VOLUME 23
NUMBER 10
NOVEMBER 2019
SUPPLEMENT 1

PAGES S1–S645
ISSN 1027 3719

The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

ABSTRACT BOOK

50th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union)

HYDERABAD • INDIA
30 OCTOBER – 02 NOVEMBER 2019

The International Journal of Tuberculosis and Lung Disease

SUPPLEMENT 2

VOLUME 22 NUMBER 11 NOVEMBER 2019

The Union would like to thank the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA) for their support in publishing the Abstract Book for the 50th Union World Conference on Lung Health.

SYMPOSIA:

THURSDAY, 31 OCTOBER 2019

S1 SP-01-E3 Leading change makers to action: TB in displaced persons in complex emergencies

S2 SP-02-B2 Advancing observational research from MDR-TB treatment cohorts: data and methods, challenges and opportunities

S3 SP-03-C1 Science and action on subclinical TB: progress in understanding, diagnosis, treatment and policy

S4 SP-04-A3 Xpert MTB/RIF ULTRA transitioning: where are we?

S5 SP-05-C10 The wheels keep on turning for specimen referrals

S6 SP-06-C4 Regional child and adolescent TB initiatives to promote efforts towards a TB disease-free generation

S7 SP-07-C11 Leveraging a community-of-practice learning model to strengthen TB and HIV data quality and use for programmatic action

S8 SP-08-B7 Lung health and well-being after TB

S8 SP-09-E3 The right to TB treatment and care to end the emergency

S9 SP-10-A3 Increasing availability of DST diagnostic: need for thinking inside the box for a better, cost-effective and sustainable network

S11 SP-11-B2 Making the switch: country-level experience with programmatic or OR implementation of fully oral, shorter DR-TB regimens

S12 SP-12-C4 Moving towards child-friendly strategies for paediatric TB laboratory-based diagnosis

S13 SP-13-C3 Unanswered questions about how best to treat MDR-TB patients: evidence from the end TB observational study

S14 SP-14-C1 Sharpening our focus: treating recent TB infection in healthcare workers in TB-endemic countries

S15 SP-15-B8 Tobacco control interventions should be implemented in TB control programmes

S16 SP-16-C1 Fulfilling Commitments from the UN High Level Meeting on Tuberculosis: Programmatic Strategies for Taking Tuberculosis Preventive Treatment to Scale

S17 SP-17-A2 The way forward for TB vaccines

S18 SP-18-B2 Reducing deaths from tuberculous meningitis

S19 SP-19-B7 Asthma: an emerging threat to health across the life course

S19 SP-20-B4 Therapeutic TB trials in children: improving knowledge and access

S21 SP-21-B1 Early scale-up and evaluation of TB case finding and systematic screening using digital chest radiography and computer-aided diagnosis in Africa and Asia

S22 SP-22-C8 Taking TB diagnostics to the fields: improving access by extending advanced point-of-care (PoC) testing to rural communities

S22 SP-23-F3 Assessing the burden and impact of zoonotic tuberculosis

S23 SP-24-C1 Scaling up TB preventive treatment: considerations on target populations and diagnostic approaches

S24 SP-25-A1 The surprising role of adipose tissue at the intersection of TB infection and immunity

S25 SP-26-A2 Leadership, science and action to advance new tools to end the TB emergency

SYMPOSIA:

FRIDAY, 1 NOVEMBER 2019

S27 SP-27-B2 From shorter to short: progress towards six-month all-oral treatment regimens for MDR-TB

S28 SP-28-A3 Modified shorter treatment regimen: using evidence, capacity building and public health approach to build sustainable and efficient MDR-TB care

S29 SP-29-C6 TB preventive therapy in pregnant women: is it safe and how should we implement it?

S30 SP-30-C12 Indian policies to stop industry interference, and their potential for sub-national levels globally

S31 SP-31-C7 Ending the socio-economic emergency for TB-affected households by improving social protection coverage

S32 SP-32-F4 Accelerating control of zTB in low- and middle-income countries

S33 SP-33-B6 The importance of tackling comorbidities to reach the End TB goals

S34 SP-34-E3 Coercion in TB: human rights and ethical concerns for the use of coercion in the TB response

S34 SP-35-C11 Action on the ground: using the ECHO virtual community of practice model to promote health equity by building local health workforce capacity

S35 SP-36-E1 Implementing national level accountability for the UN HLM on TB: key recommendations and opportunities

S36 SP-37-C4 Ending paediatric TB through action: operationalising shorter TPT regimens in children

S37 SP-38-C8 MATCH: access analysis and diagnostic network optimisation

S38 SP-40-C7 Addressing mental health and substance use disorders in TB: a must for people-centred TB care

S38 SP-41-B1 Saving lives: Improving access to TB LAM testing

S39 SP-42-D1 Food for thought: impact of malnutrition on the TB epidemic

S40 SP-43-A3 New and repurposed drug resistance emergence: current status and prevention strategies

S41 SP-44-C3 Sustainable models for strengthening pharmacovigilance of TB medicines and diagnostics: global and regional perspectives and country examples

S42 SP-45-B2 MDR-TB operational research on oral regimens: spectrum of approaches and next steps

S43 SP-46-C9 Ready yet? The implications of donor financing transition on national TB programmes

S44 SP-47-C1 Accelerating the curve: TB prevention through short rifamycin-based regimens for hard-to-reach groups

S45 SP-48-E2 Mobilising youth as agents of change for a TB-free world

S46 SP-49-C8 It's time to scale up: progress in rolling out TB contact investigation in high-burden settings

S47 SP-50-C12 How to protect children from tobacco industry interference: a review of treaties, strategies, challenges and progress

SYMPOSIA:

SATURDAY, 2 NOVEMBER 2019

S48 SP-51-D6 Preventive therapy: time to roll out population-based treatment to reach the goal of TB elimination?

S48 SP-52-B2 Anticipating changes in care for DR-TB

S49 SP-53-C6 Confronting the crisis: emerging research in maternal-child TB

S50 SP-54-C1 Tuberculosis Preventive Treatment (TPT): implementation, scale-up and realities

S51 SP-55-C7 Putting evidence into action: integrating mental health treatment to end the TB emergency

S52 SP-56-E1 Shifting the gender paradigm in the TB response: women's voices

S53 SP-57-B1 Lessons learned from national TBPSs using culture and Xpert MTB/RIF: TB or not TB?

S54 SP-58-C8 Strategic initiative for finding the missing people with TB

S54 SP-59-E1 Amplifying the voices of the TB-affected community through OneImpact: a mobile community-based monitoring (CBM) technology system

S55 SP-60-C8 TB-HIV care cascade analysis to inform programmatic management and quality service delivery

S56 SP-61-C9 Making informed and smart choices: evidence-based optimisation of national strategies to end TB

S57 SP-62-C4 Improving access to TB care for children: successful approaches and upcoming opportunities

S57 SP-63-B7 Fighting to breathe: living with asthma, COPD and chronic respiratory diseases, and how to end the silence

S58 SP-64-D8 Modelling to support ending the emergency: science, leadership, action

S59 SP-65-C8 Reaching the missing men: strategies to improve men's access to TB diagnosis and treatment

S60 SP-66-E2 Taking action: addressing the oft-neglected stigma of TB within the healthcare setting

S61 SP-67-D1 Using TBPSs to catalyse the response towards ending TB in the African region

ABSTRACT PRESENTATIONS
THURSDAY, 31 OCTOBER 2019

ORAL ABSTRACT SESSIONS

S63 OA01 Will we get there? Challenges to ending tuberculosis

S67 OA02 Tuberculosis infection: from latent to eliminated

S72 OA03 Clinical investigation for tuberculosis

S77 OA04 Anti-tuberculosis treatment in patients with comorbidities

S80 OA05 Epidemiology of tobacco use and effects and some quick facts behind tobacco farming

S84 OA06 Multidrug-resistant tuberculosis: pearls and wisdom

S89 OA07 Highlights from the laboratory

S93 OA08 Has MPOWER empowered nations to tackle tobacco epidemic?

S96 OA09 Diagnosis, screening, prediction of disease in people living with human immunodeficiency virus and for diabetes

S101 OA10 National policymaking to achieve HlM & end TB goals

S105 OA11 TB training and education initiatives to build capacity and improve outcomes

SHORT ORAL ABSTRACT SESSIONS

S110 SOA-01-B1 Thinking beyond current diagnostics

S115 SOA-02-D1 The prevention cascade: prevent, treat, retain

S122 SOA-03-C7 Person-centred care: a spectrum of activities

S127 SOA-04-C1 TPT: old and new regimens

S134 SOA-05-E1 Patient detection and care innovations

S140 SOA-06-D2 Defining the TB epidemic in children to inform action

S146 SOA-08-C3 Different approaches to combating DR-TB

S151 SOA-09-D9 Achieving UHC: understanding and eliminating catastrophic patient costs in TB care

E-POSTER SESSIONS

S156 EP-01-C7 Person-centred care for improved experiences, services and outcomes

S160 EP-02-D7 Finding the "missing" cases: TB, HIV, hepatitis and depression

S165 EP-03-C12 Fighting back: keeping the tobacco industry at bay

S169 EP-04-D6 TB epidemiology and prevention interventions

S174 EP-05-C8 Active case finding in key populations

POSTER DISCUSSION SESSIONS

S180 PS-01-B6 Diabetes mellitus & tuberculosis: "nothing sweet about this comorbidity"

S185 PS-02-C13 MPOWER lessons from Southeast Asia

S188 PS-03-D1 Still far from zero TB deaths

S195 PS-04-E1 Community involvement in finding missing cases

S201 PS-05-E1 A bit of everything: stigma, community engagement, media & technology

S205 PS-06-A3 Molecular testing and resistance

S211 PS-07-B1 Quality and efficacy for TB diagnostics

S217 PS-08-D9 Money matters: analyses of societal and household TB expenditures

S222 PS-09-B1 GeneXpert

S226 PS-10-C8 Quality assessment and improvement in care

S232 PS-11-C2 Supporting patients for better TB treatment outcomes

S239 PS-12-C1 TPT: How can we increase uptake?

S243 PS-13-C8 World tour: innovations in finding "missing persons" with TB

S249 PS-14-C10 They're out there somewhere: TB case finding strategies

ABSTRACT PRESENTATIONS
FRIDAY, 1 NOVEMBER 2019

ORAL ABSTRACT SESSIONS

S255 OA-12-C8 Active TB case finding: one size does not truly fit all: part 2

S259 OA-13-B1 Genotyping: state of the art

S262 OA-14-C1 Towards TB elimination: the missing 30 million LTBI treatments

S268 OA-15-A3 Rapid genetic TB testing: performance and quality

S271 OA-17-C3 MDR-TB treatment outcomes

S276 OA-18-C1 TB infection control and prevention across households, hospitals, workplaces and prisons

S281 OA-20-A2 Drug dosing and the patient achieving a cure

S285 OA-21-D1 Providing quality care for TB patients with comorbidities

S290 OA-22-D8 Vulnerability to TB has many faces

S295 OA-23-E4 Rights-based considerations in TB person-centred care

SHORT ORAL ABSTRACT SESSIONS

S300 SOA-10-C2 Pharmacokinetics, pharmacovigilance and chain supply in the treatment of TB

S306 SOA-11-C8 Active case finding: thinking outside of the box

S310 SOA-12-C12 Enduring the power of MPOWER

S315 SOA-13-C2 Quality TB care along the cascade

S320 SOA-14-C10 Improving laboratory diagnostics

E-POSTER SESSIONS

S326 EP-06-C13 How are we doing?: tobacco control compliance post regulations

S330 EP-07-C6 TB in pregnancy: optimising diagnosis and treatment

S334 EP-08-C8 Matching people and numbers: role of TB data quality in ending TB

S339 EP-09-C2 TB and mental health

S344 EP-10-A3 TB diagnostics innovation

POSTER DISCUSSION SESSIONS

S350 PS-15-C11 Global education and training activities

S357 PS-16-B1 Optimising diagnostic tools in predictive TB

S362 PS-17-F Zoonotic tuberculosis: from basic science to One Health

S366 PS-18-C3 Challenges for DR-TB treatment

S373 PS-19-D10 A potpourri of tobacco issues

S376 PS-20-E1 Enhancing services and supporting care

S382 PS-21-C2 Treatment outcomes: DS-TB

S386 PS-22-C1 Everything about TB infection

S391 PS-23-C8 Let's talk about contact management and active TB case finding

S397 PS-24-D1 Trends in TB epidemics across the world

S403 PS-25-D8 Financing advocacy, modelling, and reporting improvements to end the TB epidemics

S407 PS-26-D6 Addressing TB in vulnerable populations (2)

S412 PS-27-C10 Optimising the use of GeneXpert

ABSTRACT PRESENTATIONS
SATURDAY, 2 NOVEMBER 2019

ORAL ABSTRACT SESSIONS

S417 OA-25-C13 Smoking cessation: from research to implementation

S420 OA-26-C3 Safety of DR-TB treatment: part 1

S424 OA-27-C2 Engaging the private sector in TB care

S428 OA-28-C3 We're vulnerable to TB: don't forget us

SHORT ORAL ABSTRACT SESSIONS

S434 SOA-15-C4 Closing the gap: addressing challenges of identification and management of childhood TB

S440 SOA-16-A3 TB diagnostic innovations

S446 SOA-17-C10 Finding the missing with TB: many paths to the same truth

S452 SOA-18-C3 Insights into the DR-TB epidemics

E-POSTER SESSIONS

S459 EP-11-D1 Addressing TB in vulnerable populations

S464 EP-12-C10 Diagnostic laboratory quality and integration

S470 EP-13-C8 PPM across different settings: models, outcomes & sustainability

S475 EP-14-B1 Digital CXRs: screening and diagnosis

S479 EP-15-C1 LTBI management: it can be done!

S484 EP-16-E2 TB testing amongst at-risk and hard-to-reach populations

POSTER DISCUSSION SESSIONS

S491 PS-28-B6 TB-HIV: African-Asian experience

S498 PS-29-A3 TB diagnostics beyond GeneXpert

S505 PS-30-C8 Private engagement across the TB care cascade

S511 PS-31-C12 Continuing to interfere: the persistence of the tobacco industry

S515 PS-32-C2 Losses and gains across the continuum of TB care

S521 PS-33-C8 Can we find "missing persons" with TB through better quality services?

S527 PS-34-B2 Curing TB: self-cure, surgery, new medications

S532 PS-35-D1 Extra-pulmonary TB: clinical and diagnostic considerations

S537 PS-36-E1Effective community interventions and advocacy

S541 PS-37-D6 Preventing disease: a focus on LTBI and transmission avoidance

S546 PS-38-B1 TB diagnostics

S552 PS-39-A1 Detection and treatment of TB

S557 PS-40-D3 Fresh air: occupational and environmental threats to lung health

S562 PS-41-C4 Strengthening TB detection and management in children

LATE BREAKER PRESENTATIONS
FRIDAY 1 NOVEMBER 2019

S569 The HIV-TB and diabetes late-breaker session / The Union student late-breaker session on lung health

SATURDAY 2 NOVEMBER 2019

S577 The Union/CDC late-breaker session on TB

S583 TBSCIENCE Oral Abstract-Driven Presentations

S596 TBSCIENCE Posters

S642 Author Index

The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

Manuscripts and correspondence

SUBMISSIONS COORDINATOR RASHA JERANDI
TECHNICAL EDITOR IRENE ROY
DIRECTOR OF PUBLICATIONS JOSE LUIS CASTRO
MEMBERSHIP/SUBSCRIPTIONS membership@theunion.org
EDITORIAL OFFICE The International Union Against Tuberculosis and Lung Disease (The Union)
68 boulevard Saint Michel, 75006 Paris, France
Tel: (+33 1) 44 32 03 60 Fax: (+33 1) 43 29 90 87 e-mail: journal@theunion.org website: www.theunion.org

AIMS AND SCOPE. *The International Journal of Tuberculosis and Lung Disease* is an official journal of The Union. The *Journal's* main aim is the continuing education of physicians and other health personnel, and the dissemination of the most up-to-date information in the field of tuberculosis and lung health. It publishes original articles and commissioned reviews not only on the clinical and biological and epidemiological aspects, but also—and more importantly—on community aspects: fundamental research and the elaboration, implementation and assessment of field projects and action programmes for tuberculosis control and the promotion of lung health. The *Journal* welcomes articles submitted on all aspects of lung health, including public health-related issues such as training programmes, cost-benefit analysis, legislation, epidemiology, intervention studies and health systems research.

DISCLAIMER. Any opinions expressed or policies advocated do not necessarily reflect those of The Union.

SUBSCRIPTION INFORMATION. *The International Journal of Tuberculosis and Lung Disease* is published monthly by The Union. Volume 22 (2018). *Individual membership*: 240€. *Electronic membership*: low- and low-middle-income countries 20€; high-middle-income and high-income countries 80€. *Institutional subscriptions*: 300€. *All payments to*: Membership Services, The Union, 68 boulevard Saint Michel, 75006 Paris, France. e-mail: membership@theunion.org. *Sample copies (libraries)*, *Missing issues*, *Address changes*: contact Membership Services.

INSTRUCTIONS TO AUTHORS. Instructions on manuscript submission can be obtained from the Union website www.theunion.org.

ADVERTISING SALES. Contact journal@theunion.org.

EXCESS PAGE CHARGE. All articles over length will be subject to an excess page charge (see Instructions to authors and website).

FULL TEXT VERSION ONLINE. The full text of the *Journal* is published online as of Volume 1, 1997. Free access to back issues. Access for 2018 is free to Union members and subscribers. Address: www.theunion.org (link) or www.ingentaconnect.com

INDEXING AND ABSTRACTING SERVICES. The *Journal* is indexed and/or abstracted in the following media: CLOCKSS, Current Contents®/Clinical Medicine, Excerpta Medica/EMBASE, the Global Health and CAB Abstracts databases, Index Medicus, ISI Alerting Services, LOCKSS, Medical Documentation Service®, Medlars, Medline, the Science Citation Index®, SciSearch® and the SIIC databases.

ISSN 1027-3719

♾ This paper meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper)

INT J TUBERC LUNG DIS 22(11):S1–S645

50th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Hyderabad, India, 30 October – 02 November 2019

SYMPOSIA: THURSDAY 31 OCTOBER 2019

SP-01-E3 Leading change makers to action: TB in displaced persons in complex emergencies

TB in complex emergencies: context, pitfalls, and opportunities in successful programme implementation

R Coninx[1] [1]World Health Organization, Genève, Switzerland. e-mail: coninxr@who.int

This talk will outline current challenges and innovative solutions with regard to tuberculosis control programs during complex-emergencies. Drawing on his extensive experience working in complex-emergencies, and with TB control programs for marginalized populations, this speaker will examine barriers to TB control programs under the circumstances of long-term displacement. Considering these unique challenges, this speaker will discuss key factors for successful implementation of DOTS and the need for effective public health response to reduce morbidity and mortality during prolonged complex-emergencies.

Unique operational issues of a long-term migrant crisis: migrant patient experiences, and TB control at the Thai-Myanmar border

S Thi[1] [1]FHI 360, Bangkok, Thailand. e-mail: seinthi@gmail.com

This talk will address strategies for engaging health professionals and displaced populations receiving treatment for TB across borders, and for successful long-term prevention and control outcomes during and after civil unrest. Discussion of lessons learned from the Thai-Myanmar border will focus on the impact of efforts to improve cross border communication and continuity of care. Evaluation and strengthening of healthcare worker systems, patient resources, and communication pathways are core components in these capacity-building efforts.

The re-emergence of TB within a large-scale migrant crisis: challenges of control in Venezuela

J Villalba[1] [1]Massachusetts General Hospital, Boston, United States of America. e-mail: Julian.villalba@mgh.harvard.edu

This talk will examine the collapse of the Venezuelan health system and the current epidemiology and management of tuberculosis in Venezuela. This talk will also provide improved solutions during this vulnerable time for preventing the spread of tuberculosis both within the nation's borders and in a broader migration context. As instability leads to migration, outbreaks of tuberculosis may contribute to the spread of disease across borders. Identifying and treating these emerging cases becomes crucial in order to prevent the exacerbation of the outbreak and acquire appropriate continuity of care for those affected by tuberculosis disease.

Intensified TB services to address the humanitarian crisis among forcibly displaced Myanmar nationals (FDMNs) in Bangladesh

S Islam[1] [1]BRAC, Dhaka, Bangladesh. e-mail: shayla.i@brac.net

Since August 2017, 921,000 nationals from Rakhaine state of Myanmar were forcibly displaced to Cox's Bazar, Bangladesh. They have been in a perilous situation due to limited food and shelter worsened by poor access to healthcare services. BRAC, a non-governmental organization, started TB interventions jointly with the government across 34 makeshift camps. This effort established 15 laboratories and deployed screeners to visit every household and conduct outreach to identify TB presumptives. Upon diagnosis, treatment is initiated by a graduate doctor and DOT ensured through local leaders called Majhi or a person nominated by them.

From September 2017 to March 2019, a total of 83,471 TB presumptives were tested, of which 3,914 were confirmed with TB. These vigilant interventions for TB help support the influx population to thrive in this fragile environment.

SP-02-B2 Advancing observational research from MDR-TB treatment cohorts: data and methods, challenges and opportunities

Observational data for individual patient data meta-analysis in MDR-TB.

J Campbell[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: jonathon.campbell@mail.mcgill.ca

Individual patient data meta-analysis (IPD-MA) has played an integral role in the evolution of the World Health Organization's multidrug-resistant tuberculosis guidelines for nearly a decade. Borne out of necessity due to the scarcity of randomized trials in multidrug-resistant tuberculosis, the vast majority of the individual patient data within these analyses come from observational studies. The content of each observational data set, and their quality, is variable, which pose challenges during data synthesis and analysis. In this presentation, the principles of IPD-MA are discussed, and we explore pathways to improve observational data collection and challenges that may be encountered along the way.

Considering regimen changes in evaluating MDR-TB treatments: why is it important and what data do we need to do it?

M Franke[1] [1]Harvard Medical School, Boston, United States of America. e-mail: molly_franke@hms.harvard.edu

The drug composition of longer MDR-TB treatment regimens often varies throughout the 20-month treatment course. Drugs may be added or removed from a regimen based on treatment response, toxicity, or drug-sensitivity test results, all of which are may influence treatment outcomes. Longitudinal datasets that permit the study of dynamic treatment regimens, regardless of how they change throughout treatment, will be critical to identifying optimal regimens and optimal approaches to regimen design. Drawing illustrative examples from HIV, we will demonstrate the importance of considering the time-varying nature of MDR-TB treatment regimens when identifying optimal treatment strategies. We will propose an approach and identify the minimum set of data required to execute it.

Answering the relevant question: how we can analyse observational MDR-TB treatment data to emulate randomised trials?

C Rodriguez[1] [1]Harvard Medical School, Boston, United States of America.
e-mail: carly_rodriguez@hms.harvard.edu

The use of observational data to draw inferences on the effect of multidrug-resistant tuberculosis treatment presents unique, yet surmountable challenges. Selection bias, confounding, and other threats to validity are more likely to be introduced when a treatment is not randomly assigned. Failure to identify and control for these biases can affect the validity of study results. Through a guided example, we will describe an approach to analysis of observational data that leverages principles drawn from randomized trials and helps to identify and circumvent common threats to validity.

Evaluating prioritised outcomes for MDR-TB treatment

G Montepiedra[1] [1]Center for Biostatistics in AIDS Research and Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, United States of America. e-mail: gmontepie@sdac.harvard.edu

Knowledge about optimal treatment strategies for multidrug-resistant tuberculosis is urgently needed, as many of the available drugs have substantial toxicity. Because conventional methods for evaluating TB treatment consider one outcome at a time, they do not provide a single comparison measure that encompasses patient-level risks and benefits. In contrast, if one conceptualizes treatment outcome as a composite of multiple measurements of a patient's treatment experience, it becomes possible to compare the overall desirability of regimens. This presentation illustrates analytic approaches for prioritized outcomes that have been used in other fields such as cardiovascular disease and HIV; these methods allow for simultaneous consideration of treatment response and adverse events, and can be useful when efficacy and toxicity comparisons between regimens suggest contradictory conclusions.

Additional challenges and pitfalls in observational data analyses of TB treatment cohorts

M Bastard[1] [1]Epicentre, Geneva, Switzerland.
e-mail: mathieu.bastard@geneva.msf.org

Analysis of observational data, retrospective or prospective, involves challenges that must be confronted during data analysis and interpretation. These challenges include selection bias, absence of randomization, data quality issues, non-comparability of study populations, and violations of assumption common to many statistical techniques. In this presentation, we will highlight

specific examples of how these biases may operate uniquely in the context of MDR-TB treatment cohorts and offer approaches to address them.

SP-03-C1 Science and action on subclinical TB: progress in understanding, diagnosis, treatment and policy

Subclinical TB: what is it, why is it relevant?

R Houben[1] [1]London School of Hygiene and Tropical Medicine, London, United Kingdom. e-mail: rein.houben@lshtm.ac.uk

This presentation will provide an overview of current scientific knowledge on subclinical TB, including definitions and why it is relevant for global TB care and prevention efforts through the potential for ongoing transmission. We will provide an estimate of the global burden of this TB disease phenotype, including changes over time where possible. Finally an overview of key remaining gaps in our scientific understanding of subclinical TB will be given, and how this currently blocks a path to policy action.

What is the natural progression and regression of subclinical TB: results from a systematic review of historical data

B Sossen[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: blsossen@gmail.com

The kinetics of the early stages of pulmonary tuberculosis, including subclinical TB, are poorly understood: in particular how people progress and regress with regard to disease extent, symptoms, bacillary load and infectiousness prior to presentation. However this has direct implications for how we estimate disease burden from national prevalence surveys and also how we model Mtb transmission. The natural history of TB disease in humans in the absence of treatment can only effectively be assessed from pre-chemotherapy literature. In this presentation we will present findings from a systematic review and analysis of this historical literature to provide novel empirical insights into early disease progression.

The impact of new insights into subclinical TB on models of TB transmission

A Richards[1] [1]London School of Hygiene & Tropical Medicine, London, United Kingdom. e-mail: alexandra.richards@lshtm.ac.uk

The presence of an intermediate subclinical stage in the natural history, from where individuals can contribute to transmission, progress to clinical disease but also regress has consequences for the modelling of TB. Informed by the unique collation of historical empirical data from the previous presentation, this presentation will explore the impact of subclinical TB on models of TB natural history, with particular focus on implications for burden estimation and contribution to transmission.

Diagnosis and treatment of subclinical TB

C Denkinger[1] [1]University of Heidelberg, Heidelberg, Germany. e-mail: claudia.denkinger@med.uni-heidelberg.de

For many years we have approached the management of TB according to a paradigm of asymptomatic latent infection and symptomatic active disease. It is becoming increasingly apparent that a proportion of those previously classified as latently infection in fact have evidence of subclinical disease. In this presentation we will explore the current approaches and future pipeline for subclinical and incipient TB diagnostics and consider the merits of different treatment strategies.

Integration of subclinical TB into global and country-level TB policy: opportunities and obstacles

F Cobelens[1] [1]Amsterdam Institute for Global Health and Development (AIGHD), Amsterdam, Netherlands. e-mail: f.cobelens@aighd.org

To make the transition from knowledge to action, this presentation will explore the potential for, and obstacles to, the integration of subclinical TB into global TB care and prevention policies. For example, should TB programmes consider implementing activities targeted specifically at diagnosing and treating subclinical TB. How should treatment guidelines for this state be developed? What current policies already can already address the burden or dynamics of subclinical TB, and what is their evidence base?

SP-04-A3 Xpert MTB/RIF ULTRA transitioning: where are we?

GLI Guideline: planning for country transition to Xpert® MTB/RIF Ultra cartridges

H Alexander[1] [1]Centers for Disease Control and Prevenetion, Atlanta, United States of America.
e-mail: drz5@cdc.gov

The Xpert MTB/RIF Ultra assay was developed to overcome the limitations of the original assay and was endorsed by World Health Organization in early 2017. The Global Laboratory Initiative (GLI) developed a practical guide to plan and implement a smooth transition from use of Xpert MTB/RIF to Xpert MTB/RIF Ultra cartridges, ensuring uninterrupted service and avoiding cartridge wastage. It includes advice on how to translate findings from the WHO Meeting Report of a Technical Expert Consultation: Non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF into an actionable implementation plan, from country-level to site-level, for adoption of the Xpert MTB/RIF Ultra cartridge. This presentation will highlight the principal activities to be undertaken by countries and where we are with Ultra transition using data from Cepheid and partners.

Ultra transitioning in HBCs: a survey of progress and barriers to uptake

K England[1] [1]Medecins Sans Frontieres - Access Campaign, Geneva, Switzerland.
e-mail: kathleen.england@geneva.msf.org

In January of 2017, an improved cartridge, Xpert MTB/RIF Ultra, was recommended by WHO to replace the original assay. As of today, there is little information about the status of transitioning to this new test. MSF recently conducted a multi-country survey (48 high burden TB countries as defined by WHO in the post-2015 era) to gain a better perspective on the status of implementation as well as challenges currently faced in adopting this new assay. From the study, only two countries have fully transitioned (S. Africa and Lesotho) with two more (Zimbabwe and Uganda) making significant progress toward transitioning to this next generation assay. Further, 19/48 (40%) of countries were noted to have procured small volumes for validation, research, or initial piloting activities prior to transition. Identified misconceptions, challenges, and barriers to transitioning are outlined in this presentation.

Implementation of MTB/RIF Ultra cartridges in Ukraine: achievements, challenges and next steps

Y Terleieva[1]

MTB/RIF Ultra cartridges have been actively introduced in Ukraine since December 2018. Prior to its full-scale introduction in the country, the performance of molecular genetic assay using MTB/RIF Ultra cartridges had undergone testing in the CRL. The MTB/RIF Ultra cartridges were distributed for further use to the healthcare facilities of the Ministry of Health, the Ministry of Defense, and the penitentiary service of Ukraine. This presentation highlights the list of program activities being undertaken by the country for the introduction of MTB/RIF Ultra cartridges. Besides, it focuses on some specific aspects of the use of the cartridges within TB service and in primary healthcare, including the difficulties faced by specialists when using MTB/RIF Ultra cartridges, further use of MTB/RIF Ultra cartridges and expected outcomes.

Transition to Xpert Ultra cartridges: preparation by NTP Bangladesh for getting there

P Kumar Modak[1] [1]NTP, Dhaka, Bangladesh.
e-mail: pronab.modak@yahoo.com

Bangladesh NTP has only 58% bacteriological confirmed TB cases and Child TB case detection is very low, clinically diagnosed pulmonary TB case detection rate is 22 % of total TB cases reported. Using Xpert Ultra tests is intended to increase the smear negative, Child TB and extra pulmonary case detection. NTP Bangladesh, with the support of USAID- funded Challenge TB project, organized two day workshops in 2018 and in March 2019 at the national level to prepare the GeneXpert network to introduce ultra-cartridges. All TB stakeholders participated in these workshops to have national consensus on its implementation. Three sites (3 hospitals) in Dhaka were selected to implement in a phased manner before country scale up. NTP procured 12,000 cartridges through Global Drug Facility (GDF) for those centers. A time line matrix was developed to materialize and monitor the transition properly and smooth scale up.

SP-05-C10 The wheels keep on turning for specimen referrals

Logistics is key: how specimen referrals are benefiting from a network approach

K Nichols[1] [1]The Nichols Group LLC, Washington, United States of America. e-mail: kameko@thenicholsgroupllc.com

Specimen referral systems continue to receive focus and the current landscape is full of great examples of countries working on strengthening activities. From introducing guidelines and clear monitoring and evaluation frameworks with specific indicators, to creating logistics efficiencies by using a network approach, to innovative mechanisms for data collection, to drone pilot projects, to using ride-hailing technology for transportation, we will learn from country examples in sub-Saharan Africa and Southeast Asia.

STRiders: increasing case detection rates in the Philippines

R Carter C. Nalda[1] [1]Philippine Business for Social Progress, Manila, Philippines. e-mail: rcnalda@pbsp.org.ph

In 2017, the Philippines had 335 GeneXpert machines in operation but notification of Drug Resistant TB (DR-TB) cases and equipment utilization were low. One reason for this was believed to be the lack of a reliable transport for Rural Health Units (RHUs) to refer eligible cases for GeneXpert testing. To address this gap, the PBSP ACCESS TB PROJECT began implementing the Specimen Transport Riders (STRiders) strategy in July 2018 using 138 STRiders serving 127 Xpert sites and 1,048 RHUs/DOTS facilities in 7/17 regions. The STRiders strategy aims to ensure that 100% of Xpert-eligible cases are tested and results' release is timely. As a result, there has been a significant increase in case detection for regions where STRIDERS are being implemented. ACCESS TB will continue to implement STRIDERS until the end of 2019. There are also plans to expand STRIDERS to other regions facing the same challenges on specimen transport.

SITRUST: an Android mobile application-based innovative approach for transport and real-time tracking of specimens in Indonesia

R Kusuma Dewi[1] [1]P2PL, Ministry of Health, Jakarta, Indonesia. e-mail: retnokd@gmail.com

Indonesia has made tremendous progress in developing laboratory capacity nationwide. Nevertheless, geographical challenges limit the access to diagnostics, resulting in significant underutilization of existing capacity. In 2018, only 13.6 % of the TB cases were diagnosed by GeneXpert and during 2015 to 2017, 5072 out of total 9852 RR cases diagnosed received phenotypic DST for both 1st and 2nd line drugs. Lack of rapid and reliable specimen transportation system remains a major cause of inefficient use of existing diagnostic services. NTP, in collaboration with Yayasan KNCV Foundation Indonesia developed an Android mobile application to order and track specimen shipments, as well as report test results electronically. National postal services were used in the first phase of implementation in 10 provinces and 50 districts. Data from January to December 2018 showed that GeneXpert utilization has been increased 200-500%. The system has shown the scalable potential with sustainable funding and commitment.

Optimising sputum transport for Lao PDR

T Sorsavanh[1] [1]National TB Centre (NTC) Lao PDR, Vientiane, Lao People's Democratic Republic. e-mail: xzhang@clintonhealthaccess.org

58% of Lao PDR's total population lives in rural areas, with 8% living in extremely remote areas without road access. Residents are distributed across mountainous terrain in the north, plateau highlands, and island communities along the Mekong River. The resulting routine sputum transport network relies upon cool boxes, motorcycles, vehicles, and boats in order to transport patient samples to the nearest GeneXpert testing devices, located at provincial TB labs. The NTC has been working towards establishing a cost-effective sample transport network that provides optimal coverage for all communities, and will share lessons learned.

Using optimisation software to improve sample referral system design

S Rupani[1] [1]LLamasoft, Inc., Cape Town, South Africa. e-mail: sid.rupani@llamasoft.com

This presentation will discuss how optimization software, such as LabEQIP, Llamasoft's proprietary Supply Chain Guru, and an under-development, open-access tool can help improve the design and performance of specimen referral systems. Country examples will be given across Kenya, Tanzania, Malawi, etc. and topics will include key questions that this type of software can address, necessary data to input into the software, potential improvement in performance, challenges and limitations, and the shift from design to implementation. The broader linkage to diagnostic network optimization will also be explained.

SP-06-C4 Regional child and adolescent TB initiatives to promote efforts towards a TB disease-free generation

The journey towards TB diagnosis and successful treatment: a patient's personal experience

N Mahamo[1] [1]Baylor College of Medicine Children's Foundation, Maseru, Lesotho.
e-mail: nteboheleng852@gmail.com

Adolescents are a much-neglected group as they often fall between paediatric and adult services and experience many challenges in accessing health care and staying on treatment. A personal experience of a patient journey will be presented by an adolescent TB survivor from the AFRO region and some reflections on what could have been done to make it better.

The role of regional leadership and collaboration in closing the child and adolescent TB policy-practice gap

M Sekadde[1] [1]National TB and Leprosy Control Programme Uganda, Kampala, Uganda.
e-mail: moorine.sekadde@gmail.com

In 2018, The Union established a regional child and adolescent TB center of excellence (COE) in the Africa region as part of the global efforts to end the TB epidemic among vulnerable populations including children and adolescents. The COE, initially targeting Uganda and Zimbabwe, aims to strengthen NTP child and adolescent TB leadership and coordination; support the development and scale up of child and adolescent TB capacity building programs such as the Union e-learning platforms, facilitate south to south learning exchanges and networks. The Union's successful DETECT project in Uganda has provided a model for implementation that is being scaled up and refined. There is a huge need to understand the burden and challenges for adolescents with TB, as per international Roadmap, which the COE aims to address in the region through collaborative partnerships, learning from affected adolescents how to develop age-appropriate models of care.

Bridging the divide: the importance of adapting adolescent HIV best practices into adolescent TB best practices: the BIPAI network experience

J Bacha[1] [1]BIPAI, Mbeya, Tanzania, United Rep.
e-mail: bacha@bcm.edu

While programs in high TB/HIV burden countries are striving for a more patient-centered, integrated, comprehensive care model for all adolescents, advances in HIV care tend to outpace advances in TB care. However, most adolescent-friendly programs and models of care designed for HIV services are easily and effectively adapted to adolescent TB and HIV/TB. This session examines several "adolescent best practices" utilized within the BIPAI network that while were initially designed for HIV care, have been successfully adapted to TB care. The aim of this session is to encourage TB clinicians and sites to utilize, adapt, and build upon the many existing "adolescent best practices" to create effective adolescent-centered, integrated TB services. Illuminating examples from the BIPAI network will include Teen Clubs, Peer Support/Teen Leaders, Teen Talks, mHealth, and social media, among others.

Isoniazid preventive therapy (IPT) implementation in Kenya: achievements, challenges and lessons learnt

S Muleshe[1] [1]National Tuberculosis & Leprosy Control Program, Nairobi, Kenya. e-mail: skmuleshe@gmail.com

In children, IPT can decrease TB disease progression by 60% and has been shown to be a cost-effective strategy in high TB burden countries. However, in 2017, globally, of the 1.3 million children estimated to be eligible for IPT, only 23% were initiated. Similarly, only 13% of eligible children were initiated on IPT in Kenya in 2017. This session will focus on the impact of key interventions implemented in Kenya to improve uptake of IPT among child TB contacts (including use of Child Contact Management registers and Community Health Volunteers to conduct household contact tracing and linking to health facilities for IPT and follow-up) & children/adolescents living with HIV as well as challenges and lessons learned.

Detection and prevention of DR-TB in children and adolescents in Africa

J Seddon[1]

Each year half a million individuals develop multidrug-resistant tuberculosis, each of whom live and interact with multiple children and adolescents. These younger people are at high risk of becoming infected with drug-resistant strains of *M. tuberculosis* and are at increased risk of progressing to disease. Little is currently done

globally to find these vulnerable children and only a tiny minority are treated for drug-resistant tuberculosis infection or disease. This talk will highlight the burden of the problem, outline strategies for how health systems might find these children and adolescents and the emerging evidence on best drug regimens to treat them.

SP-07-C11 Leveraging a community-of-practice learning model to strengthen TB and HIV data quality and use for programmatic action

Developing and sustaining an M&E curriculum to strengthen data quality and use for HIV and TB communities of practice

S Ghosh[1]

Smita Ghosh, will facilitate this symposium and present a comprehensive process for development, and pilot testing a multi-module, multi-session Monitoring and Evaluation (M&E) curriculum developed by CDC. Smita will share experience and lessons learned from pilot testing this M&E curriculum for HIV, and TB in several countries. She will also share lessons learned and explore avenues for promoting this curriculum through use of virtual communities of practice such as the Extension of Community Health Outcomes (ECHO) model. Building capacity and sustaining it using a mentorship design through virtual communities of practice for the M&E activities in various country settings shall be explored.

Experience of pilot-testing the M&E curriculum to promote data quality and use in Ethiopia

B Eskinder[1] [1]CDC-Ethiopia, Addis Ababa, Ethiopia.
e-mail: vey0@cdc.gov

The first country to pilot test CDC's M&E curriculum was Ethiopia. Co-taught by U.S. and Ethiopian Center for Disease Control and Prevention (CDC) officials, a week-long capacity building training for 40 M&E Officers from regional health bureaus around the country was inaugurated in February 2019. This training built capacity of regional M&E leaders to more effectively monitor public health programs, collect reliable data, and identify areas for patient management and program monitoring and improvement. The 2015 strategy for the United States President's Emergency Plan For AIDS Relief (PEPFAR) involves the use of all available data at the facility level to inform decisions about priority locations, populations, interventions, and partnerships within a target country in order to achieve epidemic control. Experience will be shared on how this training has been applied to build communities of practice to promote patient level data quality improvement.

Experience using ECHO to promote TB data use to build a community of practice in Kenya

E Carter[1] [1]Brown University, Nairobi, Kenya.
e-mail: e_jane_carter@brown.edu

TB Data 4 Action is an innovative approach to analyzing and utilizing routinely collected program data at facility level. This approach allows TB supervisors to evaluate program effectiveness and compare facilities, and counties to find the missing cases to improve quality of care along the care cascade. Project ECHOTM - TB Data for Action, developed by The Union, Centre for Health Solutions and the Kenya NTP now supports this method that was originally developed in Zimbabwe. Adoption of this TB Data 4 Action method through the combination of real time data analysis and short didactics bimonthly is building communities of practice to scale up data use efforts throughout the country

Experience using HIV curriculum to build capacity using ECHO in India

R Aggarwal[1] [1]CDC-India, New Delhi, India.
e-mail: mdx6@cdc.gov

Implementation of integrated care for prevention and management of TB in PLHIV in India is compounded by having two separate vertical national programs for HIV and TB with separate implementation systems warranting a need for capacity building program for co-management of dual infection. Reshu will discuss the implementation of HIV-TB ECHO called e-National Initiative to Strengthen Collaboration between HIV-TB (e-NISCHIT) that began in May 2018 . She will share experience and lessons learned from implementing e-NISCHIT curriculum that includes various TB-HIV related topics to ensure HIV –TB care continuum from prevention, diagnosis and treatment, to retention. Thirty sessions including case and didactic presentations, as well as enriching discussions have included 115 participating ART clinics and 25 experts from HIV and TB as expert facilitators. Initial evaluations of impact of HIV-TB ECHO demonstrates improvement in knowledge, self-efficacy, professional satisfaction and decrease in professional isolation.

SP-08-B7 Lung health and well-being after TB

Patient perspectives

I Schoeman[1] [1]TB PROOF, Cape Town, South Africa. e-mail: ingrid.tbproof@gmail.com

The importance of understanding the perspective of patients and families affected by TB disease was highlighted in The Union meeting, 2018. This agenda will be continued here, with a presentation highlighting key challenges that patients and their families face on completion of treatment. Priorities for research and clinical care, from a patient / TB survivor perspective, will be presented for discussion. Gaps in our current understanding will be highlighted.

Burden of disease

B Allwood[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: brianallwood@gmail.com

Existing data on the burden of residual post-TB pathology amongst TB survivors will be presented. The high prevalence of post-TB lung damage, and the increased risk of recurrent TB disease faced by this population will be highlighted. Gaps in our current understanding of the epidemiology of post-TB lung damage and associated outcomes will be explored.

Clinical picture and definitions, across the life course

M van der Zalm[1] [1]Stellenbosch University, Cape Town, South Africa. e-mail: mariekevdzalm@sun.ac.za

The clinical spectrum of post-TB lung damage across the life course will be reviewed, including that seen in paediatric, adolescent and adult populations. Approaches to measurement will be described, and the case definitions / classification approaches considered at the recent post-TB symposium will be presented for discussion.

Socioeconomic and quality of life outcomes

O Ivanova[1] [1]Ludwig Maximilians University, Munich, Germany. e-mail: olena.ivanova@lrz.uni-muenchen.de

Existing data on the long-term impact of TB on the social and economic well-being of patients and their families, beyond TB treatment completion, will be explored. Measurement tools for these important outcomes will be discussed, and key knowledge gaps will be highlighted.

Integrated approaches to post-TB management

U Egere[1] [1]Liverpool School of Tropical Medicine, Liverpool, United Kingdom. e-mail: uzochukwu.egere@lstmed.ac.uk

At present there remain no guidelines for the follow-up and clinical management of TB survivors. In this session strategies for the clinical management of patients with post-TB lung damage will be discussed, and the need for early diagnosis of recurrent-TB disease will be highlighted. Health system challenges to patient follow-up will be considered, and gaps in evidence highlighted.

SP-09-E3 The right to TB treatment and care to end the emergency

The realities of not being able to access new TB treatments

N Venkatesan[1] [1]Economic Times, Mumbai, India. e-mail: nandita.venky@gmail.com

TB -- one of the biggest public health crisis today-- and human rights are linked intricately. Often TB sufferers are shortchanged at every step through the cascade of care. It starts with delayed diagnosis to no monitoring of drug side effects till little support during recovery phase. Nandita Venkatesan had her first episode of TB in 2007 and completed 18 months of treatment, and unfortunately developed TB again in 2013. During her second round of treatment she suffered catastrophic profound deafness and endured a number of emergency surgeries to save her life. Nandita will outline the pain, inequities, and challenges faced by people with tuberculosis and how new treatments and policies for the TB care must be made available to people with TB.

Care cascades of TB: revealing poor quality TB care in LMICs

M Pai[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: madhukar.pai@mcgill.ca

Everyone has a right to TB care, but TB care coverage must of high quality. Poor quality of TB care is widespread in both public and private sectors in high burden countries. Gaps in the cascade of care have been documented for all forms of TB, for adults and children, and in all settings. Poor quality care is a major driver of TB mortality, and most deaths are among the most vulnerable and poorest. TB programs must go beyond coverage and address quality. TB programs must also modernize TB care and adopt the best in class tools to ensure high-quality care.

How human rights and the law must be harnessed to ensure access to good quality TB and DR-TB treatment and care

B Citro[1] [1]University of Chicago Law School, Chicago, United States of America.
e-mail: citro@law.northwestern.edu

Human rights law at international, regional and national levels establishes clear content and corresponding legal obligations for governments related to the availability and accessibility of medicines and other health technologies. Yet, this body of law has not hardly been utilized in support of promoting access to good quality drugs and diagnostics for TB. While some examples exist in the TB context, the legal principles and their application in other contexts, including HIV, provide concrete examples of how human rights and the law can be used to support other efforts to increase access to new TB drugs and diagnostics, in particular. This talk will introduce and discuss these legal principles, highlight some key cases, and suggest possible courses of action to harness human rights and the law in support of access to good quality TB treatment and care.

How patent opposition can help access to treatments: the experience with bedaquiline in India

L Menghaney[1] [1]Medecins Sans Frontières, New Delhi, India. e-mail: leena.menghaney@geneva.msf.org

Experience from increasing access to medicines for HIV treatment, has highlighted that dependence on donations and single suppliers is not sustainable in the long run. To encourage generic supply of both adult and paediatric formulations in fixed dose combinations -people living with HIV, rights organisations and MSF - spent a decade challenging patents of pharmaceutical corporations that presented barriers to access, ensuring that over 21 million receive lifesaving treatment with affordable antiretrovirals. Now to ensure access to new drugs in MDR-TB regimens, Indian civil society together with MSF is starting to challenge patents that are limiting access to drugs like bedaquiline. Reducing the length of patent barriers will encourage the early entry of alternative suppliers and is an important strategy to reduce prices. The objective is to increase access to bedaquiline in DR-TB programmes globally using public health safeguards in the Indian patent law.

Experience of successful use of human rights law to improve TB care approach in Kenya

A Maleche[1] [1], Nairobi, Kenya.
e-mail: amaleche@kelinkenya.org

The session seeks to share the experience KELIN has had working with various stakeholders to use the law as a tool to safe guard the rights of persons with TB, through litigation, trainings with judicial officers, advocacy with the community and undertaking legal environmental assessments. All this has been undertaken with a view to creating an enabling policy and legal environment that is critical in ensuring that a rights based approach is at the centre of the TB response in Kenya and beyond.

SP-10-A3 Increasing availability of DST diagnostic: need for thinking inside the box for a better, cost-effective and sustainable network

Diagnostic capacity for DR-TB: where are we three years into the End TB Strategy?

K England[1] [1]Medecins Sans Frontieres - Access Campaign, Geneva, Switzerland.
e-mail: kathleen.england@geneva.msf.org

In 2015, the End TB strategy outlined specific polices for increasing diagnostic capacity across all high TB burden countries to address gaps in diagnosis of DS/DR-TB. The policies prioritized rapid molecular diagnosis using Xpert MTB/RIF over smear microscopy as the initial test for TB and universal DST for RR-TB. Further, the strategy emphasized the need to build capacity to evaluate 2nd-line drug resistance using recommended technologies: Hain MTBDRsl and MGIT culture DST. Here we review the progress of capacity building across the recognized 48 countries with high burdens of TB/HIV-TB/MDR-TB from data collected via WHO over the past three years. In general, countries have significantly increased the number of facilities for both smear and Xpert, while capacity building for LPA and cDST remain limited. In the era of updated treatment regimens using newer drugs, capacity building for drug resistance must become a high priority for all countries.

Moving towards universal DST: India's experience

S Chadha[1] [1]International Union Against Tuberculosis and Lung Disease, New Delhi, India. e-mail: drsschadha@gmail.com

In the last 5 years India has significantly increased its lab capacity for both genotypic and phenotypic DST. Over 1100 Xpert sites, 50 LPA and liquid DST labs have been established. In 2017, over 1 million Xpert tests and 100,000 first line LPA tests were done resulting in the diagnosis of ~40,000 R-R/MDR patients. ~30,000 second line DSTs were performed diagnosing 9000 pre XDR and over 2500 XDR patients. The establishment of such a large lab network was fraught with challenges including: identification of sites, establishment of TB containment lab, procurement of equipment, training of staff, ensuring uninterrupted supply of consumables and reagents, and communication of results for patient management.

New tools for first-line resistance detection combined with centralised models for universal DST: solutions here and now

N Ismael[1] [1]National Institute for Communicable Diseases, Johannesbourg, South Africa. e-mail: naziri@nicd.ac.za

Drug resistant TB is chronically under detected and is expected to increase over the coming decade, threatening the End TB 2035 targets. The ability to diagnose rifampicin resistance has significantly improved with the introduction of molecular diagnostics leading to improved detection and getting people onto treatment earlier. However, regimens for drug resistant TB require at least 4-5 effective drugs for successful outcomes to be realized. Universal drug susceptibility testing is urgently needed but is often unavailable even at National TB Reference laboratories. The landscape for front line technologies for rapid detection of rifampicin and isoniazid resistance is expanding and provides great opportunities to close the gaps. Universal drug susceptibility using sequencing is maturing however the availability is likely to be limited and considerations to look at centralized models does offer an important and cost-effective bridge to delivering high quality services and improve outcomes.

Appropriate solution for improving DST and specialised testing at the NRL (modular containment model)

J Semuto Ngabonziza[1] [1], Kigali, Rwanda. e-mail: cldsemuto@gmail.com

Early, rapid, and accurate diagnosis of tuberculosis (TB) is the cornerstone for TB management and control, complete DST is essential to achieve treatment success and complete cure. In Rwanda, universal access to DST has been achieved through countrywide implementation of Xpert MTB/RIF assay that substantially reduced the diagnostic delay; therefore shortening the time to initiate appropriate treatment. However, some category of patients including those detected with rifampicin resistant TB and re treatment require complete DST profiles for their optimal management, which require prior culture. While other specialized TB testing, such as whole genome sequencing, will first required culture and inactivation before further molecular steps. Since 2014, the NRL Rwanda has been utilizing a furnished modular containment laboratory as a rapid and effective solution for ensuring adequate infrastructure. The success, challenges, and solutions for improving DST and specialized testing using this modular laboratory will be discussed in detail during the presentation.

Use of minimal inhibitory concentration (MIC) to redefine anti-TB drugs dosing strategy

D Cirillo[1] [1]San Raffaele Scientific Institute (HSR), Milan, Italy. e-mail: cirillo.daniela@hsr.it

Drugs susceptibility testing (DST) is critical to provide data for a proper therapy or to confirm the susceptibility to a started treatment. Routine DST is performed at a "Critical Concentration" upon which strains are classified as "sensitive" or "resistant". For drugs such as rifampicin, isoniazid, fluoroquinolones and injectable agents, this classification does not always reflect the clinical outcome or correlates with the presence of molecular determinants of resistance. Testing the MIC represents a better strategy to align phenotypic tests to mutations conferring resistance. MIC identification has the advantage of providing a range of values as presumptive indication of sensitivity to the drugs (i.e. the lower the MIC, the higher the chances that the plasmatic concentration is sufficient to inhibit bacterial growth). Although commercial plates exist, MIC testing has not been fully standardized yet. International regulators such as EUCAST are working toward protocol standardization to define MIC distributions of new drugs.

SP-11-B2 Making the switch: country-level experience with programmatic or OR implementation of fully oral, shorter DR-TB regimens

Collaboration of national tuberculosis programmes and implementing partners on research planning and oversight: experience in Ukraine

N Lytvynenko[1] [1]The F.G. Yanovsky NAMSU National Institute of Phthisiology and Pulmonology, Kyiv, Ukraine. e-mail: dr.n.lytvynenko@gmail.com

An estimated 10,000 people develop RR-TB in the Ukraine each year, and treatment success rates hover around 51% (2015 cohort). In order to address these poor outcomes – along with the significant burden of fluoroquinolone resistance – the National TB Institute began offering expanded access to new and repurposed drugs through an operational research project. With the 2018 WHO recommendations supporting modified, all-oral short course regimens implemented through operational research, the National TB Institute expanded this research project in partnership with MSF and the National TB Program to offer an all-oral regimen in Zhytomyr Oblast. This presentation will describe the processes followed to expand operational research in the country for all oral short regimens for RR-TB.

Successful cycles of implementation planning in Uganda in response to rapid advances in RR-/MDR-TB management

R Katuramu[1] [1]Minsitry of Health, Kampala, Uganda. e-mail: rkaturamu@gmail.com

505 cases of RR-/MDR-TB were started on treatment in Uganda in 2018, with a treatment success rate of 64% in the 2016 cohort. The National TB and Leprosy Control Program (NTLP) has initiated its strategic planning to enable rapid transition to the 2019 WHO guidelines, with an implementation plan for a modified, fully oral shorter MDR-TB regimen modeled on the introduction of the standardized shorter regimen in March 2018 and the roll out of bedaquiline from 2016. This presentation will describe the key elements of success for timely, sequential country level adaptations in response to innovations in MDR-TB treatment and subsequent normative guidance updates.

Building research capacity at the National Center for Tuberculosis and Lung Diseases in Georgia

N Tukvadze[1] [1]National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia. e-mail: marikushane@yahoo.com

The capacity for conducting operational and clinical research has been developed at the National Center for TB and Lung Diseases in a step-wise approach since 2004. Research planning and oversight is now led by the National Center for Tuberculosis and Lung Diseases, in collaboration with National institutions and international expertise. Professional development of research staff and data analysis to translate findings into policy and practice has led to a positive feedback loop of essential resources to conduct further research, including close monitoring of programmatic use of a fully oral modified shorter regimen beginning in May 2019.

Building on national rollout of the shorter regimen to implement WHO guidelines and increase access to Group A drugs in Democratic Republic of the Congo Republic of Congo

M Kaswa[1] [1]National Tuberculosis Control Program, Kinshasa, Congo, the Democratic Republic of the. e-mail: meckkay2002@yahoo.fr

The Democratic Republic of Congo has scaled up programmatic management of DR-TB since 2007 and now has an estimated 7,500 RR-/MDR-TB cases per year, with 912 laboratory-confirmed cases and 854 cases started on treatment in 2017. The country has implemented the 2016 WHO shorter regimen, with over 825 patients started on the standardized shorter regimen as of March 2019; similarly, bedaquiline is now available for all patients with MDR-TB drug intolerance or resistance, including as a drug substitution within the shorter regimen. While continuing to strengthen programmatic capacity to reduce diagnostic and treatment gaps, the National TB Program is building upon their experience in responding to WHO guideline updates in order to provide modified, fully oral shorter RR-/MDR-TB treatment regimens to eligible patients under operational research.

Programmatic nurse-led management of fully oral, modified shorter regimens in Northern Cape, South Africa

N Ndjeka[1] [1]Drug-Resistant TB, TB & HIV, National Tuberculosis Control Programme, Johannesburg, South Africa. e-mail: Norbert.Ndjeka@health.gov.za

After programmatic implementation of the WHO recommended standardized shorter regimen in 2017, South Africa introduced a modified, injectable free shorter regimen for RR-/MDR-TB in July 2018. The Northern

Cape Province, with experience using bedaquiline for pre-XDR/XDR-TB since 2015, has placed over 80% of RR/MDR-TB patients on shorter regimens by end 2018. This session will describe the province's experience with modified shorter regimens; interim treatment outcomes for the first cohort of patients at national and provincial level; and the role of nurses in the management of RR-/MDR-TB in the province's strategy to provide patient-centered, decentralized care.

SP-12-C4 Moving towards child-friendly strategies for paediatric TB laboratory-based diagnosis

Improving access to lab-based diagnosis for children: experience from the Challenge TB-funded paediatric TB project in India

A Kalra[1] [1]FIND India, New Dehli, India.
e-mail: aakshi.kalra@finddx.org

The diagnosis of tuberculosis can be challenging in children. In the large-scale implementation project in 10 major cities of India, GeneXpert testing was offered on available samples (pulmonary/extrapulmonary) free of cost, thereby paving way for better TB care. A high throughput lab was established in each city and linked to various providers in the public and private sector, through rapid specimen transportation and electronic reporting. For 94,415 presumptive paediatric TB cases (Apr'14-Mar'18), a total of 6,270 (6.6%) TB patients were detected, of which 545 (8.7%) were rifampicin resistant. Overall detection rates on GeneXpert were three-fold higher than smear microscopy. For 94% patients, results were reported within 24 hours of sample receipt at lab. Project demonstrated the feasibility of rolling out rapid & upfront GeneXpert testing for presumptive paediatric TB cases. The project is now being scaled up by the National Programme in India.

Availability and accessibility of TB diagnostic services for paediatric TB at the primary healthcare level: a multicountry survey

E Wobudeya[1] [1]Makerere University, John Hopkins University, Research Collaboration, Kampala, Uganda.
e-mail: ewobudeya@gmail.com

The TB-Speed project, funded by Unitaid and the 5% initiative, includes an operational research to evaluate impact of decentralizing childhood TB diagnosis at Primary Health Center (PHC) on case finding in six countries. At baseline, the project undertook a cross sectional-survey to assess childhood TB diagnostic capacities in 179 PHC facilities in 32 rural/semi-rural districts in Cambodia, Cameroon, Cote d'Ivoire, Mozambique, and Uganda. 83 (46.4%) PHCs diagnosed TB while 96 (53.6%) referred children to another level for diagnosis. Of 125 (69.8%) PHCs performing microbiological samples collection only 12 (6.7%) specifically collected paediatric samples (7 GA, 0 NPA, 8 induced sputum, 1 stool). 82 (45.8%) PHCs had onsite laboratory; 6 (3.3%) had Xpert MTB/RIF available, 78 (43.6%) performed smear microscopy. Childhood TB diagnostic capacity is limited at PHC level in those high TB-burden countries, specifically in terms of paediatric sample collection and access to molecular testing for TB.

Using simple OneStep stool method for rapid TB screening and diagnosis of children at decentralised level, what is the impact?

E Klinkenberg[1] [1]KNCV Tuberculosis Foundation, The Hague, Netherlands.
e-mail: eveline.klinkenberg@kncvtbc.org

During last year's Union meeting KNCV presented a simple one step method for processing of stool for diagnosis of TB in children. This simple stool processing method based on the Xpert technology uses the same supplies and equipment as needed for Xpert sputum processing. No additions are required and thus can be done at every site were a GeneXpert is available. This simple processing method will bring the diagnosis to were sick children mostly present themselves, the lower level of the health system. KNCV is currently testing the Simple One Step Stool (SOS) method alongside routine diagnostics and result thereof will be presented. Analysis will besides concordance between using stool and routine practice, also focus on increasing access to a diagnosis for children in line with the patient centered care approach.

Optimisation of use of stool as a sample for paediatric TB diagnosis

P Nabeta[1] [1]FIND, Geneva, Switzerland.
e-mail: pamela.nabeta@finddx.org

FIND, in partnership with Rutgers State University (Rutgers), University of Cape Town (UCT) and 42 Technology (42T), has developed a centrifuge-free stool processing kit (SPK) that is compatible with rapid molecular assays, and could replace existing invasive sampling methods required for diagnosing paediatric TB. Its introduction, in conjunction with the WHO endorsed Xpert MTB/RIF Ultra, will bring TB and drug resistant TB diagnosis within reach of the 80% of children who currently remain undiagnosed. Usability testing, optimization and analytical validation have been completed, results of which will be presented. A comparative evaluation of the SPK (FIND), One-Step (KNCV) and Sucrose Flotation (TB-Speed) methods in a uniform, controlled setting has been initiated. Data on performance,

operational characteristics and costing will be collected, analysed and compiled in a dossier for WHO review towards potential policy recommendation.

Solving the TB diagnostic problem in children: how far are we on the road to decentralised, child-friendly testing?

N Heinrich[1] [1]Ludwig Maximilians University, Munich, Germany. e-mail: heinrich@lrz.uni-muenchen.de

Sputum-based pathogen detection methods are difficult to perform, and often miss TB, especially in small or very ill children. WHO target product profiles call for new tests that work with "child-friendly" samples. Algorithms of screening and confirmatory tests are desirable if no single test fulfils the criteria. An overview of the current test candidates, and their current state of development will be provided, including the TAM-TB test. The absence of a good reference standard diagnostic poses a challenge for treatment, but also for validation of new tests. Most children will only be diagnosed clinically, with substantial uncertainty about true disease status. New tests should confirm TB in more patients from this group. The EDCTP – funded RaPaed TB study evaluates several new candidate diagnostics in 1,000 sick children, and requires rigorous case classification, based on TB laboratory confirmation, exclusion of TB, or cases without clear diagnostic certainty.

SP-13-C3 Unanswered questions about how best to treat MDR-TB patients: evidence from the endTB observational study

Effectiveness of new WHO all-oral long regimens

M Rich[1] [1]Partners In Health, Natick, United States of America. e-mail: mrich@pih.org

WHO has recently revised treatment guidelines for MDR-TB treatment, radically revising the hierarchy of MDR-TB drugs. Yet there is still very little evidence about the effectiveness of MDR-TB regimens that are designed according to this new hierarchy. The endTB Observational Cohort is the largest prospective cohort of patients treated with drugs that are prioritized in the new WHO guidelines (e.g. bedaquiline, fluoroquinolones, linezolid, clofazimine and cycloserine). In this session, we will present treatment outcomes of endTB patients who received regimens consistent with the latest WHO guidelines, and attempt to extrapolate outcomes as the WHO guidelines are adopted globally.

Safety of long-term use of linezolid in MDR-TB treatment

M Bastard[1] [1]Epicentre, Geneva, Switzerland. e-mail: mathieu.bastard@geneva.msf.org

Linezolid is increasingly used for the treatment of MDR-TB and is strongly recommended in the latest revision of the WHO MDR-TB treatment guidelines. Linezolid, however, can produce serious side effects such as peripheral neuropathy, myelosuppression and optic neuritis. The toxicity of long-term usage of linezolid, as a part of multidrug regimens including other drugs with overlapping toxicities, has not been well documented. The vast majority of patients enrolled in the endTB Observational Study are receiving linezolid as part of treatment for MDR-TB, providing a unique opportunity to understand the long-term toxicity of the drug. In this session, we will present data about the most common toxicities observed in patients receiving linezolid for MDR-TB treatment.

Prolongation and combination of bedaquiline and delamanid

C Hewison[1] [1]Médecins Sans Frontières (MSF), Paris, France. e-mail: cathy.hewison@paris.msf.org

Two of the most important unanswered questions about bedaquiline and delamanid are: (1) Can they be used in combination with each other? (2) What is the optimal duration of treatment? The combination of bedaquiline and delamanid is increasingly being used at country level, for reasons of effectiveness and safety. This combination has been shown to be safe in the recent DELIBERATE clinical trials, but there is limited data in field settings. Likewise, bedaquiline and delamanid are routinely used for more than 24 weeks in the field, even though current WHO guidelines recommend a maximum of 24 weeks. In this session, we will present safety data from the endTB Observational Study, which includes the largest number of patients treated with bedaquiline and delamanid combination under programmatic or trial conditions. Data about combined use and extension for more than 24 weeks will be presented.

Final outcomes of patients in the endTB observational cohort

M Franke[1] [1]Harvard Medical School, Boston, United States of America. e-mail: molly_franke@hms.harvard.edu

Many of the patients in the endTB Observational Study, particularly in the initial stage, were infected with highly resistant strains of TB and had received multiple courses of treatment with second-line TB drugs. Co-infection like HIV, hepatitis B/C, and co-morbidities like malnutrition and diabetes, were also very common. Culture conversion at six months has been encouraging, but due to the highly complex nature of the patient population,

a high rate of late treatment failure or death, specifically reconversion to positive after initial culture conversion, could be expected. In this session, we will present final outcomes of over 1,000 patients treated with bedaquiline or delamanid, and analyze factors associated with poor outcome.

Lessons learnt from the endTB observational study

U Khan[1] [1]Interactive Research & Development, Dubai, United Arab Emirates. e-mail: uzma.khan@ird.global

The endTB Observational Study is the largest multi-country prospective study of patients receiving bedaquiline or delamanid for MDR-TB under programmatic conditions. Patients are treated according to national protocols, consent to have their data analyzed in the study, and are followed closely for treatment response and adverse events. During implementation of the endTB Observational Study, many barriers needed to be overcome, such as importation of drugs, clinical capacity building, and data collection and cleaning. Many important lessons have been learnt that are directly applicable to the introduction of other new drugs and treatments for other diseases.

SP-14-C1 Sharpening our focus: treating recent TB infection in healthcare workers in TB-endemic countries

The epidemiology of TB in healthcare workers in high-incidence countries

S Adams[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: shahieda.adams@uct.ac.za

Dr. Adams will speak about the importance of focusing on identifying and treating latent tuberculosis infection in high risk populations such as HCWs. There is limited data on the epidemiology of TB in HCWs in high-incidence countries. Work by Dr. Adams and colleagues has demonstrated that the annual rate of tuberculosis infection in South African healthcare workers is very high, irrespective of the testing method used, and may be explained by occupational exposure, as the rate was considerably higher than non-healthcare workers from the same community. Dr. Adams will discuss the optimal approach to TB screening in HCWs in high-incidence countries.

The timetable of TB disease

M Behr[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: marcel.behr@mcgill.ca

Multiple longitudinal epidemiological studies from the pre-antibiotic era show that the vast majority of TB disease manifests soon after infection, with disease following remote infection being rarer. These include natural history studies, the control arm of Isoniazid trials, the MRC trial of BCG vaccination in the UK and the household contacts of TB patients randomized to home treatment in Madras. This appreciation of the natural history of infection and disease should be useful in strategizing preventive efforts, including identifying and intervening on incident TB infection in healthcare workers. Furthermore, if TB infection is not lifelong (i.e. spontaneous clearance of infection occurs), then people with longstanding tuberculin reactivity may not be persistently infected at the time of a new exposure. The latter has implications for the prevention of TB disease in individuals with a recent exposure to active TB, depending on whether tuberculous infection confers transient or sustained protection against disease.

Is latent TB infection more harmful or helpful to the host?

E Nardell[1] [1]Brigham and Women's Hospital, Boston, United States of America. e-mail: enardell@gmail.com

Although there is little direct evidence that treating latent infection lessens the limited protection it affords the host, fear of loss of protection has been raised as a rationale not to treat latency. Dr. Nardell will make the case that the protection of LTBI is unlikely to be lost, given the long-term protection of BCG vaccine, a self-limited mycobacterial infection, and the protection of a recently developed killed mycobacterial vaccine.

HCW TB screening: needs and challenges

H van der Westhuizen[1]

Healthcare workers have at least a two-fold higher risk of developing TB and six-fold higher risk of developing drug-resistant TB, in comparison to the populations they serve. Although TB is recognized as an occupational disease, occupational health systems in TB-endemic countries are absent or weak and thus TB screening, even for active TB disease is rarely performed. Dr. van der Westhuizen will discuss the needs and challenges related to healthcare worker TB screening for active and latent TB from the perspectives of healthcare workers in a high incidence country.

Experiences with LTBI screening of HCWs in an Indian referral hospital

D Christopher[1] [1]Christian Medical College, Vellore, India.
e-mail: djchris@cmcvellore.ac.in

India ranks first among all countries in terms of the burden of TB, and HCWs in India are exposed to TB on a regular basis. Paradoxically, in India and other high burden countries, HCW screening and protection against TB transmission are lacking. Among HCWs, nurses spend more time in contact with infectious TB patients, and are at high risk for acquisition of TB infection and disease. A systematic review showed that LTBI prevalence among nurses ranged from 43% to 87%, and in almost all studies, LTBI prevalence in nurses was 1.3% to 35.6% higher than in other HCWs. Therefore, our initial studies were centered around screening nursing students and we have devised a pragmatic policy for prophylaxis. More recently, we have also screened medical students. Our experiences in studying TB risk in HCWs, particularly young health care trainees, offering LTBI prophylaxis and developing hospital infection control strategies will be discussed.

SP-15-B8 Tobacco control interventions should be implemented in TB control programmes

Association between exposure to tobacco smoke and tuberculosis

C Chiang[1] [1]The Union, Taipei, Taiwan.
e-mail: cychiang@theunion.org

Smoking is associated with an increased risk of active tuberculosis (TB) and latent TB infection (LTBI). Passive exposure to tobacco smoke has been reported to be associated with both active tuberculosis and LTBI. Smoking has been reported to be significantly associated with delay in TB diagnosis and treatment, positive smear and cavitary pulmonary TB. Studies have reported that smoking is associated with delayed sputum conversion, unfavourable treatment outcome of TB, recurrent TB. To strengthen early diagnosis of TB and enhance effective TB treatment, tobacco cessation and smoking awareness program should be integrated into TB control, smokefree health facilities must be established and health care workers must be engaged and trained in providing tobacco control services.

How effective is the systemic integration of smoking cessation into TB control programmes in creating smoke-free environments?: a pilot study in an urban setting in the Philippines

A Ohkado[1] [1]Research Institute of Tuberculosis (RIT), Japan Anti-Tuberculosis Association (JATA), Tokyo, Japan.
e-mail: ohkadoa@jata.or.jp

We conducted a prospective observational study, whereby an intervention group comprised of people with tuberculosis (TB) receiving the modified ABC Smoking Cessation approach, and a control group of people with TB receiving only regular health education, at selected health centers in Manila City. We also conducted a series of focus group discussions (FGDs) to explore perceptions of quitting smoking. We enrolled in 1,145 and 1,028 people with TB as an intervention and a control group, respectively. Both smoking and the secondhand-smoking (SHS) rates at the 6th & 12th month of TB treatment were lower in the intervention group than those in the control group. The TB treatment success rate in the intervention group was significantly higher than that in the control group ($P<0.001$). FGDs indicated that the experience of being diagnosed with TB did prompt many to either reduce the number of cigarettes or to quit temporarily.

Cross-country comparison of awareness of TB and smoking

G Fong[1] [1]University of Waterloo, Ontario, Canada.
e-mail: geoffrey.fong@uwaterloo.ca

This presentation describes findings from 20+ International Tobacco Control Project countries on smokers' awareness of harms of smoking and secondhand smoke (SHS) on lung health. Smokers were most aware that smoking causes lung cancer, but some countries were lower (e.g.,80% in China) than others (e.g., 99% in France). Interestingly, awareness that smoking causes TB was greater among smokers in India and Kenya (both 71%), than in 5 EU countries (e.g., Germany 42%, Spain 56%). Awareness that smoking causes emphysema ranged from 85-90% in Canada, US, and Australia) to 69% Hungary and 76% China. Awareness that SHS causes lung cancer was lowest of all but varied across countries (e.g., 91% Mexico and 81% Brazil vs. 65% Greece and 56% the Netherlands). Low awareness that smoking causes TB and other lung diseases points to the need to raise public awareness, especially, and surprisingly, in many high-income countries.

National framework on joint TB-Tobacco collaborative activities: an experience from India

L Swasticharan[1] [1]Ministry of Health and Family Welfare, Govt. of India, New Delhi, India.
e-mail: swasticharan.l@nic.in

Exposure to tobacco smoke increases risk of developing TB by 2.5 times; risk of relapse by 3 times; and increases tuberculosis mortality and resistance to anti–tubercular drugs by 4 times. National Framework for Joint TB-Tobacco Collaborative Activities was developed in 2017 and officially launched in eight states in August 2018. India is the first country in SEA region to develop such Framework. This aims to reduce the burden of co-morbidity thorough collaborative activities between two national programmes viz. Revised National Tuberculosis Control Programme (RNTCP) and National Tobacco Control Programme (NTCP). Joint coordination mechanism at national, state, district levels with collaborative functional activities at all levels is the key to success The implementation includes 'Brief Advice' for tobacco cessation in RNTCP and similarly screening of active 'TB symptoms complex' among registered tobacco users in NTCP and digital linkage between National Tobacco Quitline/m-cessation programme and TB missed call initiative.

Approaches to integrate TB and tobacco control health messaging

R Perl[1] [1]Vital Strategies, New York, United States of America. e-mail: rperl@vitalstrategies.org

Vital Strategies collaborated with the Ministry of Health and Family Welfare, Government of India, in the message testing, development and implementation of a national mass media campaign called "TB Cough", which was globally the first ever campaign that linked TB and Tobacco, and graphically depicted how smoking and second-hand smoke exposure increases the risk of TB and dying from it. This session will present the approaches towards integrating messaging around TB and Tobacco Control using population level communication channels of mass media complemented with social and earned media.

SP-16-C1 Fulfilling Commitments from the UN High Level Meeting on Tuberculosis: Programmatic Strategies for Taking Tuberculosis Preventive Treatment to Scale

Global TB Preventive Treatment (TPT) Updates

A Kanchar[1] [1]WHO, Geneva, Switzerland.
e-mail: kanchara@who.int

Following the release of the updated 2018 WHO Latent tuberculosis infection guidelines for Programmatic Management, global TB preventive treatment (TPT) targets were set as part of the UN High Level Meeting on TB held in New York in September 2018. Nations are now working to set national targets and accountability frameworks, as well as they are working with key partners and funders to rapidly scale up TB preventive treatment. This presentation will review the global landscape for TPT implementation as well as share an overview of several global initiatives currently underway.

Approaches and Lessons from Early Implementation and Scale-up of TPT for People Living with HIV and Child Contacts in Uganda

S Muchuro[1] [1]Uganda National TB and Leprosy Programme (NTLP), Kampala, Uganda.
e-mail: smuchuro@defeat-tb.urc-chs.com

Uganda's TB/HIV co-infection rate is 40%. The country has low TPT coverage of 2% and 17% among PLHIV and child contacts, respectively, and low completion rates (27%). Integration of TPT into HIV surge activities, pairing of INH with pyridoxine and antiretroviral therapy (ART), continuous quality improvement, and increased accountability through a weekly reporting contributed to a quadrupling of enrollments among new PLHIV from 20,820 in Jan-Dec 2018 to 21,742 in Jan-Mar 2019, and from 17% to 35% among child contacts over the same period. Improved coordination between the MoH and national warehouses, prioritization of clinics for the limited isoniazid, web-based monitoring of clinic stock levels and ordering of isoniazid and pyridoxine contributed to a improvement in completion rates from 27% in 2017 to 67% in 2018. However, improvements in contact screening, family targeted behavior change communication, and community-based approaches to TPT are required to improve coverage among the child contacts.

Programmatic Implementation of TB Preventive Treatment (TPT) in Child Contacts <5 Years in Rwanda

P Migambi[1] [1]Tuberculosis & other Respiratory Communicable Disease Division, Institut of HIV/AIDS Disease Prevention Control, Rwanda Biomedical Center(RBC), Kigali, Rwanda. e-mail: patrick.migambi@rbc.gov.rw

Management of latent tuberculosis infection (LTBI) is one of the globally recommended key interventions to end TB. Rwanda has over 10 years of experience implementing LTBI management among child contacts less than 5 years of age. The number of child contacts screened increased from 89% in 2014 to 98% in 2018. Over the last five years, 94% of child contacts were screened and among them presumptive TB rate was 12% and 12% of these were diagnosed with TB. Seventy-three percent of eligible child contacts initiated TPT. The completion rate was 98% on average over the same period. The good uptake of IPT over the years was due to integration of screening in Integrated management of childhood illness (IMCI) and use of community health workers for contact tracing and follow up. Further effort is needed to increase the initiation of IPT among eligible children.

Scaling up TB Preventive Treatment (TPT) in South Africa: "Claiming our Former Glory"

H Mabuza[1] [1]Centers for Disease Control and Prevention, Johannesburg, South Africa. e-mail: ysf2@cdc.gov

South Africa accounts for the largest proportion of patients initiated on TPT globally (~45%). While South Africa is the largest contributor to global TPT numbers (in the form of IPT, or isoniazid preventive therapy), challenges of national coverage remain. Only ~38% of eligible newly diagnosed people living with HIV (PLHIV) received IPT. In order to understand challenges with IPT uptake among PLHIV, stakeholders convened a TPT consultative round table discussion in 2017, bringing together PEPFAR funded implementing partners. A national TPT circular was developed to address and clarify some confusion around TPT and it was disseminated at a national TB/HIV stakeholder's meeting. CDC then introduced a Quality Improvement project to scale up TPT in select high burden districts and high volume facilities, resulting in an increase in weekly IPT initiations from ~700 to ~5000 in nine months.

Scaling up TB Preventive Treatment Beyond People Living with HIV (PLHIV) and Child Contacts in India: Roadmap and Challenges

K Sachdeva[1] [1], Delhi, India. e-mail: ddgtb@rntcp.org

India has the highest burden of LTBI globally, with nearly 40 per cent of the Indian population having LTBI. The programme is expanding the eligible population from PLHIV and child contacts of pulmonary TB patients as per new WHO recommendations, which would further increase the target population multi-fold. The sheer magnitude of the numbers offers challenges in capacity building for the programme and acceptability among the beneficiaries. India has committed to achieving the UN High level meeting targets for TPT, with a commitment of nearly 7 million rupees between 2018-2022. India's plan for scaling up LTBI would offer good learning experience for all countries.

SP-17-A2 The way forward for TB vaccines

Advances and novel concepts in preclinical and early clinical development of new TB vaccines

D Lewinsohn[1] [1]Stop TB Partnership Working Group on New TB Vaccines, Portland, United States of America. e-mail: lewinsod@ohsu.edu

Recent research has highlighted the potential for vaccines to prevent or eliminate TB infection or disease. This talk explores cutting-edge research in pre-clinical development of new TB vaccines, with a focus on novel vaccination strategies. This will include insights provided by vaccination with rhesus cytomegalovirus (rhCMV), intravenous BCG, and mucosal vaccination. Novel concepts for antigenic targets, mechanisms of action, and routes of delivery will be discussed.

The potential impact of new and repurposed TB vaccines

R Harris[1] [1]LSHTM, London, United Kingdom. e-mail: rebecca.harris@lshtm.ac.uk

Following on from recent phase IIB efficacy results, this talk will explore the epidemiological impact and cost-effectiveness that could be expected with current late-stage candidates in different epidemiological settings. Using available mathematical modelling evidence, consideration will be given to informing design of phase III clinical trials and future implementation, by an exploration of which characteristics could be most impactful, and which populations should be vaccinated to maximise population-level impact.

The role of multisector partnerships in TB vaccine development

B Kana[1] [1]University of the Witwatersrand, Johannesburg, South Africa. e-mail: Bavesh.Kana@nhls.ac.za

Successful vaccine development involves a multitude of stakeholders, including vaccine developers, researchers, cross-product bodies, civil society, advocates, affected communities/patients, funders and many more. This talk will explore the involvement of these stakeholders in the development and implementation of new and repurposed TB vaccines, and how each stakeholder group can contribute to more effective cross-sector partnerships as we scale-up efforts to develop vaccines for TB. Roll out of adolescent/adult vaccines will bring unique challenges, so consideration will be given to how the field can prepare to ensure rapid and equitable access once candidates are successful in clinical trials.

Response from CS

B Kumar[1] [1]Global Coalition of TB Activists, New Dehli, India. e-mail: blessi.k@gmail.com

An informed and engaged civil society is essential to the successful development and implementation of new vaccines. Civil society and affected communities should be involved in research and development from early stage and preclinical research through to clinical trials and eventual uptake of new TB vaccines once licensed. The speaker will provide a civil society response and perspective on the preceding presentations, and on the role of new TB vaccines in global efforts to end TB.

SP-18-B2 Reducing deaths from tuberculous meningitis

Improving the diagnosis of tuberculous meningitis

K Sharma[1] [1]Postgraduate Institute of Medical Education and Research, Chandigarh, Chandigarh, India. e-mail: sharmakusum9@yahoo.co.in

The diagnosis of tuberculous meningitis (TBM) is difficult and poses a significant challenge to physicians worldwide. Delay in effective treatment results in significant morbidity and mortality. Conventional diagnostic armamentarium like microscopy and culture has a limited role due to low sensitivity and prolonged turnaround time in clinically relevant time frame. The diagnostic challenge for microbiologists is the paucibacilliary nature of the disease and the low volumes of CSF available in real life clinical settings. Timely and accurate diagnosis, along with information about susceptibility of drugs with good CSF penetration is needed for the initiation of appropriate therapy in TBM patients. I will discuss the limitations of current technologies and the role of upcoming molecular methods, including nucleic acid amplification techniques, XpertMTB/RIF, Xpert Ultra, Line probe assays, LAMP, HRM ,newer DST platforms and whole genome sequencing.

Optimising anti-tuberculosis drug treatment of tuberculous meningitis

H Alsdurf[1] [1]McGill University, Montreal, Canada. e-mail: hannah.alsdurf@mail.mcgill.ca

The current treatment regimen for tuberculous meningitis (TBM) recommended by the WHO is based on data from, and just follows, the treatment of Pulmonary TB. But treatment is challenging because the drugs must cross the barrier into central nervous system and only free fraction of the drug can cross the barrier. Some anti-TB drugs including rifampicin - a key drug for TB - penetrate poorly. The optimal chemotherapy regimen needs to be defined. In the last ten years, effort has been made to explore how we can optimize the use of old and new anti-TB drugs, such as using high dose rifampicin, quinolones, linezolid and isoniazid. This is included for specific patient groups like HIV co-infection and children. Optimal research strategies are needed towards better treatment of this devastating disease.

Adjunctive therapy for tuberculous meningitis

G Thwaites[1]

Reducing deaths for tuberculous meningitis (TBM) requires the bacteria to be killed quickly, but the intracerebral inflammatory response also needs to be controlled. Adjunctive corticosteroids have been used for many years, with good evidence that they reduce deaths in HIV-uninfected individuals. However, corticosteroids do not work for all patients. There is little evidence they benefit HIV-infected individuals with TBM and other drugs may be more targeted and effective. The list of alternative adjunctive agents that may reduce deaths is growing. They include aspirin, thalidomide, and other biological agents that inhibit tumour necrosis factor (TNF). I will review the current evidence surrounding corticosteroids and the likely future for other agents.

The complications of tuberculous meningitis: their spectrum, basis, and effect upon outcome

U Misra[1] [1]Sanjay Ghandi Post Graduate Institute, Lucknow, India. e-mail: drukmisra@gmail.com

The complications of tuberculous meningitis (TBM) include raised intracranial pressure, stroke, paradoxical worsening, hyponatremia, status epilepticus and drug induced hepatitis. These complications occur at different time points and often worsen the outcome of patients. Stroke is attributed to vasculitis mechanical stretching of vessels, compression by basal exudates. Associated cerebral salt wasting (CSW) and hyponatraemia can also result in cerebral hypoperfusion. Raised intracranial pressure is attributed to multiple etiologies such as tuberculoma, infarction, hydrocephalus and brain edema, which it is best managed by External ventricular drainage or ventriculo-peritoneal shunt. Osmotic diuretics are of limited and temporizing value. It is important to anticipate and manage these complications appropriately to reduce the mortality and morbidity.

The pathogenesis and management of HIV-1-associated tuberculous meningitis

R Wilkinson[1] [1]Institute of Infectious Disease and Molecular Medicine, , South Africa. e-mail: Robert.Wilkinson@crick.ac.uk

In patients who are co-infected with HIV 1, TBM is one of the commonest forms of meningitis and can have a mortality approaching 50%. The clinical, radiographic and laboratory features exhibit differences those found in HIV-1 infected persons. In particular paradoxical deterioration may be particularly severe (TBM-IRIS) in the context of otherwise life-saving combined anti tubercular and antiretroviral therapies. Observational analyses implicate inflammasome activation and neutrophils as detrimental inflammatory mechanisms contributing to morbidity and mortality. Via drug interaction and shared side-effects, antiretroviral therapy may also complicate the antibiotic treatment of TBM: itself recognised to be suboptimal. The role of the commonly used adjunctive anti-inflammatory therapies (corticosteroids, aspirin and thalidomide) is less well-defined in HIV-1 co-infected patients. This presentation will review these features and recent research and give pointers to how the mortality and morbidity might be decreased in this difficult set of circumstances.

SP-19-B7 Asthma: an emerging threat to health across the life course

Asthma in African children: the South African perspective

R Masekela[1] [1]University of AberystwythKwaZulu Natal, Durban, South Africa. e-mail: masekelar@ukzn.ac.za

This talk will review of the burden of asthma and drivers of poor asthma control in South African children. The current gaps in the literature with regards to asthma in LMICs and the relationship between asthma and allergies in that context. A description of an ongoing pan African school-based study into asthma control.

Bronchiolitis and asthma: emerging links

J Grigg[1] [1]Queen Mary University of London, London, United Kingdom. e-mail: j.grigg@qmul.ac.uk

Bronchiolitis is a major cause of respiratory morbidity. It is also followed by persistent respiratory symptoms in many infants. This presentation will review the evidence for the link between bronchiolitis and the subsequent development of school age asthma. It will review both epidemiological data and mechanistic data - and evidence from therapies that reduce the risk of RSV bronchiolitis infection in infancy.

SP-20-B4 Therapeutic TB trials in children: improving knowledge and access

Evidence-based dosing of first-line drugs for African and Indian children: data from SHINE

H McIlleron[1] [1]Univesrity of Cape Town, Cape Town, South Africa. e-mail: helen.mcilleron@uct.ac.za

Most paediatric tuberculosis is paucibacillary. Evidence for tuberculosis treatment in children is largely extrapolated from adult studies. Trials in adults with smear-negative disease suggest that treatment can remain effective if shortened from 6 to 4 months. New fixed-dose combinations for TB treatment in children have been introduced, enabling revised dosing recommended by WHO, although the safety of exposure to higher drug concentrations has not been assessed in large paediatric studies. SHINE is a multicentre, open-label, parallel group, non-inferiority, randomised controlled 2-arm trial comparing a 4-month treatment regimen to the standard 6-month regimen using revised WHO paediatric anti-tuberculosis drug doses in children. We enrolled 1,200 African and Indian HIV-infected and uninfected

children below 16 years with non-severe TB. Intensive sampling was completed in 60 children and pharmacokinetics of rifampicin, isoniazid and pyrazinamide characterized using noncompartmental analysis using AUC24 as primary measure. These findings have significant implications for evidence-based dosing in children.

Optimising rifampicin exposure in children towards treatment shortening and treatment of severe disease: OptiRif Kids trial

A Garcia-Prats[1] [1]Desmond Tutu TB Centre, Stellenbosch University, Cape Town, South Africa.
e-mail: garciaprats@sun.ac.za

For equivalent rifampicin dosages, children typically require approximately twice the mg/kg body weight dosage to reach serum concentrations equivalent to those of adults. Adult data ndicate that higher doses of 35 mg/kg of rifampicin are safe, well tolerated, and have increased antimycobacterial activity. Increased rifampicin doses may also be beneficial in children with severe forms of tuberculosis. We aimed to establish the dose and safety of rifampicin in children required to match rifampicin exposure targets in adults of 35 mg/kg dose over 15 days. Multiple dosing cohorts were evaluated until target rifampicin exposures were achieved during 15 days during the intensive phase of treatment. Incremental dose escalation was completed in each cohort, and single-dose within-cohort dose escalation. 60 children in 3 dosing cohorts were enrolled. Data for all dosing cohorts are reported here, including Day 1-14 60 mg/kg rifampicin (9 weight bands), and Day 15 75 mg/kg (9 weight bands).

Site of disease pharmacokinetics in children with complicated intrathoracic TB

E Lopez Varela[1] [1]IS Global, Barcelona, Spain.
e-mail: elisa.lopez@isglobal.org

For successful treatment of TB, drugs used need to reach their molecular targets at the site of disease at adequate concentrations. Little is known regarding the pharmacokinetics of antituberculosis drugs at the site of disease in children, including tissue penetration in lung. The aim of this proof-of-concept study was to characterize drug concentrations at the site of disease for rifampicin, isoniazid in children with intrathoracic TB, and compare drug concentrations to those in plasma. We evaluated drug concentrations in broncho-alveolar lavage (BAL) and in intra-thoracic lymph node tissue in 20 children with complicated intrathoracic TB undergoing bronchoscopy or transthoracic surgical lymph node decompression in Cape Town, South Africa.Intensive plasma sampling was completed; samples were analysed using standard liquid chromatography tandem-mass spectrometry. Lymph tissue was analysed using LC/MS-MS, laser capture microdissection or matrix-assisted laser desorption/ionization mass spectrometry.

Optimising therapeutic approaches in children with malnutrition and implications for clinical trial design

R Savic[1] [1]UCSF, San Francisco, United States of America.
e-mail: rada.savic@ucsf.edu

Malnourished and young children are vulnerable to severe tuberculosis and poor treatment response. Current WHO dosing guidelines are based on weight, and does not account for age and nutritional status, which may lead to systematic under-dosing and worse outcomes in most vulnerable children. We quantified the population impact of current WHO guidelines for drug-susceptible tuberculosis in children in the 20 countries with highest disease burden and high malnutrition rates, using an integrated model which links country-specific individual-level demographic data to pharmacokinetic, outcome, and epidemiological models. We estimated that 11-55% of all children (n=374,810) and >70% of underweight children (n=103,215) were underdosed with WHO dosing. A simple change in dosing procedure to include age and nutritional status would equalized outcomes by nutritional status and save at least 1/3 of all children with unfavourable treatment outcomes. This approach requires no additional measurements or new drug formulations and could be implemented immediately.

From clinical trial data to improving drug formulations required in the field: experiences from PADO, GAP-f

M Penazzato[1] [1]World Health Organization, Geneva, Switzerland. e-mail: penazzatom@who.int

For TB, clinical evidence is lacking to define appropriate paediatric doses, paediatric formulations do not exist for most drugs and time to market lags compared to adults. Key challenges that hamper rapid development and introduction of optimal paediatric formulations include market fragmentation, lack of child-friendly TB formulations, complexity and cost of the projects, internal prioritization within companies, lack of market incentives/small markets, and difficult and slow market uptake. TB PADO builds on HIV PADO, which identified key priority products since 2013 to ensure a consistent clear message to manufacturers regarding needs through collaborative and coordinated action: TB PADO prioritizes based on current and expected WHO guidelines and provide a vision for policy change, providing guidance on product development to industry. GAP-f is a collaboration platform that promotes faster, more efficient and focused approaches to paediatric clinical and formulation development and introduction leveraging public and private investments.

SP-21-B1 Early scale-up and evaluation of TB case finding and systematic screening using digital chest radiography and computer-aided diagnosis in Africa and Asia

An overview of automated reading software for CXR: products, approaches and evaluation results

J Creswell[1] [1]Stop TB Partnership, Geneva, Switzerland.
e-mail: jacobc@stoptb.org

Currently, only one automated CXR reading software (CAD4TB) is commercially available and evaluated in peer reviewed literature. However, many new products are being introduced and need evaluation before they can be used by implementers. Using chest x-rays collected through different case finding approaches from TB REACH projects across Asia and Africa, we present the results of multiple automated reading software packages including Qure.ai and Lunit using different TB screening and testing approaches. We tested the different software packages against both bacteriological and human reference standards. We present the differences across the a number of products now available, how they can become more user friendly, and discuss some thinking on new developments in the AI field for reading CXR.

Intensified TB case finding in primary care in Blantyre, Malawi using computer-aided chest X-ray detection

P MacPherson[1] [1]Liverpool School of Tropical Medicine, Liverpool, United Kingdom.
e-mail: peter.macpherson@lstmed.ac.uk

Adults attending primary care in sub-Saharan Africa have a high prevalence of TB symptoms. Current sputum-based screening approaches are impractical and unaffordable for health systems, and result in long treatment delays, high out-of-pocket costs and missed opportunities for treatment. The PROSPECT Study being conducted in Blantyre, Malawi is a three-arm pragmatic randomised trial investigating the cost-effectiveness of intensified TB screening using computer-aided chest x-ray detection (TB-CAD). From 15th November 2018, all adult clinic attenders with an acute illness have been screened for TB symptoms and if eligible, randomly allocated to trial interventions. Here we report on the prevalence of TB symptoms among acute adult clinic attenders, patterns of abnormalities on chest x-ray identified through TB-CAD screening and compared to radiologist reference read, and comparison of patient costs incurred by participants receiving TB-CAD and standard sputum-based interventions.

Computer-aided interpretation of digital chest X-rays in Vukuzazi, a population-based survey of HIV, TB and diabetes in rural KwaZulu-Natal

E Wong[1] [1]African Health Research Institute, Durban, South Africa. e-mail: emily.wong@ahri.org

KwaZulu-Natal is in the midst of three intersecting epidemics -- HIV, tuberculosis and non-communicable diseases. In the uMkhanyakude district in Northern KwaZulu-Natal, the Africa Health Research Institute has been undertaking demographic and HIV surveillance in a population of approximately 120,000 individuals for over 15 years. In May 2018, in an effort to better understand the intersection of communicable and non-communicable diseases in our population and to establish a platform for interventional studies, we launched Vukuzazi, a population survey that offers community-based screening for HIV, TB, diabetes to all individuals over 15 years and old. In the TB screening algorithm, presence of symptoms and computer-aided interpretations of digital chest x-rays are used to identify individuals for sputum M.tb testing. Here we report on the use of CAD4TB in the TB screening algorithm of Vukuzazi.

Utility of CAD4TB in mobile surveillance vans in Nigeria fills necessary gap in national TB programme

R Eneogu[1] [1]KNCV TB Foundation Nigeria, Abuja, Nigeria.
e-mail: reneogu@usaid.gov

In Nigeria, where according to the WHO Global Tuberculosis Program, it is estimated that the TB treatment coverage in 2017 is 24% (95% CI: 23-38%), the mobile TB surveillance vans provide one of the few alternatives to the patient-initiated pathway surveillance and targeted screening to capture TB from the general population. We report on the number needed to screen by age, gender and setting, the operating costs per TB patient identified and the geographical differences in the cascade of subjects attending community TB screening using CAD4TB and reported symptoms to identify presumptive TB cases that are then tested with GeneXpert machines. We also evaluate the contribution of mobile vans to validating sub-national TB prevalence estimation.

Roundtable discussion: lessons learned in the early scale-up of digital chest X-ray plus CAD

L Corbett[1]

Speakers together with implementers with practical experience of using digital chest X ray plus computer-aided detection in Asia (Pakistan and India) - and Africa (National TB Programme, Malawi and Kenya) will discuss key lessons learnt and challenges. This will include mobile reporting technologies, and the need for expert

readers alongside CAD as well as the practical challenges of implementing radiology in resource limited settings with little existing radiological infrastructure and training.

SP-22-C8 Taking TB diagnostics to the fields: improving access by extending advanced point-of-care (PoC) testing to rural communities

Reviewing the diagnostic outreach to rural populations: How are we doing and where do we go from here?

M Pai[1] [1]McGill International TB Centre, Montreal, Canada.
e-mail: madhukar.pai@mcgill.ca

This presentation will discuss various efforts to improve TB diagnostics at the point of care in decentralized settings, including primary care and rural areas. The landscape of POC technologies will be reviewed.
In addition, the presentation will cover novel strategies to reach missing patients, including engagement of community health workers, pharmacies, GPs, and private health providers.

Performance of advanced diagnostics in low-income countries: comparison of LAMP and GeneXpert with applications for TB control programmes in rural settings.

L Nakiyingi[1] [1]Makerere University, Kampala, Uganda.
e-mail: lydiakiyingi@gmail.com

This talk gives an update about newer technologies for TB diagnosis, focusing on LAMP and GeneXpert. Details of studies done comparing their performance, utilization, and cost effectiveness when applied to rural settings in Uganda, will be presented. The goal of this presentation will be to consider the applicability and make recommendations on utilization of these diagnostics to TB control programs.

Utilising chest ultrasound as a PoC diagnostic test for TB programmes in a rural setting.

P Agostinis[1] [1]Ospedale San Antonio Abate, Tolmezzo, Italy. e-mail: agostinispaolo@gmail.com

Dr Agostinis has studied the use of point of care ultrasound for the diagnosis of various pulmonary conditions including tuberculosis. Here he will present the possible findings on ultrasonography that could suggest TB. He will furthermore discuss the effectiveness of this technology for accurate diagnosis in the field. The goal of this presentation will be to consider ultrasound as a complementary diagnostic tool that can be utilized by TB programs in low resource countries.

SP-23-F3 Assessing the burden and impact of zoonotic tuberculosis

Improving our understanding of the burden of zTB

A Dean[1] [1]WHO, Geneva, Switzerland.
e-mail: deanan@who.int

The 'Roadmap for Zoonotic TB' calls for a stronger evidence base to improve our understanding of the burden of zoonotic TB and guide an effective response. Globally, WHO estimated that there were 142,000 human cases of zoonotic TB in 2017. However, the true burden is likely to be underestimated, as high quality data are lacking from many countries. Improving the surveillance of zoonotic TB will require overcoming barriers to accessing health care, investing in the development and roll-out of appropriate diagnostic tools, and strengthening case-based recording and reporting systems. In the interim, targeted surveys among possible high risk groups in certain settings may provide valuable data at the sub-national level. In parallel to these efforts, there is a need for more comprehensive data on the prevalence of bovine TB in animal populations as well as investigation of drivers of transmission to people.

Zoonotic tuberculosis: progress, challenges, and opportunities to assess its global burden

F Oleo-Popelka[1] [1]Western University / Schulich School of Medicine & Dentistry, London, Canada.
e-mail: francisco.olea-popelka@schulich.uwo.ca

Efforts during the past six years that resulted in successfully creating and increasing global awareness of zoonotic tuberculosis (ZTB) will be presented. The benefits of multi-institutional collaboration will be highlighted, and progress towards accomplishing the ZTB Roadmap milestones will be discussed, emphasizing the need for additional work to implement and improve routine surveillance of Mycobacterium bovis (M. bovis) as the causal agent of human TB.
Remaining challenges, opportunities, and a few examples of current field work and activities in different countries/regions will be presented. The need for targeted approaches that are suitable for different epidemiological and logistical scenarios in different countries/regions will be emphasized.
The importance of generating robust scientific evidence locally, nationally, and at a global scale in order to create

an investment case to advocate for funding and political commitment to address the challenges posed by zoonotic TB will be discussed.

Ecology and evolution of the Mycobacterium tuberculosis complex

S Gagneux[1] [1], , Switzerland.
e-mail: sebastien.gagneux@swisstph.ch

Recent studies of large globally representative collections of whole genome sequences from human-adapted Mycobacterium tuberculosis complex (MTBC) lineages have considerably enhanced our understanding of the global population structure, phylogeography and evolutionary history of these pathogens. In contrast, there is little information on the various animal-adapted ecotypes of the MTBC, despite the fact that these pathogens represent the primary causative agents of TB in livestock and cause zoonotic TB in humans. This presentation will highlight the current state of knowledge in phylogeographical population structure of animal-adapted MTBC organisms and discuss how differences in host tropism as well as how key events associated with domestication of cattle, animal husbandry, human migration and trade may contribute to the spillover risk and impact of zTB in humans.

Exploring the proportion of human TB due to zTB

M Behr[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: marcel.behr@mcgill.ca

The End TB Strategy imposed by the World Health Organization aims to reduce TB-related deaths by 90% by 2030. The Mycobacterium tuberculosis complex (MTBC) consists of M. tuberculosis (M. tb) as well as other species including M. bovis and M. orygis. The latter are typically associated with non-human hosts, but can be transmitted to humans, to cause zoonotic TB (zTB). A recent WGS-based phylogeny of the MTBC suggests that M. orygis may be to Bos indicus as M. bovis is to Bos Taurus. If true, published studies on zTB may have underestimated zTB in countries such as India. This presentation will summarize the current state of knowledge and highlight critical needs and opportunities for accurately assessing the proportion of TB that is attributable to zTB.

Challenges for laboratory identification of agents of zTB in a routine diagnostic laboratory

J Michael[1] [1]Christian Medical College, Vellore, Vellore, India. e-mail: joymichael@cmcvellore.ac.in

With 2.7 million cases in 2017, India accounts accounts for a quarter of the world's TB burden. While Mycobacterium tuberculosis (Mtb) is the most common cause of tuberculosis in people in India, the incidence of other Mtb complex agents including M. bovis, M. orygis, and others agents known to cause zoonotic tuberculosis (zTB) remains unknown. This is because while current protocols in a routine mycobacteriology diagnostic laboratory including MPT 64 immunochromatographic test, nitrate reduction, susceptibility to paranitrobenzoic acid, and niacin production are able to differentiate between agents of M. tb complex and non-tuberculous mycobacteria, they do not differentiate between the agents of zTB including M. bovis, M. caprae, M. orygis, etc. from Mtb. This presentation will highlight our recent findings from application of new molecular diagnostic techniques for assessing the burden of these potentially zoonotic pathogens in people in India.

SP-24-C1 Scaling up TB preventive treatment: considerations on target populations and diagnostic approaches

WHO guidelines on TPT and evaluation of target population

A Kanchar[1] [1]WHO, Geneva, Switzerland.
e-mail: kanchara@who.int

WHO published the consolidated and updated guidelines for programmatic management of latent TB infection in 2018. Previous (2015) LTBI guidelines recommended differentiated approach for low and high TB burden countries. For the first time, 2018 guidelines provided recommendations to expand TB preventive treatment services in high burden countries. These included expansion of target groups for TB preventive treatment and use of TST/IGRA for detection of latent TB and radiography for TB screening in PLHIV on ART. These guidelines also recommended shorter rifamycin based TB preventive treatment regimen including 3HP and 3RH. Further, at the first ever UN high level meeting on TB, member states endorsed target to provide 30 million individuals with TB preventive treatment by 2022, including specific targets for PLHIV and household contacts of TB patients. The 2018 WHO guidelines provide necessary guidance to enable scaleup of preventive treatment to achieve global targets.

Implementing IGRA: practical experiences from Zambia, considerations for other countries

K Shanaube[1] [1]Zambart, Lusaka, Zambia.
e-mail: kshanaube@zambart.org.zm

Tests for Tb infection may have specific challenges when used in settings with high rates of TB infection and high HIV prevalence. We describe studies of IGRAs compared to TST in such settings and the challenges of interpretation. In addition there are many logistical challenges of using IGRAs in community testing. We present some of our experience of how to conduct testing in these environments.

TPT among household contacts using chest X-ray as the principal tool for ruling out active disease: experience from Bangladesh

T Rahman[1] [1]Interactive Research and Development, Dhaka, Bangladesh. e-mail: toufiq.rahman@ird.global

In the absence of an effective vaccine that can prevent the progression of active tuberculosis (TB), the National TB Control Programs (NTP) largely depend on TB preventive therapy (TPT). However, prioritizing target population and use of available diagnostics to determine eligibility of TPT is critical. From February 2018 to January 2019, 3,193 household contacts of 883 index pulmonary TB patients from 12 NTP centers in Dhaka were approached. Of these 2,149 (67%) were verbally screened for symptoms of TB and invited for a chest X-ray (CXR). A total of 1,804 (84%) contacts agreed for CXR; 39 (2%) people were identified with TB and started treatment. Remaining 1,765 (98%) contacts with normal CXR, negative sputum test, and favorable clinical opinion were considered eligible for TPT and of these 1,308 (74%) agreed to initiate TPT. CXRs were crucial to identify people with early disease and to rule out TB for preventive treatment.

Asymptomatic contacts aged 5–14 years and TB preventive treatment: what diagnostic approaches to consider?

S Graham[1]

The traditional focus for the provision of TB preventive therapy (TPT) in resource-limited, TB endemic countries has been on high-risk populations such as child household contacts < 5 years and people living with HIV, once active TB is excluded. A wide policy-practice gap is well recognised but there are increasing efforts to address it. While TPT for young child contacts is important to reduce TB-related child morbidity and mortality, it provides limited benefit to reduce ongoing TB transmission in the community. The potential individual and public health benefits of TPT for a wider age range of household contacts (including older children and adolescents) is now recognised. The possibility of regimens that are shorter, safer and as effective as IPT adds impetus. However, effective implementation of TPT for this age group will require important additional challenges, including access to care, effective evaluation for diagnosis or exclusion of active TB, and treatment support.

SP-25-A1 The surprising role of adipose tissue at the intersection of TB infection and immunity

Changes in body composition during TB treatment: fat versus lean body mass

G Praygod[1] [1]National Institute for Medical Research - Mbeya Medical Research Centre, Mbeya, Tanzania, Dar es Salaam, Tanzania, United Rep..
e-mail: gpraygod@yahoo.com

Tuberculosis patients have significant weight deficits at the beginning of treatment, related to the severity of disease, which contribute to treatment outcomes including mortality. Although survivors regain weight during treatment, many patients remain undernourished after treatment completion. Often, disease management is not optimal to meet the increased dietary requirements to replenish weight lost and compensate for continuing nutrient loss and inefficient metabolism. Importantly, studies from tuberculosis endemic countries have shown that a larger proportion of weight regained during treatment is fat mass (adipose tissue) rather than lean mass. This is a key distinction because lean mass rather than fat mass recovery has been associated with survival and functional benefits. In this symposium, we will review evidence on body composition changes during tuberculosis treatment and discuss their implication during treatment and for long-term health.

The contribution of adipose tissue in the containment or progression of TB

J Nagajyothi[1] [1]Public Health Research Institute, Newark, United States of America. e-mail: jfn31@njms.rutgers.edu

Adipose tissue is a highly active endocrine organ that regulates whole-body immune and metabolic homeostasis by secreting various humoral factors and inflammatory cytokines. Adipocytes communicate with other cells locally and afar via the autocrine/paracrine functions of secreted adipokines. Dysfunctional adipose tissue with deregulated adipokines signaling is implicated in various diseases including metabolic syndromes, cancer, and chronic infectious diseases such as Chagas cardiomyopathy. Although the lungs are the port of entry and the predominant site of tuberculosis disease mani-

festation, we and others have demonstrated that *M. tuberculosis* persists in adipose tissue of aerosol-infected animals and alters adipose tissue physiology and adipokines, which in turn drives whole-body immune and metabolic homeostasis. Using a novel transgenic murine tuberculosis model, we demonstrate that ablation of adipocytes leads to elevated pulmonary bacterial burden and pathology. Our work supports an emerging view that adipose tissue pathophysiology plays a major role in the progression of tuberculosis.

Adaptations of M. tuberculosis to lipid-rich host environments

S Gandrota[1] [1]CSIR-Institute of Genomics and Integrative Biology, New Delhi, India. e-mail: sheetal.gandotra@igib.in

Caseating granulomas are the hallmark of tuberculosis in humans. Drug discovery against bacilli in this extracellular, lipid rich niche requires models that can mimic this environment. Towards this goal, we use the adipocyte model of Mycobacterium tuberculosis infection. Peculiar to the model is the ability of the bacilli to infect and grow within the cells, followed by necrotic lysis of the cells yet persistent growth attached to cell remains. We compared the physiology of M. tuberculosis in adipocytes and preadipocytes. Both cell types demonstrated growth, necrotic lysis, and sustained growth attached to the cellular remains; however, the adipocyte host offered a lipid rich environment thereby affecting lipid metabolism of the bacilli. The key finding from these experiments was the discovery that lipid-rich environments offer an iron-rich niche to the bacilli, with tolerance to oxidative stress. These discoveries have implications for the drug discovery pipeline.

Pas de deux: Diabetes, adiposity, and the efficacy of anti-tuberculosis therapies

D Van Aartsen[1] [1]University of Virginia, , United States of America. e-mail: DJV3WG@hscmail.mcc.virginia.edu

Diabetes is associated with an increased risk of tuberculosis (TB) treatment failure, death, and relapse compared to patients without diabetes. In addition to the negative impacts on the TB patient's immune response, co-morbid metabolic disease influences the pharmacokinetics of anti-TB drugs. The magnitude of this relationship may be sufficient to diminish TB treatment efficacy. In this symposium, we will review the clinical data that link metabolic diseases with altered pharmacokinetics and pharmacodynamics of TB treatment, and discuss possible mechanisms using a translational research framework.

SP-26-A2 Leadership, science and action to advance new tools to end the TB emergency

Progress in the pipeline: advances in the development of new, more effective TB vaccines

D Tait[1] [1]IAVI, Cape Town, South Africa. e-mail: dtait@iavi.org

We will not end the TB emergency without a new vaccine. There has been significant recent progress in TB vaccine research and development and results published last year from recent efficacy trials demonstrate that developing new, more effective vaccines and delivery strategies is not only feasible but that a promising candidate is ready to move towards Phase 3 development. Multiple candidates are in various stages of clinical development, trials with novel designs that could streamline and accelerate TB vaccine development are underway and some have yielded results, and new preclinical approaches are being tested and providing important insights. The progress and opportunity in TB vaccine R&D are unprecedented. This presentation will discuss the state of the field and future directions in developing new TB vaccines, with a focus on vaccines in clinical development.

Accelerating access to TB diagnostics to find the "missing millions" and achieve the targets of the Global Plan to End TB

M Pai[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: madhukar.pai@mcgill.ca

The Global Plan's 90-90-90 progress report highlights that the greatest gap in the cascade of TB care is in access to diagnosis. Over 3 million people still go "missing" every year – they are either not diagnosed or not being reported. Finding these "missing" cases is central to ending TB. Key commitments made at the UNHLM on TB stress that point-of-care (POC) and child-friendly diagnostics as well as drug susceptibility tests are the need of the hour. Though the TB community has made progress in the area of rapid molecular DST and urine-based LAM tests for TB-HIV, we still need rapid, simple, non-sputum based POC tests for TB disease, and a predictive test for TB infection. We will not achieve the targets of the Global Plan to End TB without at least an extra US$1.3 billion every year for R&D to accelerate the development of new tools.

Progress and challenges on the road to better TB treatment

B Laughon[1] [1]National Institutes of Health/ National Institute of Allergy and Infectious Disease, Bethesda, United States of America. e-mail: blaughon@niaid.nih.gov

Today's treatments for TB are intensive, expensive, and may be as long as 24 months or more for drug resistant forms of TB. We need to accelerate the speed of development of lifesaving new cures to improve TB therapy. This presentation discusses the current new drug candidates, progress made in TB drug R&D, who is funding the work, and what is needed to complete the global TB research pipeline and make an impact on the TB epidemic. The presentation will also highlight the need for a global strategy over the next 5 years to drive the momentum in TB drug development toward meeting the commitments made at last year's UN High-Level Meeting on TB.

Political opportunities and partnerships for advancing TB R&D

N Gebreselassie[1] [1]Global TB Programme, World Health Organization, Geneva, Switzerland. e-mail: gebreselassien@who.int

The End TB Strategy stipulates that major technological breakthroughs are needed by 2025, so that the rate at which TB incidence falls can be dramatically accelerated compared with historic levels. Developing and diffusing the right medical innovations is a top priority to deliver on these targets. Specific priorities include a vaccine to lower the risk of infection, a vaccine or new drug treatment to cut the risk of TB disease in the 1.7 billion people already latently infected, rapid diagnostics for use at the point of care, and simpler safer, and shorter drug regimens for treating TB disease. Reaping the benefits of innovation at the global and national levels requires governments and other stakeholders to undertake the investments, innovative partnerships and policy reforms necessary for accelerating innovation. It also requires mechanisms and practices to ensure equitable access to international public goods such as medicines, vaccines and diagnostics.

SYMPOSIA: FRIDAY, 1 NOVEMBER 2019

SP-27-B2 From shorter to short: Progress towards six-month all-oral treatment regimens for MDR-TB

NiX-TB trial experience: safety reporting and recommendations for programmatic implementation of the regimen

F Conradie[1] [1]University of Witwatersrand, Houghton, South Africa. e-mail: fconradie@witshealth.co.za

The Nix-TB clinical trial, a short (6 months) regimen in XDR and refractory MDR-TB, is the pivotal phase 3 trial whose final results supported application for regulatory approval of pretomanid by the FDA. This presentation will describe the rigorous safety assessments and delicate re-introduction of drugs after adverse events to achieve treatment success in very sick patients in the trial. Recommendations on how to implement an aggressive and yet safe approach in clinical practice outside clinical trials will be explored.

Who could benefit from six-month MDR-TB regimens?: lessons from TB-ReFLECT

R Savic[1] [1]UCSF, San Francisco, United States of America. e-mail: rada.savic@ucsf.edu

Large multicentre randomised trials of four-month fluoroquinolone-containing regimens (REMoxTB, Rifaquin, OFLOTUB) were unable to achieve non-inferiority as compared to standard control regimen. These experimental regimens did, nonetheless, achieve 80% cure rates suggesting that a significant proportion of global TB burden may be eligible for shorter courses of treatment if major determinants of unfavourable outcome could be identified. Is there a prospective approach to data analysis that will add evidence to patients likely to benefit from the 6 months regimens? This presentation will explore the key determinants of success and how to standardise their measurement.

Short (six-month) all-oral MDR-TB regimen cohort studies in an NTP

A Skrahina[1] [1]The Republican Research and Practical Centre for Pulmonology and TB, Minsk, Belarus. e-mail: alena.skrahina@gmail.com

WHO 2018 recommendations encourage programmes to implement short regimens under operational research settings. Most countries are exploring the modified shorter (9-12 months) regimens but there is increasing interest in 6 months regimens. What are the regimens being studied and how does a national TB programme go about implementing a short regimen under operational research conditions.

Integrating the patient voice in MDR-TB treatment studies

K Schwartzman[1] [1]McGill University, Montreal, Canada. e-mail: kevin.schwartzman@mcgill.ca

As we endeavour to implement patient-centred care, we need to ensure our research studies include patient-reported outcomes as a critical component. Non-inferiority trials assume that apart from the safety and efficacy outcomes being measured, the investigational regimen has other beneficial attributes. What if a shorter (9-12 months) regimen had a slightly lower risk of relapse to a short (6 months) regimen, but within the non-inferiority margin? Which regimen would a patient choose? What information would they need to decide? This presentation will share current evidence integrating patient reported outcomes, such as health related quality of life and other measures, from TB treatment trials and observational studies.

TB-PRACTECAL clinical trial: towards short, all oral MDR/XDR-TB treatment regimens

B Nyang'wa[1]

TB-PRACTECAL is a phase II-III randomised, controlled clinical trial, studying three short (6-months), all-oral treatment regimens containing bedaquiline, pretomanid and tapered dose (600 -> 300mg) linezolid for both quinolone susceptible and quinolone resistant MDR-TB. In this session we present the rationale behind the regimen choices, 6 months duration choice and the trial design. We'll also update on progress of the trial.

SP-28-A3 Modified shorter treatment regimen: using evidence, capacity building and public health approach to build sustainable and efficient MDR-TB care

Outcome of short treatment regimens for MDR-TB modified either by reduced duration of injectables or by type of fluoroquinolone core drug

A Van Deun[1] [1]Institute of Tropical Medicine, Antwerp, Belgium. e-mail: avdeun@itg.be

Excellent treatment outcomes have been reported with a standardized 9-12 months short treatment regimen (STR) from Bangladesh, Niger and Cameroon. This original STR regimen was based on gatifloxacin with kanamycin for four months. Later cohorts had either two months of kanamycin to reduce ototoxicity, or moxifloxacin or very high dose levofloxacin because of unavailability of gatifloxacin. Across the three settings, gatifloxacin was bacteriologicaly superior over the two other fluoroquinolones, allowing exceptional failures or relapses and not a single case of acquired resistance to the core drug, in contrast with particularly the moxifloxacin cohorts. Restricting the injectable to only two months yielded 87.5% relapse-free success of that gatifloxacin cohort, but failures and relapses reached 10%, with some acquisition of fluoroquinolone resistance. We conclude that for optimal results of STR, gatifloxacin and kanamycin should are needed until the newer drugs have proven to be equally efficacious. .

Programmatic performance of STR in African countries and perspectives on modification for improvement of effectiveness and safety

A Trébucq[1] [1]The Union, Paris, France. e-mail: atrebucq@theunion.org

We discuss here the epidemiological trends, multidrug resistant tuberculosis programme performance and clinical outcomes of short treatment regimen (STR) in nine African countries. We focus on effectiveness and safety under programmatic conditions. Considering programmatic effectiveness of STR, we analyse the theoretical efficacy of modified STR based on the clinical and bacteriological principles for building rational drug-resistant regimens. Finally, we discuss resources availability for implementing a modified STR in nine African countries.

National scaling up of nine-month MDR-TB regimen in the Philippines: the challenge of adverse reactions

M Santiago[1] [1]The Union, Taipei Medical UniversityTB Innovations and Health Systems Strengthening Project - Family Health International 360, Makati, Philippines. e-mail: msantiago@fhi360.org

The World Health Organization recommended the short treatment regimen (STR) in May 2016. Patients with resistance to rifampicin and isoniazid and without resistance to fluoroquinolones and second line injectables were eligible. These indications are important in the Asian setting where there is documented higher prevalence of fluroquinolone resistance. We describe here, how the STR was planned in Philippines, patient's enrolment bacteriological and clinical follow-up with especial focus on pharmacovigilance. We draw conclusions on possible modifications on STR due to challenges in monitoring hearing loss and adverse events remain as the reason for Los to Follow-up(LTFU).

Use of linezolid to replace kanamycin in short MDR-TB regimen in case of hearing loss: experience in Niger

A Piubello[1] [1]The International Union Against Tuberculosis and Lung Disease, Niamey, Niger. e-mail: apiubello@theunion.org

Niger is a country of West-Africa that is facing enormous challenges on multidrug resistant tuberculosis control. First, resources for controlling TB are very limited, health staff is scarce in number and access to care is limited by geographical challenges and security threats. Nevertheless, Niger has pioneered STR implementation and yield successful outcomes since more than 10 years. A key factor for success was the active TB drug-safety monitoring and management strategy (aDSM).
We illustrate here the enabler factors for implementing a successful modified STR where Second Line Injectables were replaced by Linezolid during the intensive phase to avoid serious hearing loss.

Capacity building for implementing a modified STR in Latin America

N Ortuno-Gutierrez[1] [1]Damien Foundation, Brussels, Belgium. e-mail: nimer.ortunogutierrez@damiaanactie.be

We describe here the approach of National Tuberculosis Programmes to implement short treatment regimen in Guatemala, Nicaragua and Bolivia. We describe the steps developed from planning to implementation, then as the World Health Organization new recommendations were publicly disseminated, we describe the approach to incorporate those according to the Latin American setting. We focus on capacity building strat-

egy that includes clinical management training and operational research workshop for preparing implementation of a modified short treatment regimen.

SP-29-C6 TB preventive therapy in pregnant women: is it safe and how should we implement it?

Treatment of LTBI among pregnant or post-partum women: uptake of WHO policy in 38 high-burden TB-HIV countries

T DeAtley[1] [1]Brown University, Providence, United States of America. e-mail: teresa_deatley@brown.edu

Tuberculosis disproportionately affects women of reproductive age with serious consequences for the mother and child. WHO recommends tuberculosis preventive treatment (TPT) to all people living with HIV, including pregnant/postpartum women. Uptake and coverage of this policy recommendation in reproductive health services is unclear. We conducted a review of latent tuberculosis infection (LTBI) policy and practice for pregnant/postpartum women residing in the 38 WHO high burden HIV/TB countries. Uptake of WHO policy to provide TPT among women accessing reproductive health services was moderate. 63% of countries provided at least one LTBI policy as recommended in the WHO's 2018 Consolidated Guidelines for Programmatic Management for LTBI. There were huge variations on the stage of pregnancy that TPT was recommended. Coverage remains unclear. Failure to provide TPT could be a missed opportunity for TB prevention strategies. Clearer understanding of coverage among pregnant/postpartum will inform WHO guidance on timing of provision of TPT.

IPT in pregnancy: leveraging population data to address clinical concerns

E Kalk[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: emma.kalk@uct.ac.za

Tuberculosis (TB) contributes significantly to morbidity and mortality in pregnant women and women of child bearing potential living with HIV. Isoniazid preventive therapy (IPT) provides protection against TB disease independent of treatment with antiretroviral therapy (ART), and at least 6 months of IPT is recommended for people living with HIV, including pregnant women. Concerns have been raised regarding the safety and efficacy of IPT during pregnancy. We have used population-wide individual-level routine electronic health data from the Western Cape, South Africa to analyze associations between IPT use during pregnancy and maternal incident TB disease, liver injury and mortality up to 12 months post-partum, and adverse pregnancy outcomes in a cohort comprising over 40 000 pregnant women on ART. Safety and efficacy results will be reported.

IPT scale-up and adverse pregnancy outcomes in programme settings in Kenya

E Onyango[1] [1]Ministry of Health, Kenya, Nairobi, Kenya. e-mail: eonyango@nltp.co.ke

Tuberculosis is a preventable cause of death among people living with HIV (PLHIV). Isoniazid preventive therapy (IPT) reduces the risk of TB and death among PLHIV. Kenya has been scaling-up IPT among all PLHIV regardless of age, sex and pregnancy. IPT and pregnancy outcomes remain unknown. We analysed Ministry of Health IPT data for 2014–2018. IPT and pregnancy outcomes were analyzed for women initiating IPT in pregnancy in 14 sites in Nairobi. Spontaneous abortion and miscarriage were considered pregnancy losses. Overall IPT uptake increased 70-fold from 9,501 in October 2014 to 667,722 in December 2017. Among 3009 pregnant women, 1028 were on IPT and (87.6%) completed treatment. Patients not on IPT were more likely to result in pregnancy loss (RR 1.13, 95% CI:1.09-1.17). IPT was scaled-up rapidly. Women on IPT did not have an increased risk of pregnancy loss.

Using a composite maternal-infant outcome measure to assess the timing of TPT in pregnant women

G Montepiedra[1] [1]Center for Biostatistics in AIDS Research and Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, United States of America. e-mail: gmontepie@sdac.harvard.edu

In P1078 (TB APPRISE), we evaluated maternal INH preventive therapy initiated during antepartum versus at week 12 postpartum with respect to maternal safety, infant safety, maternal TB and infant TB. These outcomes were analyzed separately, not necessarily providing a cohesive picture of the overall risk-benefit differences of the study arms. Using a novel approach, maternal and infant outcomes may be combined into one composite measure and then used to compare the two study arms in a superiority framework. We show how a composite measure was developed from a survey where stakeholders scored each of the possible maternal-infant events according their severity. For example, the worst score of 100 would be assigned to the event that both the mother and infant died during the study and a score of 0 if neither experienced any event. We analyze the P1078 data and compare study arms with respect to this measure.

Feasibility and acceptability of integrating TB-HIV services in reproductive, maternal, newborn and child health (RMNCH) settings: a mentor's perspective

P Dlamini[1] [1]ICAP Eswatini, Mbabane, Eswatini. e-mail: rs2462@cumc.columbia.edu

ICAP at Columbia University, in collaboration with the U.S. Centers for Disease Control and Prevention and the Ministry of Health in eSwatini, provided technical assistance to nurses and cough monitors at four health facilities in Manzini region, eSwatini, to enhance integration of tuberculosis (TB)/HIV and Reproductive, Maternal, Newborn and Child Health (RMNCH) services. Technical assistance focused on improving intensified case finding, contact tracing, isoniazid preventive therapy, and TB infection prevention and control measures, through training, mentorship and introduction of a longitudinal TB register, contact tracing tool and TB services capacity tool. Ms Dlamini is a nurse who provided training and mentorship to frontline staff that led the effort of TB integration in RMNCH services. Ms Dlamini will present best practices and challenges from implementation of the program in eSwatini.

SP-30-C12 Indian policies to stop industry interference, and their potential for sub-national levels globally

India: how essential are its policy guidelines to stop tobacco industry interference?

P Lal[1] [1]International Union Against Tuberculosis and Lung Disease, South-East Asia Office, New Delhi, India. e-mail: plal@theunion.org

This presentation will examine two policy aspects - first, the existing provisions in India's policy framework which support tobacco control, and second, additional policies that have been formulated to prevent tobacco industry interference in India. This presentation will also examine the current weakness, challenges and limitations in policy provisions and offer possible remedies from global good practices.

Tobacco industry interference: its implication throughout the UN system and the need to act at the sub-national level

D Dorado Torres[1] [1]Corporate Accountability International, Bogota, Colombia. e-mail: ddorado@corporateaccountability.org

The presentation would offer a clear picture of the current debate at the United Nations (UN) to replicate Art. 5.3 Framework Convention on Tobacco Control (FCTC) into the UN system. This presentation would ignite the discussion for national and sub-national governments to considering Art. 5.3 FCTC guidelines and Conference of the Parties (COP) decisions regarding to maximizing transparency and protection of public health policies with respect to tobacco control from commercial and other vested interests of the tobacco industry.

Industry interference: the case of Indonesia for sub-national guidelines on article 5.3

E Chairah[1] [1]Indonesian National Commission on Human Rights, Jakarta, Indonesia. e-mail: elfan.suri@gmail.com

The presentation would describe a general overview of industry interference in Southeast Asian. Particularly attention would be placed into the situation of Indonesia. Also, how the subnational policies from India can be assessed under the national context of Indonesia.Similarly, an overview of the potential next steps to stop industry interference from a human rights approach.

Industry interference and action: experience of the Philippines – how to stop commercial interest in tobacco control by using sub-national guidelines?

M Limpin[1] [1]University of Santo Tomas, Manila, Philippines. e-mail: ecblmd2015@gmail.com

The presentation will address the current situation of industry interference in the Philippines. Furthermore, it will contain the necessary steps to stop such interference. It will highlight practices of countering tobacco industry interference and cite instances that will show what works and what do not. Lastly, it will try to compare best practice in the Philippines to those being done in India with regard to Indian success of Art.5.3 guidelines.

Sub-national policies to stop tobacco industry interference in Bangladesh: their potential and limitations based on the Indian experience.

S Mahbubul[1] [1]The Bangladesh Anti Tobacco Alliance, Dhaka, Bangladesh. e-mail: smalam@theunion.org

The speaker would explain how the sub-national policies on Art 5.3 approved in Bangladesh could assist to stop tobacco industry interference in other countries.
Civil society organisations in Bangladesh are escalating their mission to prevent tobacco industry interference in public health policy. Despite making good progress in other areas of tobacco control, legal measures are not yet in place to stop tobacco lobbyists from influencing policymakers. Proponents of these preventative measures are making their case through research, advocacy and education nationwide.
Suspecting that low-levels of understanding were in part responsible for Article 5.3's low-priority status, Union grantees 'Working for a Better Bangladesh' [WBB], carried out a survey amongst members of tobacco control taskforces across 10 districts of the country. 59 percent of respondents displayed a lack of knowledge about the requirements of Article 5.3. Bangladesh's tobacco control taskforces are made up of local government representatives, medical professionals and magistrates, and are responsible for ensuring strong implementation of tobacco control laws.

SP-31-C7 Ending the socio-economic emergency for TB-affected households by improving social protection coverage

Social protection coverage among TB patients in HBCs: a multicountry analysis of national TB patient cost surveys

K Viney[1] [1]Australian National University, Canberra, Australia. e-mail: kerri.viney@hotmail.com

National TB patient cost surveys have been conducted in many countries to determine the proportion of TB patients who experience catastrophic costs and assess availability to socioeconomic support. In these surveys, a nationally representative sample of TB patients are asked questions about their income, the costs of TB care, and access to social protection schemes and other forms of financial support. This presentation presents a pooled and comparative analysis of social protection access and coverage based on a multi-country survey data set. The presentation also discusses the implications of the results for future policy and outlines possible intervention options to boost access to and coverage of social protection schemes for TB affected households.

Income security in times of sickness or disability in low- and middle-income countries: a review of policies, coverage and effects

K Lönnroth[1] [1]Karolinska Institutet, Stockholm, Sweden. e-mail: knut.lonnroth@ki.se

Income security in times of sickness or disability is essential in order to enable access to health care services, as well as to mitigate poverty effects related to reduced ability to work and limited access to the labor market. Income loss is a major component of the economic burden for TB patients while few patients are covered by income security mechanisms such as disability grants or sickness insurance. In order to understand the broader policy context of the lack of such mechanisms for TB patients, this review mapped the spectrum of existing general policies for income security in times or sickness or disability in low- and middle-income countries and analysed their coverage and effects. Few countries have universal schemes and the most vulnerable part of the population is usually not covered. Entitlements are often modest and access restricted by strict eligibility criteria that are difficult to fulfill.

Developing a locally appropriate socio-economic support package for TB-affected households in Nepal

T Wingfield[1] [1]University of Liverpool, Liverpool, United Kingdom. e-mail: t.e.wingfield@liverpool.ac.uk

WHO's 2015 End TB Strategy advocates social and economic (socioeconomic) support for TB-affected households to improve TB control. However, evidence concerning the most appropriate and impactful socioeconomic support for TB-affected households remains limited, especially in low-income countries. This presentation will describe results from two complementary projects from a mixed-methods study in four regions of Nepal. Project 1 is a case-control study with 400 participants evaluating the social determinants and consequences of TB for TB-affected households; and Project 2 is working in collaboration with 50 key, in-country stakeholders to create a shortlist of feasible and locally-appropriate interventions to mitigate this impact. This study will inform the design of "BEYOND TB", a planned program of mixed-methods research including pragmatic randomized-controlled trials of socioeconomic support packages for TB-affected households in multiple countries with a high TB burden.

Evaluating the impact of Cash Plus transfers on TB Care: The ExaCT TB Study

P Shete[1] [1]University of California San Francisco, San Francisco, United States of America. e-mail: priya.shete@ucsf.edu

Evaluating the Impact of Cash Transfers Plus on Tuberculosis (TB) Care (The ExaCT TB Study) is a multicenter trial that aims to evaluate the effectiveness of a multi-faceted social protection intervention incorporating cash transfers plus social support on improving TB diagnostic evaluation outcomes among patients using a quasi-experimental approach. Formative research and stakeholder engagement using methods in implementation science, economics and social epidemiology led to the development of the multi-modal intervention. The intervention evaluation will include assessment of : 1) feasibility of implementing a social protection implementation through public health systems; 2) effectiveness of social protections in improving health and socioeconomic outcomes; and 3) modifying targeted patient-centered barriers to TB care as a way to inform operationalizing of context-specific social protections as a tool for enhanced TB prevention and care.

Coordinating health and social care for TB patients in Mozambique: the CHEST study

S Atkins[1] [1]Tampere University, Tampere, Fiji. e-mail: salla.atkins@tuni.fi

The connection between poverty and ill health is long recognized. Tuberculosis is one of the key diseases related to poverty, treatable with simple and effective treatment. Most people with TB are poor, and TB, with the associated stigma,possible loss of work, and indirect costs of treatment can result in deepening poverty. The Coordinating Health and Social care for tuberculosis patients in Mozambique aims to connect patients with tuberculosis with social protection, and clients of social services with tuberculosis diagnosis and care. The project involves a situation analysis of Mozambican social support available for patients with tuberculosis; the co-development of an intervention with decisionmakers and policy actors, and the eventual mixed method evaluation of the intervention. It is hoped that the project will inform multisectoral action on TB in Mozambique, but also other low-and middle-income countries.

SP-32-F4 Accelerating control of zTB in low- and middle-income countries

Bovine TB in low- and middle-income countries (LMIC): accelerating control

J Wood[1] [1]University of Cambridge, Cambridge, United Kingdom. e-mail: jlnw2@cam.ac.uk

The talk will review the evidence of the significance of cattle infection with *Mycobacterium bovis* and other pathogenic mycobacteria in different regions, also assessing the variable significance of zoonotic transmission. The success of different control measures will be considered against the range of different tools available and how they have been implemented, also touching on the importance of both political leadership and farmer involvement. Opportunities for accelerated control using vaccination to reduce transmission below critical thresholds, combined with new suites of tests that can differentiate infection and vaccination that may become available will be highlighted, with an emphasis on moving away from centrally-driven, socially and economically unacceptable test and slaughter programs.

The quest for controlling bovine TB at the wildlife/livestock/human interface

A Michel[1] [1]University of Pretoria, Onderstepoort, South Africa. e-mail: anita.michel@up.ac.za

Bovine tuberculosis caused by Mycobacterium bovis (M. bovis) remains an impediment to livestock production in a number of countries around the world. However, low and middle income countries with a lack of adequate resources for disease control and the presence of a wildlife reservoir are facing multifaceted challenges that limit opportunities for effective livestock and zoonotic disease control. In South Africa, M. bovis is maintained by domestic cattle in the commercial and subsistence farming sectors as well as by African buffalo from which it has spread to at least 20 other wildlife species some of which are endangered. This presentation will highlight the need for different research approaches including the development and evaluation of diagnostic tests, establishing the role of M. bovis in wildlife populations, in humans and the mechanisms and risks of transmission between them, as well as critically evaluating the future of practical and affordable control strategies.

New approaches for diagnosis and control of bovine TB in India

V Maroudam[1] [1]CisGEN / Penn State, Chennai, India.
e-mail: vmaroudam@gmail.com

Bovine tuberculosis (bTB) is a major zoonotic disease of cattle that is endemic in most of the developing world, limiting livestock productivity and representing a global public health threat. India has the largest population of livestock and highest milk production in the world. bTB is endemic in India with more than 12 million skin-test positive adult milch animals. Control of bTB in India is complicated due to the fact that "Test-and-slaughter'' is not feasible for socioeconomic reasons, thereby favouring the persistence and transmission of the disease. This presentation will outline the potential for use of BCG vaccination of cattle to reduce infection and onward transmission, applied together with fit-for-purpose defined skin test reagents that can differentiate infected from vaccinated animals for bTB control in India and similar geographies. Together, these and similar approaches are needed to help bring bTB diagnosis and control from 19th century roots into the 21st century.

SP-33-B6 The importance of tackling comorbidities to reach the End TB goals

My life preceding TB diagnosis and risk factors

G Acharya[1] [1]Touched by TB, Mumbai, India.
e-mail: thanesahara@gmail.com

When people present with TB, it is often not their only health issue. Accessing TB treatment as well as accessing other health care services can present multiple challenges for people with TB. People with TB who have other co-morbidities often feel isolated and have to spend time and money on their other co-morbidities that can affect the outcome of their TB treatment. Ganesh will outline his journey with TB and some of the co-morbidities that he experienced. He will give a TB survivors perspective on the importance of co-morbidity policies and discuss the importance of quality TB care to ensure that co morbidities are addressed throughout a person's journey with TB.

Experience of addressing nutritional support and screening within TB services in India

K Sachdeva[1] [1], Delhi, India. e-mail: ddgtb@rntcp.org

Government of India has introduced Cash Transfer scheme under the National TB Programme for nutrition support to TB patients. INR ₹500 is given for each month to every TB patient till completion of treatment. The financial support is provided digitally, direct to the bank account of TB patients. The scheme has been initiated since April 2019. An integration has been established between on line system of TB programme – NIKSHAY and public finance management system of the department of financial services to put in place direct benefit transfer scheme across 36 state/UTs and 750 districts. The benefits are provided for all TB patients irrespective of providers they seek care to, duration of treatment, drug resistant pattern. Since its inception, the scheme has covered 1.68 million TB patients with at least one benefit. Through 2.3 million electronic transactions, ₹2.7 billion INR (39 million USD) has been paid to TB patients.

Experience of incorporating tobacco cessation services into routine TB care in China

Y Lin[1] [1]The International Union Against TB and Lung Disease, Beijing, China. e-mail: ylin@theunion.org

Recommended in the Union guideline on smoking cessation intervention for TB patients, TB doctors in China were trained to ask/record patient's smoking status and offer brief advice to quit. This initiative was integrated into TB service in routine program setting and achieved 66.7% abstinence rate at the end of 6-month treatment. The patients were traced back after 5-years to re-assess their smoking status. This presentation will describe how this intervention was integrated into TB care and the long-term outcomes of the intervention, particularly in those who are at risk of smoking relapse and need continuing cessation support.

Bi-directional screening for TB and diabetes by the diabetes and TB services in Zimbabwe

T Mapuranga[1] [1]Zimbabwe National TB control programme, Harare, Zimbabwe.
e-mail: drplanks@gmail.com

Africa is estimated to have almost 42 million people with diabetes by 2035. In 2017, the prevalence of DM among adults in Zimbabwe was reported to be 1.3%, translating to 99,400 living with DM, with 76.3% estimated to be undiagnosed. An operational research project of bi-directional screening of notified TB patients for DM and DM patients for TB at the selected facilities was conducted. The screening process sought to assess the burden of DM among TB patients and vice versa as well as feasibility of screening the sane during routine care. The pilot assessment was measured by 1) the yield of DM among TB patients screened, 2) the yield of TB among DM patients screened 3) the number of patients screened and 4) trend of screening over time. The findings from this project will be presented and how this can inform possible scale up of this in Zimbabwe.

SP-34-E3 Coercion in TB: human rights and ethical concerns for the use of coercion in the TB response

Towards a taxonomy of coercion in the context of tuberculosis

L Ruhl[1] [1]Simon Fraser University, Burnaby, Canada.
e-mail: leo_ruhl@sfu.ca

This presentation gives a brief overview of the different kinds of coercion commonly used in TB response. A taxonomy of coercion is presented and developed using examples of coercion, including information on who or what uses coercion, which kinds of persons or groups are subject to coercion, and toward what ends. Several cases of coercion are discussed, including new forms of technological DOTS and treatment adherence surveillance systems, incentives used to increase medication adherence, and the detention of persons with TB in prison.

SP-35-C11 Action on the ground: using the ECHO virtual community of practice model to promote health equity by building local health workforce capacity

Nationwide expansion of the Delhi MDR-TB ECHO programme to support TB elimination & capacity building of HIV clinicians to treat TB with ECHO support

R Sarin[1] [1]National Institute for Tuberculosis and Respiratory Disease, New Delhi, India.
e-mail: r.sarin@nitrd.nic.in

The National Institute of Tuberculosis and Respiratory Diseases (NITRD) started the MDR-TB ECHO Program in November 2016. The goal of the TB ECHO program is to develop the capacity of district TB medical officers by discussing the complex issues of MDRTB, sharing best practices and treatment or solutions. As a result of NITRD's successful program, five other Indian states have initiated their own MDRTB ECHO programs. NITRD also launched a successful TB-HIV co-infection ECHO program in partnership with NACO. This program connects ART centers with experts and other stakeholders to discuss best practices and review cases regarding TB-HIV diagnosis, testing and treatment. The Government of India has recognized the value of the ECHO model for accelerating it's goal of TB elimination by 2025 and formally incorporated it into the National Guidelines for Programmatic Management of MDR TB setting it up for country-wide expansion.

Strengthening nurse case management of TB and TB infection in NM

D Fortune[1] [1]New Mexico Department of Health, Santa Fe, United States of America.
e-mail: diana.fortune@state.nm.us

The New Mexico (NM) Department of Health (DOH) launched the TB ECHO program in 2015 to ensure effective nurse case management of persons diagnosed with active TB. With less than 40 cases per year, the ECHO model continues to ensure quality nursing case management in the realm of decreased nursing and financial resources. In order to eliminate TB, it is essential to treat persons prior to developing active TB to break the chain of infection. Beginning June 2018, the 4th TB ECHO clinic was launched. This program is designed to meet the needs and develop expertise with community providers to diagnose and treat TB infection. During each TB Infection ECHO session, an expert presents a 15-minute didactic on relevant clinical topics and community providers present their cases of persons with TB infection. CMEs are awarded after completion of the evaluation of each session.

Ensuring quality TB and specialty care for underserved patients

M Buziashvili[1] [1]National Center for Tuberculosis and Lung Diseases, Tbilissi, Georgia.
e-mail: mari.buziashvili@yahoo.com

Despite universal access to tuberculosis (TB) diagnosis and treatment in Georgia, TB patients with co-morbidities from rural and underserved areas of Georgia still lack the access to multi-disciplinary specialty care and rural area doctors also lack the access to latest updates and innovations to TB diagnosis, patient care and treatment. To overcome the challenges of delayed treatment initiation and minimize time and costs of patient travels to central facilities, project TB-ECHO was implemented in late 2017 and was fully functional since early 2018. Throughout the year, numerous patients from rural areas of Georgia have accessed the quality TB and specialty care on time from the multi-disciplinary hub team at the central facility. The actual impact of the project implementation is yet to be measured by a long-term outcome, however a significantly decreased number of lost to follow-up cases, increased treatment success and enhanced capacity of human resources are anticipated countrywide.

SP-36-E1 Implementing national level accountability for the UN HLM on TB: key recommendations and opportunities

Role of civil society in driving national- and regional-level accountability in the Asia Pacific region

R Marte[1] [1]APCASO, Bangkok, Thailand.
e-mail: rdmarte@apcaso.org

RD will speak on the role of civil society organisations and networks in fostering and implementing accountability at the national and regional levels for delivering on the UN HLM on TB political declaration. RD will also speak about the amendments being made to the TB Law in Philippines that was passed in 2016, including forming a cross-government department accountability body, and the role civil society has played within this.

Supporting strengthening of accountability using the WHO multisectoral accountability framework

D Weil[1] [1]World Health Organization, Geneva, Switzerland.
e-mail: weild@who.int

The presentation will introduce the WHO Multisectoral Accountability Framework to accelerate progress to end TB with its four components; commitments, actions, monitoring and reporting, and review, at national, regional and global levels. The framework was requested by the World Health Assembly and the UN General Assembly. The speaker will also introduce tools and documentation of good practice that can help national governments and partners in formalising and strengthening their national frameworks for accountability to increase effective multistakeholder and multisectoral action to reach the SDG, End TB and UN TB high-level meeting targets.

National HLM on TB in Brazil and the role of national parliamentary TB caucuses

T Nair[1] [1]New Delhi, India.
e-mail: tushar.nair@globaltbcaucus.org

The Global TB Caucus in a network of over 2,500 parliamentarians from more than 150 countries, united by their shared commitment to end tuberculosis, including four regional networks; Africa, Americas, Asia Pacific and Europe. Since the UN High-Level Meeting on TB, parliamentarians have played an important role in driving accountability at the national, regional and global levels for the commitments made; from the commitment to mobilise a National High-Level Meeting on TB and launch an inter-ministerial committee in Brazil to convening a side event on TB on the sidelines of the Asia Pacific Parliamentary Forum on Global Health (APPFGH). This presentation will focus on the work of the Caucus in the Asia Pacific region, including engagement with APEC, ASEAN, APPFGH and G20.

Civil society and parliamentary collaboration on TB accountability in Ukraine

Y Chorna[1] [1]Kiev, Ukraine. e-mail: chorna@tbcoalition.eu

In order to implement the commitments of the political declaration adopted at the UN HLM on TB in September 2018, accountability processes at the national level are a key. Civil society is an important player in holding governments to account and should therefore be involved in all related process; from preparation for the UN HLM on TB to agreeing on the new national targets informed by the political declaration. The potential role of civil society in accountability processes, including in partnership with parliamentarians, in Ukraine will be presented, including examples of successes and lessons learnt throughout UN HLM on TB process.

Development of a national strategic plan for TB in Kenya and the Nairobi Strategy on TB and Human Rights

R Mwaniki[1] [1]KANCO, Nairobi, Kenya.
e-mail: bmwaniki@kanco.org

Since the UN HLM on TB, Kenya has finalised a new National Strategic Plan on TB. Rahab will talk about the 2-year development process, including the influence of the UN HLM on TB and the results from the National Patient Cost Survey, and Legal, Gender and Key Population Assessments, as well as the involvement of civil society in the process. The new plan has a specific focus on reaching the "missing" people with TB and the role of communities in this, and the attention paid to adequate resourcing. Rahab will also speak about the development of the Nairobi Strategy on Tuberculosis and Human Rights, led by Kenya Legal and Ethical Issues Network on HIV and AIDS (KELIN).

SP-37-C4 Ending paediatric TB through action: operationalising shorter TPT regimens in children

A systematic approach for developing attributes for a discrete choice experiment on preferences for TPT in children in Eswatini

Y Hirsch-Moverman[1] [1]Columbia University Medical Center, New York, United States of America.
e-mail: yh154@cumc.columbia.edu

The PROTECT Study uses a discrete choice experiment (DCE) to examine preferences regarding TB preventive treatment (TPT) regimens for children in Eswatini among children, their caregivers and healthcare providers. DCEs require an important developmental phase, often using qualitative methods, to inform selection of attributes for inclusion in the design, but there is limited guidance about this process in the literature. We developed an initial list of 13 attributes and conducted in-depth interviews with 80 stakeholders, including children, caregivers, and healthcare providers, to refine these attributes and understand how they may influence TPT decision-making and service delivery. Seven attributes were found to be important across stakeholder groups: clinic visit cost, wait time, pill formulation/size, pill taste, dosing frequency, treatment duration and visit frequency, and clinic hours. These attributes were incorporated into the DCE to assess TPT preferences. In this presentation, we will detail our process in developing the DCE attributes.

Implementing three months of a daily preventive treatment (3HR) regimen in three high TB-incidence countries in Africa: lessons from the Titi study

V Schwoebel[1] [1]The Union, Paris, France.
e-mail: vschwoebel@theunion.org

The Titi study was conducted from 2015 to 2018 in Benin, Burkina Faso, Cameroon and Central African Republic to demonstrate the feasibility of implementing contact investigation among children under routine programmatic conditions in urban settings. The shorter WHO-recommended preventive treatment (PT) regimen of 3 months of rifampicin and isoniazid (3RH) was used in 3 of these countries taking advantage of the new pediatric formulations with correct drug dosage. Close to 1,500 children were enrolled in these 3 countries. They were evaluated during home and clinic visits and received PT if found to be free of active TB. Children were followed-up monthly during therapy and three-monthly thereafter for 12 months. Results indicate that the regimen was effective and well tolerated. We will report on implementation challenges concerning initial clinical and paraclinical evaluation, children follow-up, staff involvement, family support, and management of special cases, e.g. contacts of MDR-TB and HIV-positive patients.

Operational challenges with the implementation of a 12-dose weekly preventive treatment (3HP) regimen from Pakistan and Bangladesh

H Hussain[1] [1]IRD Global, Singapore, Singapore.
e-mail: hamidah.hussain@ird.global

Pakistan and Bangladesh are high TB-burden countries with an annual incidence of 267 and 221 per 100,000 population, respectively. Screening household contacts and initiating children < 5 years on TB preventive treatment is the national policy but with scarcity of resources is implemented sporadically. We initiated a donor-funded project to screen household contacts of TB patients in Pakistan and Bangladesh and start all eligible contacts on 12-dose weekly preventive treatment (3HP). Here we illustrate our experience of contact screening and treatment initiation using cascade of care analysis, and operational challenges of implementing TB preventive services under programmatic conditions. Need for investigations especially a chest x-ray to rule out TB disease is a bottle neck in starting symptom free contacts on TB preventive treatment. We also provide a comparison of screening and treatment completion in populations offered 3HP vs. 6-months' isoniazid preventive treatment (6H).

Early experiences with preventive treatment for child contacts in an MDR-TB high-burden community in Papua New Guinea

S Majumdar[1] [1]Burnet Institute, Melbourne, Australia.
e-mail: suman.majumdar@burnet.edu.au

A high burden of TB (2021/100,000 population) is reported from Daru Island, Western province of Papua New Guinea, with ~19% of cases having multidrug resistant (MDR)-TB. Household contact screening for drug-susceptible and drug-resistant TB in all ages was introduced in mid-2016, and >2,500 contacts were screened by end of 2018. Isoniazid preventive treatment (6H) was offered to all eligible, < 5 years child contacts of drug-susceptible TB cases, along with the establishment of a community-based clinic for follow-up and family-based peer counselling services. In January 2019, preventive treatment for eligible child contacts of drug-susceptible TB cases was changed from 6H to 3-months' isoniazid and rifampin (3HR), and 6-months' levofloxacin was introduced for < 5 years child contacts of MDR-TB cases with evidence of infection (TST-positive). An update will be provided including cascade of care and challenges for implementation, such as evaluation for active TB in contacts screened as symptomatic.

Indonesian experience with four months of rifampin (4R) and nine months of isoniazid (9H) for TPT in child contacts

L Apriani[1] [1]TB-HIV Research Centre Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia.
e-mail: likaaji@gmail.com

Indonesia has the third highest number of incident TB cases in the world, with an incidence rate of approximately 320/100,000 population in a country of around 264 million people. There are Indonesian national guidelines on TB preventive treatment in child contacts aged less than 5 years, but these guidelines are rarely followed. As part of a large trial that included children (0 to 17 years of age), we screened 557 children and randomly assigned 157 children to receive either 4R or 9H.
All children were followed for 28 months after randomization. In this presentation, we will report the acceptance, characteristics, tolerability and adherence in the two study arms. We found that both regimens were safe while the treatment completion rate was higher in 4R. Active TB was found in one child who received 9H. Implementation challenges with the 4R regimen will be discussed.

SP-38-C8 MATCH: access analysis and diagnostic network optimisation

Spatial analysis of TB services to improve population coverage in Pakistan

A Latif[1] [1]Ministry of National Health Services Regulation & Coordination, Islamabad, Pakistan.
e-mail: abdullah.latif@gmail.com

Pakistan's NTP aims over the coming years to geo-locate all public, private and informal health facilities, laboratories or commercial vendors providing TB diagnostic and/or treatment services. To pilot this initiative the NTP and KIT developed an ODK-based survey to collect GPS coordinates, data on basic service provision and staff capacity from all public and engaged private TB providers in Islamabad Capital Territory and Khairpur. Survey data were used to assess population coverage of TB services, and to reallocate diagnostic equipment to reduce distance between population centers and TB facilities. The NTP will share challenges and lessons learned during the pilot, and further considerations to scale the survey to the national level.

Applying the MATCH framework to improve diagnostic networks in the DRC and Tanzania

E Nkiligi[1] [1]National Tuberculosis and Leprosy Program, Dodoma, Tanzania, United Rep.
e-mail: enkiligi2015@gmail.com

To improve access to TB care, it is critical to rationally use subnational data for strategic placement of scarce diagnostic resources. With different amounts of subnational data available, the NTPs of DRC and Tanzania have conducted Global Fund supported MATCH access analyses with KIT to improve access to advanced diagnostics. In the DRC, optimum diagnostic placement required strategic thinking from multiple angles: dealing with insecure areas, providing services in hard-to-reach areas, and planning service delivery in regions where key data are missing. Results will be shared on how the MATCH approach and a tailor-made diagnostic network algorithm were utilized to improve access to diagnostics. In Tanzania, the PPA highlighted misalignments between population demand and service delivery, while MATCH access analyses indicated that placement of diagnostics in specific health facilities could potentially yield many missed TB cases. The presentation addresses how these complementary analyses enabled the NTP to improve diagnostic placement.

Innovating access to rapid molecular testing in Andhra Pradesh

S Achanta[1] [1]RNTCP, Vishakhapatnam Area, India.
e-mail: achantas@rntcp.org

With the recent introduction of Molbio Truenat technology in India, rapid diagnosis of TB through real-time PCR is increasingly accessible in primary health settings. This has been approved by the Indian authorities for use in India, and is currently being evaluated for WHO approval. Results are available in under one hour on a battery-operated machine with built-in SIM card, enabling testing and results data to be automatically shared for real-time monitoring. The Andhra Pradesh experience will be shared, in which the NTP guarantees the supplier consumption of a minimum number of tests (e.g. per month), while the supplier maintains the equipment. This presentation will also address how real-time Molbio Truenat testing workload and results data can be used to modify machine placement and possible re-allocation, with the objective of maximizing diagnostic access to catchment communities and achieving the largest yields possible in case notifications.

SP-40-C7 Addressing mental health and substance use disorders in TB: a must for people-centred TB care

Mental health, substance use disorders and TB: overview of the joint burden

K Viney[1] [1]Australian National University, Canberra, Australia. e-mail: kerri.viney@hotmail.com

Mental health and substance use disorders are frequently reported by TB patients and act as both a social determinant and a social consequence of TB. Integrated care for all conditions presents an opportunity to improve outcomes for patients, yet they are infrequently reported. This presentation will describe the burden and associations between mental health and substance use disorders and TB, building upon work published in a recent systematic review co-authored by Dr Viney, which describes the prevalence of mental health conditions such as anxiety, depression and psychosis among TB patients. The presentation will conclude by highlighting the potential benefits of integrated care for these conditions.

Practical approaches to addressing mental health needs and harmful substance use among socially vulnerable populations: lessons from London

A Story[1] [1]University College London Hospitals NHS Trust, London, United Kingdom. e-mail: al.story@nhs.net

Find&Treat have pioneered an integrated early case detection and treatment model for homeless people, drug and alcohol users and socially vulnerable populations in London. The populations served are characterised by complex co-morbidities, including a high prevalence of harmful substance use and mental health problems. This presentation will provide an overview of the screening and onward care model using examples to illustrate how the teams approach has been tailored to improve engagement and treatment outcomes. Practical examples will cover assessing capacity, the essential role of peer workers with lived experience of homelessness and addiction, psychologically informed and trauma aware approaches including mental health first aid (MHFA), and the importance of direct and ongoing liaison with allied specialist mental health and substance misuse services.

Integrating TB services as part of a comprehensive package of harm reduction for people who use drugs: experience from South Africa

H Hausler[1] [1]TBHIV Care, Cape Town, South Africa. e-mail: hhausler@tbhivcare.org

This presentation will give an overview of TB HIV Care's experience in delivering peer led outreach services for people who use drugs that include a comprehensive package of harm reduction and TB and HIV screening and linkage to care, as well as substance use screening and behavioural interventions for hospitalized TB patients.

SP-41-B1 Saving lives: Improving access to TB LAM testing

Updated WHO guidelines for the use of LAM assays

C Gilpin[1]

TB is the leading infectious disease killer of PLHIV, accounting for roughly one third of AIDS related deaths. In 2015, WHO issued guidelines for the use of a urine lipoarabinomannan (LF-LAM) test to assist in diagnosis of TB in people living with HIV. Despite evidence that the LF-LAM test has been shown to reduce mortality in the sickest patients, uptake and implementation of this test has been poor. WHO has now evaluated updated evidence for the use of the Alere LF-LAM Ag test and for a new test developed jointly with FIND and Fujifilm which has the potential to dramatically change the way TB is diagnosed in people with advanced HIV disease. Updated guidelines for the use of LAM assays will be presented during this symposium.

Country adoption and uptake of urine LAM test: current landscape and barriers

M Pai[1] [1]McGill International TB Centre, Montreal, Canada. e-mail: madhukar.pai@mcgill.ca

We conducted a questionnaire study in 31 high TB and HIV/AIDS burden countries to assess the current landscape, and to determine the barriers to LF-LAM uptake. Based on initial results from 23 countries, 10 (43%) have adopted LF-LAM policies within their National TB or HIV programs. Specifically, 6 countries have LF-LAM policies in both NTPs and NAPs, 3 countries have policies in only NTPs and 1 country reported to have LF-LAM policies in their NAP only. Interestingly, only 4 countries who stated they have an LF-LAM policy in a national program are actually using the test. Budget limitation was a barrier to LAM adoption, followed by

a lack of pilot studies and a low priority due to the relatively small size of the affected population. Regulatory challenges, lack of buy-in and the absence of LF-LAM's in the national TB or HIV programs' mandate were also cited as hurdles.

Médecins Sans Frontières: experience implementing and using TB LAM

H Huerga[1] [1]Epicentre - MSF Paris, Paris, France.
e-mail: helena.huerga@epicentre.msf.org

Médecins Sans Frontières (MSF) provides HIV and TB care in multiple countries around the world. To date MSF is using LAM to diagnose TB at 35 sites in 14 countries. MSF will present their findings on the use of LAM in different settings and patient populations: ambulatory, hospitalized, with and without symptoms, according to or regardless of CD4. LAM positivity rates in the MSF supported programs varied across settings and with different use. Here we share the MSF experience on the operational aspects of implementing LAM such as patients' provision of sputum/urine samples, LAM users' acceptability, organisation of workload and workspace, use of the reference card for reading the LAM result, and LAM inter-reader agreement.

Evaluation of TB LAM implementation in Uganda

S Turyanabwe[1] [1]Ministry Of Health, Kampala, Uganda.
e-mail: turyahabwestavia@gmail.com

As part of its strategic plan, Uganda piloted the implementation of TB LF-LAM for diagnosis of TB in people with advanced HIV disease at selected regional referral hospitals. In preparation for countrywide roll out, the TB/HIV programs decided to evaluate the use and implementation of this test in October 2018 in order to guide national roll-out. Here we outline our overall findings that led to the development of a national strategy to improve uptake and use of TB LAM in Uganda.

Supporting countries in lateral flow LAM (LF-LAM) rollout: insights from the GLI Practical Guide

M Casenghi[1] [1]EGPAF, Geneva, Switzerland.
e-mail: martina.casenghi@gmail.com

GLI has worked on a Practical Guide on the use of the LF-LAM. The objective of the Guide is to provide national TB Program (NTP) representatives, national HIV programs, Laboratory staff and implementers, with an overview of the necessary steps required for in country introduction of the test. The document also includes practical considerations and lessons learnt from early implementers on critical areas including but not limited to the choice of settings for intended use, target populations, placement in TB diagnostic algorithms, laboratory procedures, training requirements, forecasting and procurement. This with the aim to equip national programs and national laboratory networks with information and material that can support successful roll-out of the LF-LAM test.

SP-42-D1 Food for thought: impact of malnutrition on the TB epidemic

Undernourished patients, undernourished populations, and the End TB Strategy

A Bhargava[1] [1]Center for Nutrition Studies at Yenepoya (Deemed to be University), Mangalore, India.
e-mail: anuragb17@gmail.com

With the advent of successful chemotherapy, the role of nutrition in TB treatment and prevention became marginalized. This presentation will discuss how undernutrition is the commonest comorbidity in TB patients and a correctable risk factor for adverse outcomes and how undernutrition remains a major driver of the TB epidemic in high TB burden countries, especially India. The presentation will discuss the evidence base for nutritional support for TB patients, how the TB incidence attributable to undernutrition may be underestimated, and how undernutrition in patients and populations should be a priority issue across all three pillars of the END TB strategy.

Impact of malnutrition on host-immune protective mechanisms against TB: what we know and what we don't know

P Salgame[1] [1]Rutgers University, Newark, United States of America. e-mail: salgampa@njms.rutgers.edu

Malnutrition is a serious global health problem that is associated with the increased risk and severity of infectious diseases, including Tuberculosis (TB). This presentation will review the literature related to the impact of malnutrition on the host's protective innate and adaptive immunity in resisting infection and progression to TB disease. The presentation will also encapsulate studies in both human cohorts and experimental animal models that provide a mechanistic understanding of the relationship between malnutrition and host immunity. The talk will also discuss recent studies on malnutrition and dysbiosis of the intestinal microbiome and how this might impinge on anti-mycobacterial immunity. It will conclude with deliberations on how to design targeted interventions in malnourished children and adults to improve host immune resistance against TB.

Impact of malnutrition on antimycobacterial pharmacokinetics/pharmacodynamics

S Heysell[1] [1]University of Virginia, Charlottesville, United States of America. e-mail: scott.heysell@gmail.com

One understudied pathway through which malnutrition affects TB treatment outcomes is by affecting the pharmacokinetics (PK) of antimycobacterial drugs. A multicountry prospective cohort was studied to determine the pharmacokinetic/pharmacodynamic targets associated with treatment outcomes in diverse populations from Tanzania and Uganda, and urban Siberia and Bangladesh. Individual PK variability was common and drug exposure was significantly below expected ranges for the majority of drugs assayed. In total, 450 people were enrolled including 340 with MDR-TB, 59 with pediatric TB and 51 with sepsis. The association of malnutrition and PK variability depended on the drug and the population. A cohort of Tanzanian children was also studied. In this cohort, severe malnutrition and stunting were common, the presence of more than one stunting pathogen was the norm, and weight gain during TB treatment worsened drug exposure. These trends and implications for further interventional study will be discussed in detail.

Dietary intake and nutritional status of TB patients in Puducherry, South India

S Sarkar[1] [1]Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India. e-mail: drsonali.jipmer@gmail.com

There is near-universal agreement that the nutritional status of TB patients needs to be improved. In India, the national TB program has started the Direct Benefit Transfer of Rs. 500 per month aiming at improving the diet of TB patients through financial support. However, what is not known is the type and extent of deficiency of specific nutrients in the diet of the TB patients in India. A planned dietary supplementation that accounts for the level of deficiency of specific nutrients in their natural diets may be of greater benefit to the TB patients. This talk will describe a study of nutritional supplementation in Puducherry, India that highlights the need for better understanding the relationship between nutritional status and TB disease and identifies crucial knowledge gaps that must be addressed before dietary supplementation can be implemented as large-scale programmatic approach.

The impact of social protection on malnutrition: epidemiologic and programmatic implications for TB elimination efforts

D Boccia[1] [1]London, United Kingdom. e-mail: delia.boccia@lshtm.ac.uk

This talk aims to present an overview of the impact of social protection interventions on indicators of child and adult malnutrition in light of TB care and control. To this end, we will discuss the potential of these programs to affect TB trends in countries where they are implemented by making vulnerable populations more resilient to TB and more likely to complete the cascade of TB care. The talk will conclude by discussing the impact of a closer integration of TB care and social protection services providing nutrition and food security support.

SP-43-A3 New and repurposed drug resistance emergence: current status and prevention strategies

Emerging resistance: the South African perspective

N Ismael[1] [1]National Institute for Communicable Diseases, Johannesbourg, South Africa. e-mail: naziri@nicd.ac.za

Use of new and re-purposed drugs has made a huge impact on drug-resistant TB outcomes. South Africa is an early adopter of regimens with these drugs however emergence of resistance is a concern. A drug resistance surveillance program was instituted for patients receiving BDQ as part of their treatment regimen and sputum samples collected at baseline, month 2 and month 6 to monitor treatment emergent resistance. Additionally patients not responding to BDQ based regimens had a full drug susceptibility profile determined for all drugs including the new and re-purposed . Testing was performed at the WHO Supranational TB Reference in Johannesburg. A national summary of the emergence of laboratory confirmed resistance including BDQ, estimated prevalence of resistance and genetic correlates of resistance will be presented. Postulated drivers of resistance and prevention strategies will also be discussed.

The global surveillance of resistance to existing, repurposed and new anti-TB drugs and the role of sequencing

A Dean[1] [1]WHO, Geneva, Switzerland.
e-mail: deanan@who.int

The Global Project on Anti-TB Drug Resistance Surveillance, hosted by WHO since 1994, is the oldest and largest initiative on the surveillance of antimicrobial resistance in the world. Data are available from more than 97% of the world's population and TB cases from either continuous routine surveillance systems or periodic surveys. Sequencing is a valuable tool for the surveillance of drug resistance, including whole genome sequencing of culture isolates or targeted next generation sequencing of preserved sputum. It has the capacity to greatly improve our understanding of resistance patterns to a wide range of existing, repurposed and new drugs from high TB burden settings.

Building a TB and DR-TB regimen

J Caminero[1] [1]The Union, Las Palmas, Spain.
e-mail: jcamlun@gobiernodecanarias.org

Antibiotic stewardship" - most basic rules to follow to build a TB regimen (number of drugs, quality of the drugs, duration of the treatment, etc) to avoid mistakes and possible amplification of the pattern of resistance. The presentation justify that just with 2-3 good drugs is enough to cure a TB avoiding the selection of anti--TB resistance. And, if the drug combination includes 2-3 sterilizing drugs is enough just with 6-9 months of therapy. And, these fundaments are the same for the susceptible and for the drig resistant TB, even the MDR-TB, especially i we can use the new and repurposed anti-TB drugs

Diagnostics policy: BDQ phenotypic and genotypic testing – where are we?

C Gilpin[1]

In 2018, internationally agreed critical concentrations for drug-susceptibility testing (DST) for bedaquiline using different methods were established and a Technical Manual developed that describes the standardized laboratory protocols for DST. Drug resistance in TB occurs mainly through specific mutations in the DNA of TB bacteria. For some anti-TB drugs these mutations are clustered together in specific genes in the DNA, while for others the mutations are spread throughout the genome of the bacterium. The molecular basis of resistance to bedaquiline is not completely understood yet strategies that can be used to rapidly identify and drug resistance among patients being treated with bedaquiline and other newer medicines will need to be implemented as part of monitoring of drug resistant-TB patient response to treatment

SP-44-C3 Sustainable models for strengthening pharmacovigilance of TB medicines and diagnostics: global and regional perspectives and country examples

Sustainable pharmacovigilance systems in Africa

M Sigonda[1] [1]African Union-New Partnership for Africa's Development, Addis Ababa, Ethiopia.
e-mail: margarets@nepad.org

The African pharmaceutical market is expected to grow by 200% between 2012 and 2020, and some analysts forecast its market size to reach 161 billion USD by 2024. Infectious diseases such as tuberculosis, malaria and HIV are among the priority targets for the pharma market. This provides ample opportunities to improve the lives of Africans. At the same time, the future scenario warrants the need to be prepared to address challenges associated with such massive expansion of the pharmaceutical market. Of particular concern is the need for strong systems to ensure the safety, effectiveness and cost-effectiveness of newly introduced products. This will require balanced, diversified and sustainable financing models and there is critical need for developing local leadership and ownership.

Global perspectives on ensuring sustainable pharmacovigilance systems for TB medicines and diagnostics

F Mirzayev[1] [1]WHO/GTBP, Geneva, Switzerland.
e-mail: mirzayevf@who.int

Since the publication of the WHO Active tuberculosis drug-safety monitoring and management (aDSM) Framework in 2015, countries started to introduce aDSM for DR-TB patients on new drugs and regimens using domestic capacity or supported by external partners. Shortly thereafter, the WHO launched a global database for the surveillance of adverse events for aDSM of anti-tuberculosis drugs (WHO Global aDSM Database) to generate reliable evidence on the safety profile of anti-tuberculosis drugs to inform future tuberculosis treatment guidelines. It is managed by the WHO Global TB Program (GTB) and the Special Program for Research and Training in Tropical Diseases (TDR). An increasing number of countries implement the aDSM core package reporting serious adverse events. Some countries have in addition chosen to report data to the Global aDSM database. This presentation will provide an overview of these developments and a first available summary of data from the Global aDSM database

Successes, challenges and opportunities in strengthening pharmacovigilance under programmatic conditions in resource-limited settings

E Tiemersma[1] [1]KNCV Tuberculosis Foundation, , Netherlands. e-mail: edine.tiemersma@kncvtbc.org

In early years when access to medicines was very limited in low-income settings, pharmacovigilance (PV) was considered a luxury. With improved availability of life-saving medicines to diseases of poverty such as tuberculosis (TB), the need for strengthened PV systems has become more and more evident. As a result, significant strides have been made over the last two decades to strengthen country PV systems. However, critical gaps still remain to be addressed. In the TB program, where newer drugs and diagnostics are now being rolled out, the need for functional PV systems cannot be overemphasized. In this presentation we will discuss our global experience in embedding active drug safety management and monitoring in comprehensive TB programs.

Active drug safety management and monitoring of new TB medicines in Tanzania

M Marko[1] [1]Tanzanian National TB and Leprosy Control Programme, Dar es Salaam, Tanzania, United Rep.. e-mail: markojmkumbo@gmail.com

Tanzania established a plan for the implementation of new DR TB drugs and regimens in June 2016. The plan includes a section on active TB-drug safety monitoring and management (aDSM) where the country chose to implement the intermediate package of aDSM. Bedaquilline was introduced in Tanzania in 2015 under compassionate use but officially Bedaquiline and Delamanid were introduced in the country in November 2017. Tanzania started the shorter DR-TB treatment regimen (STR) in January 2018. By 2018 there were 75 DR-TB treatment facilities in the country, 45 are covered with the diagnostic and treatment monitoring capacity. In the first half year of 2018, 104 patients have been enrolled on STR and 25 patients were on Bedaquilline and Delamanid. Of 141 adverse event reports received from 20 health facilties, 126 were adverse events of special interest, 14 were serious adverse events (SAE) and one belonged to "other" category.

SP-45-B2 MDR-TB operational research on oral regimens: spectrum of approaches and next steps

Successful outcomes for patients switched from kanamycin to linezolid in a modified oral short regimen for MDR-TB in Niger

A Piubello[1] [1]The International Union Against Tuberculosis and Lung Disease, Niamey, Niger. e-mail: apiubello@theunion.org

The short regimen has been implemented in Niger since 2008 with excellent outcomes. However, ototoxicity secondary to injectable is a concern and data on modified oral short treatment regimens are lacking. A prospective longitudinal study is being conducted on a modified short regimen replacing kanamycin with linezolid in case of hearing loss at baseline or during treatment. Objectives of the presentations include review of efficacy, safety, implementation feasibility and cost.

RISE-TZ, (r)emoved (i)njectable modified (s)hort-course regimens for (e)xpert MDR-TB: programmatic feasibility and clinical effectiveness in Tanzania

S Mpagama[1] [1]NTLP Tanzania, Kibong'oto, Tanzania, United Rep.. e-mail: sempagama@yahoo.com

The RISE-TZ protocol will assess the treatment outcomes of patients treated with a modified 40-week injectable-free MDR-TB regimen for patients with FQ-susceptible MDR-TB in Tanzania. Objectives of the operational research is to evaluate safety and tolerability, efficacy including microbiological response or risk of TB recurrence and implementation feasibility and cost.

BEAT-Tuberculosis: a strategy trial of a six-month oral regimen for MDR-TB and XDR-TB in South Africa

F Conradie[1] [1]University of Witwatersrand, Houghton, South Africa. e-mail: fconradie@witshealth.co.za

BEAT-Tuberculosis is an open label, randomized controlled trial to establish the efficacy and safety of a study Strategy consisting of 6 months of bedaquiline, delamanid, linezolid, levofloxacin and clofazimine, compared to the current South African Standard of Care for 9 months for the treatment of rifampicin resistant tuberculosis. Objectives of the presentation include review of efficacy, safety, tolerability and implementation feasibility. The trial is funded by USAID and is firmly embedded within the South African National TB Program.

BEAT-Tuberculosis: a strategy trial of a six-month oral regimen for MDR-TB and XDR-TB in South Africa

K Selibas[1] [1]Wits Health Consortium, Johannesburg, South Africa. e-mail: kselibas@witshealth.co.za

BEAT-Tuberculosis is an open label, randomized controlled trial to establish the efficacy and safety of a study Strategy consisting of 6 months of bedaquiline, delamanid, linezolid, levofloxacin and clofazimine, compared to the current South African Standard of Care for 9 months for the treatment of rifampicin resistant tuberculosis. Objectives of the presentation include review of efficacy, safety, tolerability and implementation feasibility. The trial is funded by USAID and is firmly embedded within the South African National TB Program.

Operational research for MDR-TB: challenges and opportunities

C Lienhardt[1] [1]IRD, Montpellier, France. e-mail: christian.lienhardt@ird.fr

Dr. Lienhardt will provide an overview of the global spectrum of operational research (OR) in MDR-TB, comparing and contrasting this with ongoing MDR-TB and XDR-TB clinical trials. Objectives of the presentation include comparing the regimens being studied in MDR-OR; contrasting these with regimens being studied in MDR-TB clinical trials; and describing the ways OR can contribute to the MDR-TB treatment guidelines process.

SP-46-C9 Ready yet? The implications of donor financing transition on national TB programmes

Building effective donor partnerships for transparent and sustainable transition

E Wandwalo[1] [1]Global Fund, Geneva, Switzerland. e-mail: eliud.wandwalo@theglobalfund.org

As low and middle income countries grow economically, they can increase spending on health, progressively moving away from donor financing toward domestically funded health systems. This is a welcome trend, but countries must be supported to do this in a way that achieves impact. In this presentation, Dr. Wandwalo will provide an overview of the transition landscape for TB funding at the Global Fund and highlight the ways that the Global Fund supports countries to support well-planned and successful transitions, highlighting key principles of the Global Fund approach to sustainability and transition.

How is donor funding allocated? The impact of transition on donor financing, opportunities and risk

N Beyeler[1] [1]UCSF, San Francisco, United States of America. e-mail: naomi.beyeler@ucsf.edu

While there is recognition that many countries can mobilize more domestic resources towards achieving the TB epidemic, major gaps exist in donor financing for key global functions of TB-specific financing, including research and development and strengthening of surveillance technologies, especially for drug-resistant forms of TB disease. Naomi Beyeler summarizes an analysis that quantifies TB-specific development assistance for health (DAH) for these global functions versus country-specific aid, in order to identify when and where donor investments can have impact, even as countries transition out of donor eligibility for TB donor financing.

The implications of transition for market-shaping strategies; threats and opportunities for maintaining equitable access

B Waning[1] [1]Stop TB Partnership / Global Drug Facility (GDF), Geneva, Switzerland. e-mail: brendaw@stoptb.org

Age-old procurement and supply chain challenges are re-emerging in HIV, TB, and malaria programs as countries move from donor-funded procurement environments to domestically-funded, national procurement of medicines and diagnostics. This session will describe macro changes in financing and procurement and the resulting threats on long-term market sustainability and access, along with new opportunities for development banks, WHO, bilaterals and others to adopt long-term strategies to sustain markets shaped by Global Fund, GDF, and others; and refocus efforts on health systems strengthening and national policy development towards universal access goals.

Will countries be able to meet these needs: are they sufficiently prepared to fill the health financing gap created as TB donors leave?

I Bharali[1] [1]Duke University, Durham, United States of America. e-mail: ipchita.bharali@duke.edu

With the support of the Bill & Melinda Gates Foundation, Duke University is undertaking a two-year study on health transitions in middle-income countries. The study is examining the interplay between the epidemiological transition, demographic changes, and shifts in both domestic and donor financing for health. Four countries in this study: India, Kenya, Myanmar, and Nigeria are high burden countries for TB, HIV/TB and multi-drug resistant TB. In this presentation, Ipchita Bharali will focus the discussion on the impact of transition on these countries.

Health diplomacy: essential soft skills for successful transition

E Goosby[1]

Recognising that increasing domestic resource mobilisation, rather than relying on donor agencies, should now be an increasingly important driver of investment; global health diplomacy is also essential to ensure that diminishing donor resources are matched to domestic priorities and catalytic of domestic investments. In this session, Dr. Goosby highlights the important role that health diplomacy can play in securing investment, and creating the enabling environment needed to secure substantive progress towards ending the tuberculosis epidemic once and for all.

SP-47-C1 Accelerating the curve: TB prevention through short rifamycin-based regimens for hard-to-reach groups

Zero TB Kids: Using 4R to treat LTBI in Tibetan child refugees

K Dorjee[1] [1]John Hopkins University, Baltimore, United States of America. e-mail: kundorj@gmail.com

Tibetan refugees in India suffer great health disparities, with especially high rates of tuberculosis (TB). In collaboration with the Tibetan Delek Hospital in Dharamsala, India, the Johns Hopkins Center for Tuberculosis Research is combatting TB in the Tibetan community through the Zero TB in Tibetan Kids (ZTBK) project. We provide comprehensive TB case-finding, treatment, and latent TB treatment services in Tibetan boarding schools in India. We have detected alarmingly high TB case-rates (916/100,000) and latent TB infection rates (19%) in Tibetan children and adolescents, but have been able to offer short-course, rifamycin-based preventive therapy to >1000 children. In recent months, the team has expanded its efforts to include the Tibetan monasteries and nunneries. With community mobilization, political will, and broad engagement of all stakeholders, the Zero TB Kids project is having a major impact on reducing the burden of TB in this high-burden population.

The implementation of 3HP for the treatment of LTBI in two remote arctic communities with a predominantly Inuit population, the Taima TB 3HP study

G Alvarez[1] [1]School of Public Health at the University of Ottawa, , Canada. e-mail: galvarez@ohri.ca

The United Nations Sustainable Development Goal to end tuberculosis (TB) by 2030 cannot be realized without "bending the curve" through preventive activities, namely treatment of latent TB infection (LTBI). Short rifamycin-based LTBI regimens, which include 12-dose weekly isoniazid-rifapentine (3HP) and 4 months daily rifampin (4R), "accelerate the curve" to end TB; these treatment regimens are shorter, have higher completion rates, and are thus more effective than traditional 9 month isoniazid (9H) regimens. This session will share successes of short rifamycin-based LTBI regimens used in challenging settings and hard-to-reach groups, and the latest research on short and ultra-short LTBI treatment regimens.

High LTBI treatment completion rates among U.S. homeless, incarcerated, and contacts in a rural state; utilization and completion rates with 3HP, 4R and 9H

R Webb[1] [1]University of Mississippi, Jackson, United States of America. e-mail: rmwebb@umc.edu

A recent meta-analysis demonstrated greater benefit to using short course LTBI regimens to prevent TB disease. Ensuring completion of LTBI treatment is an important aspect of controlling active TB. In Mississippi, a rural state in the United States, the TB program started using 3HP in 2011. Seven years prior to the use of 3HP, LTBI completion rates ranged from 60-75%. In subsequent years with 3HP as the preferred regimen, completion rates ranged from 78-85%, and as high as 95% among contacts of known TB cases. A comparison between the use of 9H, 4R, and 3HP in this rural state over an eight-year period will be reviewed with completion rates, adverse events and benefits of shorter course regimens among contacts of TB cases, homeless and incarcerated populations.

3HP use among household contacts in the Zero TB Pakistan project

H Hussain[1] [1]IRD Global, Singapore, Singapore. e-mail: hamidah.hussain@ird.global

In the absence of an effective vaccine to prevent the progression of LTBI to active tuberculosis (TB) disease, National TB Control Programs largely depend on TB preventive therapy (TPT) to accelerate efforts to end TB. Prioritizing target populations for available diagnostics and TPT is critical. From October 2016 to February 2019, 50,407 household contacts of 12,948 index pul-

monary TB (PTB) patients in Karachi were approached. Of these 36,393 (72%) were verbally screened for TB symptoms and invited for investigations including a chest X-ray (CXR). In total, 15,686 (43%) contacts were investigated; 338 (2%) were diagnosed with TB and initiated on treatment. The remaining 15,348 (98%) contacts with normal CXRs, negative sputum tests, and unremarkable clinical evaluations were considered eligible for TPT; of these 6,067 (40%) agreed to initiate TPT with 3HP. Currently, the completion of 3HP is 65%. 3HP is a feasible TPT option in programmatic settings in high-burden countries.

Short course TB preventive therapy regimens: how short can we go?

G Churchyard[1] [1]Aurum Institute, Houghton, South Africa.
e-mail: gchurchyard@auruminstitute.org

Short course regimens are associated with fewer side effects, better adherence and higher treatment completion rates, and represent a new era for TPT. The World Health Organization recommends the following short course rifamycin containing regimens for use in high burden countries: three months of weekly high-dose isoniazid and rifapentine (3HP) for people with HIV (PWHIV) and household contacts>2 years, and three months of daily isoniazid and rifampicin (3HR) for children,

SP-48-E2 Mobilising youth as agents of change for a TB-free world

Engaging young TB survivors as powerful advocates to end TB

N Venkatesan[1] [1]Economic Times, Mumbai, India.
e-mail: nandita.venky@gmail.com

TB primarily affects youngsters during their most productive years. Apart from the physical and emotional toll, the disease also has immense financial implications. A disease long shrouded in silence, some young survivors are now speaking up, voicing the challenges they face and are taking charge of the narrative to push for a change that was long overdue. A survivor herself, Nandita will suggest ways to harness the unspent potential of survivors and sufferers, turn them into powerful advocates to make national TB programs more efficient and person-centric.

Mobilising young people from key populations and young people living with HIV in the TB response: opportunities and challenges in Asia and the Pacific

J Acaba[1] [1]APCASO, Bangkok, Thailand.
e-mail: jeffacaba@apcaso.org

Six of the 30 high-burden countries that were identified to have a high number of TB-HIV co-infection are found in Asia and the Pacific. While current trends in TB incidence rates have been decreasing since 2000, HIV cases among those who have been diagnosed with TB, particularly among young key populations, in these countries have been increasing. Engaging young people from key populations in HIV is vital to ensure that these populations are reached by TB responses. This presentation looks at opportunities and challenges around mobilizing young key populations to HIV in the TB response in the Asia Pacific region.

Using music to mobilise youth: experience from Kenya

S Otieno[1] [1]TB advocate, Nairobi, Kenya.
e-mail: steveotioti@gmail.com

Youth are the most affected population by TB. In Kenya for example the TB prevalence survey of 2016 indicated that the most affected people were youths aged 24-35. Even with these facts, there are no youth friendly TB interventions and strategies. Music for example is a strategy that easily captures the attention of youths. I have been using my music talent to mobilize youths around TB in Kenya, to encourage them to go for screening while promoting treatment adherence to those already infected. I have also used music it to reach different stakeholders to play their role in Ending TB.

Engaging youth and patient support in the Russian Federation

K Schenina[1] [1]TB People, Moscow, Russian Federation.
e-mail: shchenina@gmail.com

When Ksenia finished her treatment of tuberculosis, she began to conduct a thematic blog about the disease 'Tuberculosis. People's stories.' She wrote about the treatment of tuberculosis in Russia, she interviewed patients and doctors. She received a lot of letters came from sick people and realized that the format of the blog does not give the opportunity to help people, as they need. This is how the online patient community 'Tuberculosis: Support and Answers' appeared, which is visited monthly by several thousand people - patients, their relatives and doctors. The community is consulted by several doctors with tuberculosis, there is a psychotherapist, as well as legal support. And also a lot of people who have already cured MDR and XDR-TB, who with their advice help others not to quit treatment.

SP-49-C8 It's time to scale up: progress in rolling out TB contact investigation in high-burden settings

Systematic review of yield of TB contact investigation in high-burden settings: comparing outcomes pre- and post- WHO guidelines

M Velleca[1] [1]University of California, San Francisco (UCSF), San Francisco, United States of America. e-mail: laterza.mariana@gmail.com

This talk will present results of an updated systematic review on the status of TB contact investigation (CI) implementation, assessing the yield of CI for detecting active TB and latent TB infection, as well as describing trends in the implementation of CI since the WHO CI guidelines were published in 2012. The outcomes will be compared for different risk groups, specifically people living with HIV, children under 5 years of age, and contacts of patients with MDR-TB. The updated findings will help inform programs of the expected outcomes and impact of CI on TB care and control.

Outcomes and costs of systematic TB contact investigation and paediatric IPT initiation in Mozambique

A Abdula[1] [1]FHI360 Mozambique, Maputo, Mozambique. e-mail: aabdula@fhi360.org

Systematic implementation of contact investigation has resulted in significant increases in case finding and uptake of IPT in pediatric patients in central Mozambique. The intervention was first rolled out in the city of Beira and findings from the first year showed a significant increase in initiation of IPT in children under 5, and a 5-fold increase in TB case-finding overall. Following those strong results, it was scaled up to four additional districts in the central region. This talk will present data on the outcomes of scaled-up CI in central Mozambique, as well as the actual and programmatic costs of CI implementation. These results aim to inform future planning and policy decisions on CI implementation.

Implementation of systematic investigation and preventive therapy in children under 5 years living with smear-positive pulmonary TB in four French-speaking African countries

K Koura[1] [1]International Union Against Tuberculosis & Lung Disease, Paris, France. e-mail: kgkoura@theunion.org

While contact investigation is strongly recommended for children under 5, it is not routinely implemented in the African region. Following a workshop organized by The Union in 2014 with national TB programs (NTP) and paediatricians from 10 countries in francophone Africa, implementation of contact investigation was selected as a priority action. An operational research project was launched in 2015 in 4 countries, Cameron, Benin, Central Africa Republic, and Burkina Faso, with financial support of the French 5% Initiative to demonstrate the feasibility of systematic investigation for contact children within the National Tuberculosis Program (NTP) framework and to document the effectiveness of this intervention. The presentation will focus on lessons learned from this project.

An integrated active TB case finding and contact investigation approach in a high-burden population in urban Zambia

M Maboshe[1] [1]FHI360 Zambia, Lusaka, Zambia. e-mail: mmaboshe@fhi360.org

The presentation will describe an approach employed to find "missing TB patients" in a high-density population of Kabwe in Zambia, combining CI with other case finding approaches. The results of an intensified screening for TB using symptom screen, digital chest X-ray and GeneXpert sputum examination as well as contact investigation of all the bacteriologically positive contacts will be shared.

The role of community-based TB contact screening in improving access to TPT among children and adolescents in Uganda

M Sekadde[1] [1]National TB and Leprosy Control Programme Uganda, Kampala, Uganda. e-mail: moorine.sekadde@gmail.com

More than half of the children estimated to have TB globally are not diagnosed and treated. The situation is worse for uptake of TB preventive therapy in this vulnerable population which is low at less than 25%. In 2015-16, the Union in collaboration with the Uganda NTP implemented a two-pronged (facility and community), DEcentralize TB Services and Engage Communities to Transform Lives of Children with TB (DETECT Child TB) model to child and adolescent TB case finding and prevention. There was a documented increase in IPT uptake IPT and child TB case finding from < 5% to 72% and 8.8% to 15% in the two implementation districts during the first 15 months.

SP-50-C12 How to protect children from tobacco industry interference: a review of treaties, strategies, challenges and progress

Tobacco-free generations: an overview of frameworks, strategies and progress

A Jones[1] [1]International Union Against Tuberculosis and Lung Disease (The Union), Sydney, Australia. e-mail: ajones@theunion.org

A review of treaties, frameworks and strategies will be presented with progress updates on examples from countries where projects aimed at protecting children from tobacco and tobacco industry interference are underway. To accelerate integrating objectives into frameworks, tools have been developed by a Union Working Group to assess needs and adapt a roadmap tool for creating tobacco-free generations in fulfilment of treaty obligations.

Can global leaders and global campaigns do more to protect children from tobacco industry interference?

P Lal[1] [1]International Union Against Tuberculosis and Lung Disease, South-East Asia Office, New Delhi, India. e-mail: plal@theunion.org

Article 16 of the FCTC and domestic legislation of most countries prohibit the sale of tobacco to minors. Yet few countries especially developing countries have been able to reduce initiation into tobacco use by minors. Global surveys reveal that the problem of underage use of tobacco is much higher than previously anticipated.

The challenge for policymakers and enforcers is compounded by the easy access of tobacco products and their affordability. Given that several global treaties protect youth and vulnerable populations, very few of these have been leverage by tobacco control advocates.

This presentation will share possible provisions from global treaties and conventions which can be used to reduce tobacco use, and mitigate the challenges posed by the tobacco industry.

The threat of e-cigarettes and new products for current and future generations: challenges and opportunities for action

G Quan[1] [1]The Union, New York, United States of America. e-mail: qgan@theunion.org

Under the guise of new products that claim to be 'safer', the industry's marketing tactics to expand and attract users of e-cigarettes and heated tobacco products is a growing threat to current and future generations. Challenges and opportunities to protect young people in particular will be discussed with focus on recommendations for actions by government, regulators and civil society.

Using human rights arguments, treaties and reporting requirements to protect children from tobacco and industry interference

L Huber[1] [1]ASH USA, Washington DC, United States of America. e-mail: huberl@ash.org

Tobacco remains the leading cause of global preventable death. Left unchecked, tobacco will kill 1 billion people this century and will cost the global economy up to two percent of its GDP, which is a substantial barrier to economic and human development. Tobacco is a barrier to achieving the Sustainable Development Goals (SDG) including Target 3.a which calls upon States to "strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries."

The "right of everyone to the enjoyment of the highest attainable standard of physical and mental health" has been recognized in the International Covenant on Economic, Social and Cultural Rights and as such governments are obligated to protect the health of their citizens through international and regional human rights treaties. Tobacco control advocates can use these human rights mechanisms and processes, including a child's right to health, to help end the tobacco epidemic.

Protecting future generations by integrating tobacco control into NCDs, SDGs and human rights treaties in Iraq

T ALHilfi[1]

Tobacco use in Iraq is a leading cause of NCD morbidities and mortalities and 10% of children are already using tobacco products (GYTS 2014). The WHO FCTC has been ratified and actions are underway to raise tobacco taxes under the newly revised Iraqi tobacco law. However, the interference of the tobacco industries is a major threat and additional strategies are needed to both protect health policies and integrate tobacco control into Human Rights, NCDs, SDGs and other healthcare strategies.

SYMPOSIA: SATURDAY, 2 NOVEMBER 2019

SP-51-D6 Preventive therapy: time to roll out population-based treatment to reach the goal of TB elimination?

Modelling approaches to determine the effect of population-based treatment in high-burden settings?

J Trauer[1] [1]Monash University, Melbourne, Australia. e-mail: james.trauer@monash.edu

Many of the novel programmatic interventions currently under consideration to improve TB control in high-burden settings are directed at cases of active disease, including case finding interventions, more accurate diagnostics and better treatment regimens. However, transmission models consistently indicate that the large pool of latent infection will make it impossible to achieve the End-TB Targets without preventive interventions. We have shown only modest reductions in incidence even under the entirely unrealistic scenario that transmission is immediately halted, across settings as diverse as Fiji, Bulgaria and the Philippines. Simpler compartmental models have similarly demonstrated that preventive therapy remains effective even in high-burden settings. However, understanding the various profiles in reactivation risk, which differ substantially by age, is also critical to planning interventions. In particular, targeting previously infected children as they age towards adolescence could be particularly effective at the population level.

SWEEP-TB Viet Nam: integrating community-wide latent TB testing and short-course preventive treatment into an island-wide health screening campaign in Viet Nam

T Dong[1] [1]Friends for International TB Relief, Hai Phong, Viet Nam. e-mail: thuy.dong@tbhelp.org

Vietnam is a high burden TB and DR TB country and despite program impressive program improvements over the past 10 years, the prevalence of TB was recently found to be higher than originally estimated by WHO. New approaches are urgently needed. In early 2019, community-wide latent TB screening and treatment was organized and coordinated as part of an island health screening campaign on the rural underserved commune of Tan Hiep, Hoi An District funded by TB REACH. At a relatively low cost, high coverage and high uptake of TPT with 3HR was achieved. Implementation, outcomes, lessons learned and cost will be presented.

TB and leprosy-free Majuro: Large-scale community-wide latent TB screening and treatment in the Republic of the Marshall Islands

M Konelios-Langinler[1] [1]Dept of Health, Majuro, Marshall Islands. e-mail: mailynnlang@gmail.com

The Republic of the Marshall Islands has one of the highest incidence rates of tuberculosis in the South Pacific (480/100,000) as well as the highest prevalence of diabetes in the world, a key driver. In 2018 RMI committed to screening the population of Majuro, the urban capital island (population 27,000), for TB including latent TB. Diabetes testing was integrated into case management and short course preventive treatment regimens (3HP or 3HR depending on availability) with weekly DOT by community health workers were used to treat LTBI. Implementation, coverage and completion of LTBI treatment will be discussed as well as lessons learned and implications for the future.

Community-wide IPT for exposed children in Guinea Bissau

C Wejse[1]

Although IPT to exposed children is a WHO recommendation, it is not implemented in many high burden areas, let alone to household contacts or latently infected at large. This is driven by fear of low adherence, toxicity and generation of resistance. In a Demographic Surveillance Site in West Africa, IPT has been implemented and was shown to be feasible with acceptable adherence rates around 80% and with a clear effect on child mortality in TB affected households. The population acceptance was high and toxicity was low, and the implications may be that preventive therapy is feasible in other high- burden populations in low-resource settings. Possible roll-out scenarios will be described as well as ethical implications

SP-52-B2 Anticipating changes in care for DR-TB

Phase III trials in DR-TB: current landscape and expectations

C Mitnick[1] [1]Harvard Medical School, Boston, United States of America. e-mail: carole_mitnick@hms.harvard.edu

This presentation will review trials and operational research studies underway to investigate new regimens for drug-resistant TB, with an emphasis on all-oral, shortened regimens. Further, it will address some of the primary questions outstanding to be answered by

these studies and ways to overcome some of the challenges of answering questions about regimens through operational research. Opportunities for implementation of improved clinical and programmatic practice, as well as research methods, will be considered.

WHO consolidated guidelines on DR-TB treatment 2019: key changes and new aspects

F Mirzayev[1] [1]WHO/GTBP, Geneva, Switzerland.
e-mail: mirzayevf@who.int

This presentation will describe the main aspects of the recent treatment guidelines established by the World Health Organization for the treatment of drug-resistant TB and will outline the near future perspectives for the global policy development in this particular area depending on availability of relevant evidence base and using an independent structured process.

Early adopter of new guidance and prospective: rapid policy changes and implementation

N Ndjeka[1] [1]Drug-Resistant TB, TB & HIV, National Tuberculosis Control Programme, Johannesburg, South Africa. e-mail: Norbert.Ndjeka@health.gov.za

This presentation will describe the implementation of new bedaquiline based regimens for MDR-TB treatment in South Africa. It will cover the preparatory phase of this important project, the second phase which focused on a study known as Bedaquiline Clinical Access Programme (BCAP) and the last phase which was a programmatic scale up of an agents that was already registered.

How to implement DR-TB guidelines at the programmatic level

V Cox[1] [1]Cape Town, South Africa.
e-mail: vivian.cox@me.com

Since 2015, the Drug Resistant TB Scale Up Treatment Action Team (DR-TB STAT) has collected information from countries on the use of newer drugs and shorter treatment regimens for drug resistant tuberculosis management. This presentation will describe different approaches from countries in early adoption of the 2019 WHO consolidated guideline recommendations.

Difficulties and solutions to accessing new TB drugs in India

Z Udwadia[1] [1]Hinduja Hospital, Mumbai, India.
e-mail: zarirfudwadia@gmail.com

This presentation will focus on the clinicians' experience in using new drugs and régimens for desperately ill drug-resistant TB patients. The difficulties in accessing newer drugs like BDQ and DLM in the Indian private sector will be enumerated. Potential solutions to overcome this problem will be enumerated so more equitable access is ensured.

SP-53-C6 Confronting the crisis: emerging research in maternal-child TB

The crisis in maternal TB: a case-based discussion of research gaps

S Naik[1] [1]Byramjee Jeejeebhoy Government Medical College, Pune, India. e-mail: shilunnaik@yahoo.co.in

Pregnancy and the postpartum period represent the highest-risk time for women to develop active TB. Yet little is known about best practices for the diagnosis, treatment and prevention of TB in pregnant women. In this talk, Dr. Naik will use a case-based approach of cases of TB in pregnancy (e.g. extrapulmonary TB, MDR-TB) to reveal the significant gaps in knowledge we have on the management of this very important population.

Revisiting the burden of TB in pregnant and post-partum women

N Mafirakureva[1] [1]University of Sheffield, Sheffield, United Kingdom. e-mail: n.mafirakureva@sheffield.ac.uk

Pregnant and postpartum women have been suggested to have an increased risk of developing tuberculosis disease, which can worsen pregnancy outcomes and expose vulnerable neonates to infection. Tuberculosis during pregnancy remains poorly recorded in many settings, leading to uncertainty in its burden. Since previous modeling estimates of tuberculosis incidence in pregnant women, World Health Organization (WHO) burden estimates have made use of new data and methods to disaggregate tuberculosis incidence by age and sex. We make use of these disaggregated WHO tuberculosis estimates, United Nations Population Division fertility estimates, and our own systematic review and meta-analysis quantifying incidence rate ratio to generate new estimates for tuberculosis during pregnancy and postpartum to at the country-, regional- and global-level.

Pregnancy status in the U.S. National Tuberculosis Surveillance System (NTSS): the 2020 Report of Verified Case of Tuberculosis form

R Brostrom[1] [1]Centers for Disease Control and Prevention, Honolulu, United States of America. e-mail: hld4@cdc.gov

Tuberculosis is a notifiable condition in the U.S. Cases are reported to the Centers for Disease Control and Prevention via the Report of a Verified Case of Tuberculosis (RVCT) entered into the National Tuberculosis Surveillance System. Introduced in 1985, the RVCT was revised in 1993 and 2009. In 2016, CDC convened a workgroup to propose new RVCT revisions, to be implemented by 2020.

Pregnancy status, not captured on the current RVCT, was proposed as a new variable. Burden was weighed against importance of data collection. Although U.S. numbers of pregnant women with TB disease may be small, untreated TB among pregnant women may lead to pregnancy complications, infant mortality, and maternal mortality. Pregnant women are often excluded from clinical trials, leading to limited data for many tuberculosis drugs and clinical outcomes in pregnancy. We will discuss the process of adding pregnancy status to routine TB data collection.

Is there a connection between gestational diabetes and TB?

M Alexander[1] [1]Byramjee Jeejeebhoy Government Medical College-Johns Hopkins University Clinical Research Site, Pune, India. e-mail: mallika.alexander@yahoo.com

Pregnancy is associated with insulin resistance similar to that found in type 2 DM. The prevalence of gestational diabetes in key TB-endemic countries, like India and China, has been rapidly increasing in the last decade. Pregnancy is also an independent risk factor for developing active TB yet little is known about the interaction of gestational diabetes and TB.

In this presentation, Dr. Alexander will review the epidemiology, immunology, and significant research gaps in understanding the interactions between gestational diabetes, pregnancy, and TB in women living with and without HIV.

Paediatric TB: innovative approaches to improve outcomes

V Rouzier[1] [1]Haitian Study Group on Kaposi Sarcoma and Opportunistic Infections (GHESKIO), Port-au-Prince, Haiti. e-mail: vrouzier@gheskio.org

Children are more than 10 times likely to die if they are infected with M. tuberculosis. While most adults infected with MTB will be asymptomatic for their entire lives, a TB-infected child has a 50% chance of death. The WHO recommends a standard 4-drug regimen for 6 months to treat TB, but the dosing was not optimized for children. In this talk, Dr. Rouzier will review the data on what we know about the pharmacokinetics of TB drugs in children as well as introduce some novel approaches to overcome the challenges in monitoring drug levels in young and malnourished children.

SP-54-C1 Tuberculosis Preventive Treatment (TPT): implementation, scale-up and realities

Treatment of latent TB and the End TB Strategy: global situation and recommended actions

D Falzon[1] [1]WHO, Geneva, Switzerland. e-mail: falzond@who.int

Tuberculosis (TB) prevention is a core element of the WHO's post 2015 End TB Strategy and treatment of latent TB infection (LTBI) one of the main means to reduce TB incidence with current tools. The presentation will discuss the current global status in expansion of LTBI treatment in the world and highlight recent changes to the WHO recommendations for LTBI treatment and key barriers to implementation, namely diagnosis and new treatment options; expanding the screening of contacts; scaling-up of shorter rifampicin-based regimens; documenting routine LTBI activities and tracing and managing contact with MDR-TB.

Scaling up screening and treatment for LTBI in resource-limited settings: a health system perspective

G Fox[1] [1]The University of Sydney, Sydney, Australia. e-mail: gregory.fox@sydney.edu.au

The scale up of treatment for latent TB infection is essential to achieving the milestones of the End TB Strategy. Systematic screening of high-risk populations such as household contacts requires a reorientation of health systems towards prevention, rather than just cure. This has important implications for health systems -particularly in resource-limited settings.

This presentation will apply recent recommendations of the Lancet Global Health Commission for quality health systems to the challenge of programmatic implementation of latent TB infection. It will examine the health system factors underpinning the successful scale-up of preventive therapy in four countries – Vietnam, Indonesia, Benin and Ghana. We will apply the Lancet Commission's four foundations of quality care: governing for quality, redesigning service delivery platforms, transformation of the health workforce and the need to

ignite demand for quality care among affected populations. These analyses are relevant to the expansion of preventive therapy in other high-burden settings.

The ACT4 Trial, an intervention for LTBI programme evaluation and strengthening: results from the multicentre, pragmatic randomised-controlled trial

R Ruslami[1] [1]Indonesia. e-mail: n.ruslami@gmail.com

This session will present results from a recent cluster randomized pragmatic trial designed to enhance the public health impact of latent TB infection diagnosis and treatment (ACT4 Trial). The trial was conducted in 24 health facilities in five countries (Benin, Canada, Ghana, Indonesia and Vietnam). Results will be discussed from the perspective of both low/middle income settings and Canadian sites. Experiences and lessons learned through the trial will be presented, as well as key considerations (cost and sustainability) for scale up.

In-country experiences from Viet Nam and Benin through the ACT4 trial

D Dr. Menonli Adjobimey[1] [1]Woolcock Institute Of Medical Research in Viet Nam/entre National Hospitalier Universitaire de Pneumo-Pthisiologie de Cotonou, Ha Noi city/Cotonou, Viet Nam.
e-mail: thuanh.nguyen@sydney.edu.au

This presentation will consist of two case studies of LTBI scale-up in a low/middle income settings. The first case study will be presented from the perspective of Vietnam (Dr. Thu Anh Nguyen) and the second from Benin (Dr. Menonli Adjobimey). Each speaker will describe their experience in going from a pilot project within ACT4 research project to national implementation of LTBI treatment in children under 5 only in Benin, and all ages in Vietnam.

Meeting the UN General Assembly targets for TPT: what will it take?

S Ahmedov[1] [1]United States of America.
e-mail: sahmedov@usaid.gov

This presentation will discuss the United National General Assembly targets for Tuberculosis Preventive Treatment and areas of need for technical support to scale up implementation efforts. Examples from USAID supported countries will be included.

SP-55-C7 Putting evidence into action: integrating mental health treatment to end the TB emergency

The effect of depression on TB treatment outcomes: a systematic review

J Scuffell[1] [1]King's College London, London, United Kingdom. e-mail: jamiescuffell@gmail.com

A presentation of findings from a systematic review conducted to determine the effect of pre-treatment depression and other mental disorders on TB treatment outcomes. Outcomes reviewed include delayed treatment initiation; TB treatment outcomes of cure, death, failure and loss to follow up; measures of adherence and treatment intermittency, and TB relapse.

The role of depression and HIV infection on delayed treatment initiation among TB patients in Botswana

D Mbatshi[1] [1]Botswana-UPenn Partnership, Gaborone, Botswana. e-mail: dimam@bup.org.bw

Botswana is a country that is hyperendemic for TB and HIV. At present, little is known regarding the effect of mental health disorders on delays in TB health seeking and treatment initiation among TB patients with or without HIV infection.
In this study, we found higher prevalence of moderate to severe depressive symptoms (PHQ-9 $\geq$ 10) among TB patients with HIV infection compared to TB patients without HIV infection. Moderate to severe depressive symptoms was associated with delayed treatment initiation (symptom duration >2 months), independent of HIV status.
Depression may be a major cause of delayed TB treatment initiation in Botswana, possibly contributing to increased TB transmission in the community. These findings have implications for integration of mental health screening and treatment as a core component of HIV and TB care.

Depressive symptomatology and TB treatment outcomes in Eastern Cape, South Africa

A Medina-Marino[1] [1]Foundation for Professional Development, East London, South Africa.
e-mail: andrewm@foundation.co.za

Despite being a curable disease, TB remains a leading cause of death globally. Depression has been shown to be highly prevalent among TB patients starting therapy, but the effect of depression on TB treatment outcomes has been understudied. This presentation will focus on the effect of pre-treatment depressive symptomatology

on TB treatment outcomes, with an emphasis on comparing this relationship between HIV-infected and HIV-uninfected TB patients.

Understanding and responding to mental ill-health among people with MDR-TB in Bangladesh and Nepal

H Elsey[1] [1]University of York, York, United Kingdom. e-mail: helen.elsey@york.ac.uk

Findings from two projects conducted by the COMDIS-HSD consortium will be presented: 1) a survey of 148 MDR TB patients in Bangladesh to estimate prevalence of depression (using PHQ9 and clinical assessment) and associations with socio-demographic factors and qualitative interviews with patients, carers and health professionals to understand the impact of mental ill-health and possible interventions. We found 33.8% (95% CI 26.7 to 41.7) of patients were depressed; 2) a mixed method study to develop and explore the feasibility of delivery of a brief psycho-social intervention to improve mental health among people with MDR TB in Nepal. Over 10 months, 135 patients were screened, of whom 12 (9%) received behavioural activation (BA) counselling, 115 (85%) received information materials, 80 (59%) received an education session and 49 (36%) received at least one group session. Both studies found high prevalence of mental ill-health and challenges to the implementation of psycho-social interventions.

SP-56-E1 Shifting the gender paradigm in the TB response: women's voices

Fighting stigma with HIV- and TB-affected women in Eastern and Southern Africa

M Murenga[1] [1]Lean on Me Foundation, Nairobi, Kenya. e-mail: maureenmurenga@gmail.com

In Eastern and Southern Africa gender-based stigma and discrimination keeps women and adolescent girls living with HIV out of reach of life saving TB diagnostics and treatment. Community and peer support as well as community mobilization and education are the best approaches to resolve these challenges. Lean on Me Foundation and partners lead this work, promoting engagement and empowerment of HIV and TB affected women.

Addressing TB among women representing key populations in Eastern Europe and Central Asia

Y Chorna[1] [1]Kiev, Ukraine. e-mail: chorna@tbcoalition.eu

Barriers to TB diagnosis and treatment for women who represent key population communities, including women living in detention settings, women who use drugs, and female migrants, are not well explored. These women face increased risk for TB due to the structural and environmental factors, and multiple barriers in accessing services. The organizations in the TB Europe Coalition have partnered with key population communities to improve TB services provision. Ways in which these approaches benefit women will be explored in the presentation as well as ways to address longer-term sustainability issues in financing these programs.

Bolo Didi: a movement of female TB survivors in India

N Venkatesan[1] [1]Economic Times, Mumbai, India. e-mail: nandita.venky@gmail.com

Bolo Didi or Say Sister is a movement started by two female TB survivors in India. Through community gatherings, social media and WhatsApp female TB survivors help other women with TB navigate complex diagnostic processes, adhere to treatment, and retain their self-efficacy and standing in their community. The power of peer support and female social networks will be explored in the presentation as well as the ultimate lack of information, stigma, abandonment, fear and isolation that many women with TB face in India.

Focus on community: how TB interventions can help shift harmful gender norms

R Abeid Khaji[1] [1]SHDEPHA+ KAHAMA, Kahama, Tanzania, United Rep.. e-mail: rabiabeid@gmail.com

Working with rural and marginalized communities impacted by HIV and TB in Tanzania, SHDEPHA community workers observed first hand how harmful gender norms prevent both women and men in the community from accessing TB and HIV services. By fostering community dialogues and utilizing empowerment techniques, and role modelling, SHDEPHA is addressing the gender disparities more broadly and at the same time succeeding in obtaining community buy-in for TB screening and HIV prevention activities.

Funding women's empowerment through TB programming

M Smelyanskaya[1]

TB REACH is a rapid funding mechanism supporting innovation in TB programming. A recent wave of funding solicited proposals focused on empowerment of women. The presentation explores whether it is possible to include empowerment of women and begin a discourse on achieving gender equality within TB programmes and how this shift impacts TB response.

SP-57-B1 Lessons learned from national TBPSs using culture and Xpert MTB/RIF: TB or not TB?

The use of Xpert MTB/RIF (or Ultra) and culture in national TBPSs: an overview

C Sismanidis[1] [1]WHO, Geneva, Switzerland.
e-mail: sismanidisc@who.int

Following results from recent national TB prevalence surveys that used both culture and Xpert, the WHO Global Task Force on TB Impact Measurement has led efforts to understand the reasons for discordant results, to identify appropriate solutions for interpretation and analysis of data, and to develop consensus around recommendations for future surveys. This presentation will provide a summary of results from recent surveys, explanations for discordant results, approaches used for interpretation and analysis of data, and draft recommendations for future surveys.

Culture and Xpert in a repeat survey, the second national TBPS in Viet Nam: Nguyen Viet Hai – Viet Nam NTP

N Viet Hai[1] [1]Vietnam Integrated Centre for Tuberculosis (TB) and Respirology Research, Hanoi, Viet Nam.
e-mail: nguyenviethai.hmu@gmail.com

After a first survey in 2006-7, Vietnam conducted a repeat TB prevalence survey in 2017-18. In addition to the methods used in the first survey (smear and LJ culture), the repeat survey also used Xpert MTB/RIF and liquid culture. Results showed discordance in test results. This presentation will discuss the main results of the survey, how discordant Xpert and culture results were interpreted, and the likely explanations for discordant results.

Minimising culture to standardise survey findings: the first national survey of Eswatini

W Sikhondze[1] [1]Eswatini/Swaziland MOH National TB Control Programme (NTCP), Mbane, Eswatini.
e-mail: welile.sikhondze@gmail.com

The first national TB prevalence survey in Eswatini was successfully implemented in 2018. The survey used an innovative diagnostic algorithm which minimized culture testing. Field- level Xpert MTB/RIF testing was done for all presumptive TB cases, with Xpert testing on two separate sputum samples (spot-spot or spot-early morning). For all those with an Xpert-positive test result, two culture tests were then performed on two additional sputum samples (spot-spot/spot-early morning) using the MGIT culture system. This algorithm performed well throughout field operations, with timely results fed back via GxAlert and minimal disruption to the routine laboratory culture testing services. Survey cases were defined based on results from the 4 tests performed as well as radiological reading. This presentation will discuss the main results and lessons learned from the survey.

Application and implications of Xpert Ultra in a national TBPS

F Ismail[1] [1]National Institute for Communicable Diseases, Johannesburg, South Africa. e-mail: farzanai@nicd.ac.za

South Africa conducted a National TB prevalence survey to estimate the burden of bacteriologically confirmed pulmonary tuberculosis in 2018-2019. The survey had a sample size of 55 000 people. All participants were screened for symptoms suggestive of TB and chest x-ray. Any screen-positive participant was tested using both Xpert Ultra and MGIT culture, on two separate sputum samples. We present comparative findings between Xpert and culture in this active case finding activity and discuss implications for the use of Ultra for community based efforts to find missing TB cases.

TB or not TB: comparison of different diagnostic algorithms in the TREATS prevalence surveys

H Ayles[1] [1]London School of Hygiene & Tropical Medicine, Lusaka, Zambia. e-mail: helen@zambart.org.zm

TREATS measures the impact of the HPTN 071 (PopART) intervention of combined, universal HIV and TB screening and treatment on the burden of TB at population level. Key to measurement is a TB prevalence survey conducted in 56,000 randomly sampled individuals from the trial communities in Zambia and South Africa. This survey initially planned to use digital CXR with CAD and Xpert ultra to measure the difference in prevalence between intervention and control arms. The operating characteristics of the Xpert ultra and experience from ongoing prevalence surveys, especially the decrease in

specificity thought to be caused by dead bacilli, caused us to rethink the algorithm to be used.
I will present on our philosophy regarding choice of algorithm and results from an intensive diagnostic phase where we tested different algorithms and novel diagnostics in an attempt to overcome the challenge of "low specificity" of Xpert ultra for prevalence surveys.

SP-58-C8 Strategic initiative for finding the missing people with TB

Progress and partners' perspectives on supporting countries to find the missing cases

E Wandwalo[1] [1]Global Fund, Geneva, Switzerland. e-mail: eliud.wandwalo@theglobalfund.org

Dr Eliud Wandwalo will present a joint talk/slide set by the TB partners including the Global Fund, WHO, Stop- TB, and USAID on supporting 13 countries with 75% of missing TB cases, identified for Global Fund Catalytic funding during the 2017-20 funding cycle. The talk will focus on progress achieved to date, and provide an overview of factors that have contributed to this, as well as more detailed granularity on approaches used by partners in their support.

Addressing human rights and gender barriers in achieving the goal of reaching the people with TB whom we currently miss

O Mumba[1] [1]EANNASO, Dar es Salaam, Tanzania, United Republic of. e-mail: mumba@eannaso.org

Many of the factors that increase a person's vulnerability to tuberculosis (TB) or reduce their access to services to prevent, diagnose and treat TB are associated with their ability to realize their human rights. A human rights-based approach to TB prevention, treatment and care can help programmer managers, civil society and other TB partners overcome the many barriers to effective TB prevention, treatment and care. Examining the gender dimensions of TB is also important for overcoming barriers to effective prevention, coverage and treatment of tuberculosis. This talk will describe work carried out to address these human rights and gender barriers.

Philippines: progress in screening and testing for TB in line with high-level commitment

A Garfin[1] [1]National Tuberculosis Programme, Philippines, Manila, Philippines. e-mail: garfinamc@gmail.com

The Philippines, one of the high burden TB countries, has recently engendered increasing political commitment towards ending the TB epidemic. The country is scaling up intensified activities in screening and testing for TB to detect and notify 2.5 million TB cases by 2022 as committed during the High Level Meeting during the United Nations General Assembly last September 2018. Finding these cases will decrease the TB incidence rate by 23%. With this commitment, there is a need to collaborate with the different sectors that can help detect and notify these TB cases. Dr. Anna Marie Celina Garfin, the NTP manager of the Philippines will be describing and exploring the reasons for the recent upsurge in enthusiasm and activities designated to end the TB Epidemic in her country.

Innovative means to find and report new TB cases in India

K Sachdeva[1] [1]Delhi, India. e-mail: ddgtb@rntcp.org

In April 2018, India launched a scheme to provide financial incentives for nutritional support, mediated via digital technologies. This Direct Benefit Transfer (DBT) scheme delivers Indian Rupees (INR) 500/month to TB patients while on treatment, taking advantage of India's universal biometric identification system (AADHAR) and Nikshay online electronic TB register. In late 2018, India also introduced an electronic tool in pilot sites to start capturing data for contacts of TB patients, providing key indicators for management of TB infection.

SP-59-E1 Amplifying the voices of the TB-affected community through OneImpact: a mobile community-based monitoring (CBM) technology system

What is CBM and how can it contribute to finding the missing people with TB?

C Smyth[1] [1]Stop TB Partnership, Geneva, Switzerland. e-mail: caoimhes@stoptb.org

Community-based monitoring (CBM) for accountability is an important element of a Community, Rights and Gender approach to TB. It enables communities to collect and interpret information about the availability, accessibility and quality of TB services and the conditions and barriers that undermine or hinder the delivery of these services. Currently this data is not collected ei-

ther routinely or periodically. As a result, TB planning is uninformed by the patient experience and responses to challenges faced are slower than they could be. To support CBM interventions Stop TB Partnership developed a CBM framework and digital solution platform and implementation handbook to facilitate CBM in TB.

CBM: improving access to information on TB in the Democratic Republic of the Congo

M Lunga[1] [1]Club des Amis Damien (CAD), Kinshasa, Congo (Democratic Rep.). e-mail: maxilunga@yahoo.fr

In 2017 DR Congo, under the Global Fund Initiative to find the missing people with TB and with the technical support of Stop TB Partnership, developed a Community, Rights and Gender strategy. They conducted several assessments and generated data and strategic information for programmatic planning and action. One of the bottlenecks identified was the absence of real time data on human rights barriers to access to inform advocacy and programmatic planning and responses. In 2018 DR Congo with technical assistance from STP conducted a needs and feasibility assessment to conduct CBM using the STP digital solution platform, an intervention that has since been integrated and adapted into the existing community health care model in Kinshasa. The data generated has demonstrated an improvement in TB knowledge among TB patients, one the barriers to access identified in the CRG assessment.

CBM: generating information on drug side effects, interfering with TB treatment completion in Ukraine

O Klymenko[1] [1]TBpeople Ukraine, Kiev, Ukraine. e-mail: olyaklymenko2910@gmail.com

The burden of drug resistant TB (DR-TB) in Ukraine is high. Urgent actions are needed to prevent further spread of DR-TB. People on DR TB treatment face many challenges, most notably side effects. Side effects such as nausea, hearing loss and fatigue, which impact a persons' quality of life. To better understand the burden and impact of side effects, Ukraine leveraged and adapted the Stop TB Partnership CBM digital platform to monitor these side effects. The intervention is being implemented in Cherkasy region by TBpeople Ukraine, supported by Public Health Center and data is routinely collected by a local peer support network who provide daily treatment adherence support. The information generated is being used to inform community advocacy on out of pocket expenses related to TB.

Using OneImpact, a digital CBM system to influence policy and programming decision-making: experiences in Tanzania

O Mumba[1] [1]EANNASO, Dar es Salaam, Tanzania, United Republic of. e-mail: mumba@eannaso.org

Using a community-driven and multi-stakeholder approach to develop and drive a digital CBM intervention, Tanzania is monitoring the availability, accessibility and quality of TB services in Kigoma. Led by TB survivors, this initiative has been able to document critical issues which have been resolved at the community, regional or national level. The outcome of the intervention development process resulted in a transparent accountability framework and to date evidence generated as demonstrated efficacies in community responses to problems reported from the patient perspective. The digital community monitoring systems is also being piloted as a mechanism to bring community feedback into the Tanzania National Coordination Mechanism (TNCM) as a way to get community feedback in programmatic management.

SP-60-C8 TB-HIV care cascade analysis to inform programmatic management and quality service delivery

Overview of the global cascade of TB-HIV activities

A Baddeley[1] [1]World Health Organization, Geneva, Switzerland. e-mail: baddeleya@who.int

Close to half a million people with HIV-associated TB were not reported to have started TB treatment in 2017, and of the 464,000 that were reported around 90,000 did not receive life-saving ART. Half of the 30 countries with the highest burden of HIV-associated TB did not report initiating TB preventive treatment. This presentation will describe the cascades from the different entry-points, and will highlight the missed opportunities and gaps in TB/HIV care continuum from data reported in 2019.

Diagnostic cascade: challenges and experience from the India

A Puri[1] [1]National AIDS Control Organization, Delhi, India. e-mail: ddgbsd.naco1@gmail.com

Presentation focuses, how India has been working to reduce the case detection gap through co-location of TB and HIV diagnostic services, developing specific strategies, focusing key populations, strengthening of HIV testing among presumptive TB cases, collaboration with the private sector, and strengthening monitoring mechanisms – crucial to address leaky cascade.

SP-61-C9 Making informed and smart choices: evidence-based optimisation of national strategies to end TB

Finding the "missing" TB patients just got easier: a faster way to conduct a patient pathway analysis

J Brown[1] [1]Linksbridge SPC, Seattle, United States of America. e-mail: jessie.brown@linksbridge.com

The Patient Pathway Analysis (PPA) methodology was developed to help TB programs understand the alignment between where people seek care and where TB services are provided. The PPA brings together data on care seeking and service availability to reveal key-gaps in access to TB diagnosis and treatment. Results from a PPA shed light on where people with TB might be missed by the current health system and offer suggested points for intervention by programs. For these reasons, the PPA has emerged as an important component of the data and evidence ecosystem to support TB policy and planning. A PPA may be implemented at the national or subnational level to better understand gaps in access to care and optimize interventions accordingly. The presentation covers the following three questions: (1) Why conduct a PPA, (2) How to conduct a PPA, and (3) How to conduct a PPA faster -introducing the PPA wizard.

Care cascade analysis: what happens where and why?

M Meis[1] [1]The Hague, Netherlands. e-mail: max.meis@kncvtbc.org

According to the Global TB Report 2018, an estimated 3.6 million TB patients were missed by health programmes in 2017. Despite significant global programme efforts, this was only a modest reduction of 400,000 from the 4 million reported in 2016, and in no way sufficient to achieve the targets set out in the Global End TB Strategy. Performing a care cascade analysis does not only inform programmes, about at which stage of their journey to cure patient's might be missed, but also, where those diagnosed and reported might be lost.
This presentation demonstrates how routine data analysis and visualisation can be effectively used to facilitate evidence based strategic planning at national, subnational and facility level. This in turn will allow for more targeted and efficient resource planning and interventions.

MATCH: using sub-national data to rationally prioritise interventions to meet local needs

M Bakker[1] [1]KIT Royal Tropical Institute, Amsterdam, Netherlands. e-mail: m.bakker@kit.nl

The MATCH Approach (Mapping and Analysis for Tailored disease Control and Health system strengthening) has been successfully applied in African and Asian countries to support strategic decision making on subnationally tailored interventions. The approach has supported NTPs to allocate scarce resources based on identified subnational variations and gaps in delivery and access to healthcare. To do this, multiple sources of geographically, temporally and demographically disaggregated data have been collated, mapped and spatially analysed to identify geographic pockets of people with TB who are likely missed throughout the pathway of care. Mapping subnational data enables triangulation of spatial variations in TB notifications, TB program efforts and TB risk factors, and very importantly, identification of local anomalies (how local areas deviate from their surrounding areas). During the presentation, a selection of examples will be shared in which the NTP applied MATCH to determine where and how to find missed cases of TB.

Maximising impact with limited resources: optimisation versus prioritisation

K Fiekert[1] [1]KNCV Tuberculosis Foundation, The Hague, Netherlands. e-mail: kathy.fiekert@kncvtbc.org

TB programmes the world over struggle trying to balance the ever-increasing calls for setting ambitious targets with inadequate availability of resources. Donors' and national governments' demands for prioritization have left many programmes with impossible decisions of having to select one intervention over another and/or focussing on one key affected population or geographic area over another. We argue that this approach has undermined the global and national End TB strategy and, in some cases, augmented health care inequalities. It is therefore time for a rethink and aim for evidence-based optimization of interventions using the People Centred Framework approach. This will ensure realistic target setting and the right balance of approaches/ interventions matched to geographic needs, target groups and available resources. The design is based on findings from the PPA, Care Cascade Analysis, GIS and other available data and corresponding to different funding scenarios.

SP-62-C4 Improving access to TB care for children: successful approaches and upcoming opportunities

Availability of paediatric TB services in sub-Saharan Africa: results from CaP TB site-level assessment in six African countries

L Denoeud[1] [1]EGPAF, Geneva, Switzerland.
e-mail: ldenoeud@pedaids.org

Data on availability of pediatric TB services in Sub-Saharan Africa are scarce. In preparation for the CaP TB project roll-out, we performed facility assessments to verify the status of pediatric TB service delivery under standard-of-care and identify key implementation challenges. Between February and June 2018, EGPAF in collaboration with NTPs collected site-level data in 203 health facilities across six African countries. We assessed the availability of key pediatric TB services availability across different child health entry points and different levels of the health care system.
Results showed high heterogeneity between countries, but some common challenges could be identified: weak integration of TB pediatric services in other child health entry points (MCH, nutrition services); limited diagnostic capacity including capacity to perform complex sample collection procedures and access to Xray and Xpert testing; poor implementation of active case finding activities (i.e contact tracing) and TB preventive Treatment. Detailed results will be presented.

Breaking the cycle: comprehensive childhood DR-TB management in Tajikistan

J Kliescikova[1] [1]Dushanbe, Tajikistan.
e-mail: tajikistan-medco@oca.msf.org

Globally, the diagnosis and treatment of children with DR-TB is neglected. Historically, challenges to case-finding, drug-susceptibility testing and regimen design have resulted in deprioritisation of this at-risk group in national programme planning. In Tajikistan, a high proportion of people is diagnosed with rifampicin resistance and transmission of resistant strains is common within households. Médecins sans Frontières have been collaborating with the National TB programme of Tajikistan since 2011 to develop and deliver a comprehensive package of DR-TB management amongst children and adolescents. The programme is based on a holistic approach that incorporates household contact tracing, molecular diagnostics, drug compounding, family observed therapy, psychological counselling and social support, use of paediatric formulations, and further plans for delivery of preventive therapy to contacts. The implementation of newer and repurposed TB drugs allowed greater use of injectable-free regimens and improved treatment responses. Lessons learnt through implementation of this programme will be discussed.

Successes in facilitating introduction of paediatric-friendly formulations of TB medicines

B Waning[1] [1]Stop TB Partnership / Global Drug Facility (GDF), Geneva, Switzerland. e-mail: brendaw@stoptb.org

The Stop TB Partnership's Global Drug Facility (GDF) plays a key role in facilitating introduction of new tools for TB. In the past few years, several paediatric-friendly TB medicines have become quality-assured. GDF has used its unique combination of in-country technical assistance programme, market-shaping and partner coordination work, procurement services and initial funding to buy products in order to get these new tools into programmes. This session will highlight successes with introducing appropriately-dosed, paediatric-friendly, fixed-dose combination products for drug-sensitive TB and paediatric-friendly formulations for drug-resistant TB and present job-aides available for programmes that would like to implement these products.

SP-63-B7 Fighting to breathe: living with asthma, COPD and chronic respiratory diseases, and how to end the silence

Drivers of the major causes of lung disease around the world

G Marks[1] [1]University of Sydney, Sydney, Australia.
e-mail: guy.marks@sydney.edu.au

Conventionally, we have sought to classify diseases as communicable or non-communicable or as genetic or environmental. Increasingly it is become clear that such simplistic distinctions are both inaccurate and unhelpful. The causes of lung disease are multi-factorial, with political, economic, social and environmental factors all important and tending to interact. Complex, multi-faceted interventions are required to make a major impact on the high burden lung diseases afflicting poor and vulnerable populations in the world today. There are some important opportunities for health gain, including active case finding for tuberculosis, effective action again tobacco, leveraging action for climate change to also include action to improve air quality and improving access to effective medicines including inhaled corticosteroids for asthma and targeted use of antibiotics for pneumonia. We need research to identify the key drivers of change in each of these domains and then advocacy and action to motivate this policy change

Post-TB sequelae

B Allwood[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: brianallwood@gmail.com

For many patients TB does not end on the completion of treatment, and there are many long-term consequences. This talk will focus primarily on the long-term respiratory consequences of tuberculosis from a physician's perspective. Content will include evidence of the magnitude of the problem and a description of the different phenotypes of post-TB lung disease. TOPD will be discussed in more detail, highlighting the mechanism of air-flow obstruction and presentation of available evidence for treatment.

Be He@lthy, Be Mobile WHO initiative for CRDs: experiences and challenges – the way forward

A El Sony[1] [1]Epidemiological Laboratory (Epi-Lab) for Public Health and Research, Khartoum, Sudan. e-mail: asmaelsony@gmail.com

The use of mobile technology including SMS, apps, telemedicine is increasingly considered as a way to improve access to prevention, diagnosis and management of non-communicable diseases (NCDs) including chronic respiratory diseases (CRDs). This talk will set the scene of fighting the global health burden of CRDs through new technology based on mobile technology, to help combat non-communicable diseases (NCDs) including (CRDs). It will shed light on the mHealth programme-specific handbooks that act as aids to policy-makers and implementers of national, or large-scale, mHealth programmes with a focus on experiences from LMICs

Global state of COPD and asthma: the need for a holistic approach

K Mortimer[1] [1]Liverpool School of Tropical Medicine, Liverpool, United Kingdom. e-mail: kevin.mortimer@lstmed.ac.uk

This talk will set the scene of the global state of COPD and asthma, highlighting the particular needs of the World's poor with – and at risk of developing – asthma and COPD. The talk will be put in the context of The Union's current Strategic Plan for Lung Health and aim to generate discussion about how to move from Strategic Thinking to Action that will help end the emergency of COPD and asthma.

SP-64-D8 Modelling to support ending the emergency: science, leadership, action

Modelling to inform "strategic" active case finding of TB cases in rural Nepal

S Shrestha[1] [1]Johns Hopkins Bloomberg School of Public Health, Balitmore, United States of America. e-mail: souryashrestha@gmail.com

Global declines in TB incidence are slow, and TB transmission remains high in many high-burden settings like Nepal. We aimed to estimate the impact of active case finding (ACF) in the context of ongoing IMPACT-TB ACF program in four districts of Nepal. Using transmission models informed by data on local demography and TB, we explored the impact of ACF under scenarios representing different sources of heterogeneity. We found substantial (> 10-fold difference) geographical heterogeneity in VDC-level (small administrative units) TB notification rates within these districts. If the observed heterogeneity in TB notifications reflected heterogeneity in transmission, targeting high-incidence "hotspots" were likely to be impactful. However, if heterogeneity primarily reflected underlying disparities in access to TB healthcare, prioritizing remote areas with low access to healthcare, could be equally important. Understanding these differences is key to ending the TB emergency in Nepal.

Optimising approaches for active case finding for TB: a modelling analysis

L Cilloni[1] [1]Imperial College London, London, United Kingdom. e-mail: l.cilloni15@imperial.ac.uk

In high-burden settings, should active case-finding efforts employ smear microscopy, rather than more sensitive (but more costly) rapid molecular diagnostics? We aimed to address this question in the context of Chennai, India. We constructed a dynamic transmission model, consistent with urban Chennai, and compared ACF approaches employing either microscopy, or GeneXpert for TB diagnosis. We compared the potential impact and cost of both approaches. Screening 50% of the slum population per year in 2019-36 would incur an incremental cost of USD 42 million (95% CI 27-74 million) and USD 40 million (95% CI 16-62 million) when using smear and GeneXpert, respectively, with comparable epidemiological impact. In the case of smear, approximately 80% of the total intervention costs would be associated with treating false-positives. Owing to its specificity, smear-based ACF may not be a cost-effective alternative to Xpert-based ACF in urban India. This is important information for ending the TB emergency in India.

Policy perspective: is modelling a useful tool to combine robust scientific evidence and leadership to identify cost-effective strategies to accelerate progress to end the emergency?

B Kumar[1] [1]Global Coalition of TB Activists, New Dehli, India. e-mail: blessi.k@gmail.com

I will describe the country and global TB policy making context, give examples of country and global modelling work, highlight future modelling needs, and give my interpretation of the advantages and disadvantages of modelling for country and global policy making and from the community perspective. Highlight how modelling can contribute to a person centered rights based care for TB.

SP-65-C8 Reaching the missing men: strategies to improve men's access to TB diagnosis and treatment

Sex disparities in TB burden and care

K Horton[1] [1]London School of Hygiene and Tropical Medicine, London, United Kingdom. e-mail: katherine.horton@lshtm.ac.uk

Global and regional TB incidence, case notifications, and deaths have been higher for men than women every year that estimates have been reported. Recent prevalence surveys, showing TB prevalence is over twice as high among men as among women, indicate this disparity is not a consequence of a female disadvantages in TB care. In fact, prevalence-to-notification ratios indicate greater gaps in detection and reporting among men than women. Men are estimated to remain infectious in the community a year longer than women in some settings, suggesting TB screening rates are much lower among men than women. Our recent modelling work in Viet Nam suggests that strategies to reduce the gender gap in TB screening by improving men's access to care could have a substantial impact on TB incidence and mortality, not only in men, but also in women and children.

What do men need, what do men want?: identifying preferences for a male-centred TB care and support initiative, Buffalo City Metro Health District, South Africa

A Medina-Marino[1] [1]Foundation for Professional Development, East London, South Africa. e-mail: andrewm@foundation.co.za

In South Africa, men with TB struggle to remain in care and have worse treatment outcomes compared to women. The impact of this is reflected in recent work revealing that TB in South Africa is a primary driver of men's lower life expectancy. Research demonstrates that men's health behaviours are influenced by the availability and exchange of resources within their networks. Guided by the Network-Individual-Resource model, we qualitatively identified men's experiences while in TB care, the mental and tangible resources needed and/or accessed while engaged in care, and how men's resources may function together to influence their TB-related health behaviours and outcomes. We will also present initial findings on men's preferences for a subsequent male-centred TB care initiative. Finally we will discuss proposed studies aimed at further identifying the importance and interaction of men's mental and tangible resources, and the need for male-centred care initiatives to improve TB-related outcomes.

Khotla ("a gathering place for men"): Lesotho's most masculine clinic

T Chakare[1] [1]Jhpiego, Maseru, Lesotho. e-mail: tafadzwa.chakare@jhpiego.org

Lesotho has the second highest TB incidence rate in the world (852 per 100,000). Gender, cultural norms, and the lack of male-friendly services has resulted in delayed detection of TB and HIV among men. In July 2016, Jhpiego and the Ministry of Health established a stand-alone male clinic aimed at providing comprehensive, integrated, client-centred health services. By providing a separate confidential space for men, the Khotla Clinic has ensured earlier case finding for chronic conditions. At the clinic, universal TB screening and sputum is collected from presumptive patients. When the clinic opened in July 2016, TB diagnoses were high (47 patients with TB in the first 3 months) with high detection rates (27% yield). These rates have dropped to 12 patients with TB per quarter (10% yield in 2019), yet still suggest a pressing TB diagnosis gap among men at clinic inception.

Improving effectiveness and efficiency of systematic screening of high-risk population using gender- and age-specific TB rates in Nigeria

R Eneogu[1] [1]KNCV TB Foundation Nigeria, Abuja, Nigeria. e-mail: reneogu@usaid.gov

Ending TB epidemic requires applying epidemiological principles for efficiency and effectiveness. Two mobile diagnostic units, each fitted with a chest x-ray and GeneXpert machines, were deployed to areas with relatively high male populations. 62,416 clients were screened with chest x-ray, sputa from 5,755 presumptive clients were tested using Xpert MTB/RIF assay, and 919 patients were diagnosed with TB including 37 RR-TB patients. The number needed to screen (NNS) and number needed to test (NNT) to diagnose one patient were 59

and 5, respectively, for males and 98 and 10, respectively, for females. The NNS for males ranged by 10-year age groups from 47 to 69, compared to 54 to 188 for females. The age groups with the lowest NNS were 25 – 24 and 35 – 44. Similar patterns were observed with the NNT. Targeted screening of men of productive age group improves the efficiency and effectiveness of systematic screening.

SP-66-E2 Taking action: addressing the oft-neglected stigma of TB within the healthcare setting

Towards TB patient-centred care: stigma reduction strategies in healthcare settings

E Mitchell[1] [1]KNCV Tuberculosis Foundation, The Hague, Netherlands. e-mail: emhmitchell@gmail.com

This talk will provide an overview of health-related stigma to open this symposium. The talk addresses common drivers and facilitators of TB patient stigmatization, such as ritual segregation, misunderstandings of transmission risk, poor working conditions, and disparagement of TB health care workers within medical hierarchies. She will analyze how these drivers of stigma within healthcare facilities can negatively impact TB care in different contexts. This talk will reiterate the importance of rigorous methods to effectively measure TB stigma in health facilities, before describing several multi-level approaches that are being tested to specifically target the main drivers of both TB stigma and drug resistant TB stigma.

Sharing stories of occupational TB-related stigma in healthcare worker interactions in South Africa

T Mosidi[1] [1]University of Cape Town, Cape Town, South Africa. e-mail: thatomosidi@gmail.com

As a doctor and survivor of XDR-TB, Dr. Mosidi will begin by recounting her experiences with stigma and discuss how the "TB-Proof" fallacy helps to perpetuate stigma between healthcare workers towards other health care workers. She will recommend actions that need to be taken to reduce workplace stigma in healthcare facilities and interventions, such as increased biosafety measures that need to be implemented to create a safer working environment for a spectrum of healthcare providers dealing with TB. In this presentation, Dr. Mosidi will also advocate the importance of sharing stories of occupational TB as an intervention strategy and the impact these stories can have on reducing stigma in healthcare settings.

Advocating for policy reform: the patient perspective on how current policies fuel TB stigma

N Venkatesan[1] [1]Economic Times, Mumbai, India. e-mail: nandita.venky@gmail.com

As a TB survivor, Ms. Venkatesan will discuss the role current policies play in increasing TB stigma in the healthcare setting and provide a unique insight into ways to combat TB stigma in health facilities in order to ensure better patient care. She will also examine what HIV advocates are doing to reduce HIV stigma and how those techniques can be translated to address TB stigma. Throughout this presentation, recommendations for modification of current policies and practices used in health facilities will be made. The presentation will include steps that healthcare providers can take to be better advocates for their patients and thus help reduce TB stigma.

Recommendations on creating stigma-free working environments to benefit TB HCWs and their patients

R Nathavitharana[1] [1]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, United States of America. e-mail: rnathavi@bidmc.harvard.edu

This talk will examine how internal and external stigma towards TB shapes health seeking behaviors in both patients and healthcare workers. Using case studies, this talk will reiterate the importance of improved training and education for healthcare personnel and emphasize the need to strengthen occupational health systems in order to address stigma. Recommendations on pathways to increasing leadership amongst TB healthcare providers will be shared.

The CRESIPT trial: a comprehensive approach to addressing TB-related stigma in Peru

C Evans[1] [1]Universidad Peruana Cayetano Heredia, Lima, Peru. e-mail: carlton.evans@ifhad.org

Persons with tuberculosis often describe the psycho-socio-economic effects of tuberculosis-related stigma being worse and more prolonged than symptoms and side-effects. Much of this stigma occurs in health establishments, worsened by infection control precautions that leave patients feeling "unclean", especially if they are required to be observed taking every dose in health establishments. The CRESIPT trial has recruited 1,617 newly diagnosed patients with tuberculosis, providing half with an integrated socioeconomic support package aiming to empower them, harnessing peer-led stigma reduction groups and educational information sessions aimed to dispel misinformation. In order to further reduce stigma, this package is integrated with evidence-based, pragmatic infection control guidelines that em-

phasise informing patients when they no longer pose any significant transmission risk. Baseline results characterising the experience of tuberculosis-related stigma in health establishments will be compared with 6-month follow-up results, to evaluate the impact of a socioeconomic intervention package in reducing tuberculosis-related stigma.

SP-67-D1 Using TBPSs to catalyse the response towards ending TB in the African region

TB impact measurement: the role of national TBPSs in the context of ending TB

I Law[1] [1]Geneva, Switzerland. e-mail: lawir@who.int

This presentation will describe the role of national TB prevalence surveys in providing more accurate estimates of TB burden. It will include an overview of the latest methodology, the global and regional progress in conducting surveys, with a focus on the African region. Finally, the presentation will highlight the key findings and lessons learnt from completed surveys in Africa since 2010.

Reprioritising active case finding following Rwanda's TBPS

P Migambi[1] [1]Tuberculosis & other Respiratory Communicable Disease Division, Institut of HIV/AIDS Disease Prevention Control, Rwanda Biomedical Center(RBC), Kigali, Rwanda.
e-mail: patrick.migambi@rbc.gov.rw

Rwanda completed a TB prevalence survey in 2012. The report, published in 2014, revealed that the prevalence was lower than previous WHO estimates. There were however still a significant proportion of missed cases. Based on the results, Rwanda adopted its active case finding strategy among high risk group (prisoners, contacts of TB patients, PLHIV, children under 15 years and people above 55 years). Findings from the survey also demonstrated a higher sensitivity of chest x-ray as a screening tool compared to symptoms, based on this the NTP introduced X-ray as part of the screening algorithm. This has resulted the increase of proportion of TB cases notified among high risk groups from 15% in 2014-2015 to 47% in 2017-2018 fiscal years.

Informed investment in TB diagnostic technologies and approaches following Zimbabwe's TBPS

C Sandy[1] [1]Ministry Of Health and Child Care, Zimbabwe, Harare, Zimbabwe. e-mail: dr.c.sandy@gmail.com

Zimbabwe's 2014 TB prevalence survey found the TB prevalence to be lower than WHO estimates. The survey informed a major programmatic shift, including increased significance (and procurement) of chest x-ray for TB screening due to its greater sensitivity than symptoms, adoption of Xpert MTB/Rif as the first test for TB, and targeted screening in selected communities. Other survey benefits include strengthening of the specimen referral system and TB laboratory network, capacity building for participating health workers and increased community awareness on TB. Mobile X-ray trucks used during the survey continue to be used for targeted screening in high risk and hard-to-reach populations. One key challenge to fully implement the recommendations from the survey is resource limitations, particularly inadequate access to CXR for TB screening and testing all presumptive TB cases with Xpert-MTB Rif.

Redefining TB care in Kenya after the national TBPS: business unusual

E Omesa[1] [1]Minisrty of Health, , Kenya.
e-mail: omesaeunice@gmail.com

Kenya's 2016 TB prevalence survey revealed a higher prevalence than previously estimated, and that >40% of people with TB were being missed. Additionally, 67% of people with TB (particularly men) did not seek care. Over 80% of people with TB symptoms who presented to health facilities were missed. As a screening tool, chest X-ray had a sensitivity of 88%; over 50% of TB cases with abnormal x-rays had no classical TB symptoms. The results prompted Kenya to re-focus on intensifying community awareness for early care seeking, and to target men and the urban poor. The TB diagnostic algorithm is being reviewed to prioritise GeneXpert and x-rays. Quality improvement was implemented in health facilities to address system gaps, and selected private providers, chemists and traditional practitioners were engaged. These approaches have resulted in a >10% increase in treatment coverage. The survey could however not provide sub-national burden estimates for geographical targeting.

Optimising TBPSs towards achieving the SDG and End TB targets in the African region

F Mavhunga[1] [1]World Health Organization, African Region (Afro), Brazzavile, Congo. e-mail: mavhungaf@who.int

This concluding presentation will focus on considerations of findings and lessons learnt from national surveys and how best they can be translated into country and regional action. There has been an upsurge in the number of African countries that have conducted TB prevalence surveys since 2010, and this has contributed immensely to the understanding of the national epidemics, as well as the regional patterns based on emerging common themes. While there has been an under-representation of West and Central Africa in the conduct of these surveys, there are critical lessons that can already be implemented in these countries in the absence of local surveys. Experiences from these surveys demonstrate the potential impact that data can have on public health practice. This presentation will highlight and discuss the need to build in post-survey implementation processes into survey design

ABSTRACT PRESENTATIONS THURSDAY 31 OCTOBER 2019

ORAL ABSTRACT SESSION (OA)

OA-01-C8 Active TB case finding: one size does not truely fit all: part 1

OA-01-300-31 Tuberculosis active case finding in high-burden areas: experience with mobile X-ray vans and Xpert MTB/RIF in Lima, Peru

DV Puma Abarca,[1] AK Millones Gomez,[1] J Jimenez Guevara,[1] MB Brooks,[2] JT Galea,[3] L Lecca,[4] MC Becerra,[2] SA Keshavjee,[2] CM Yuen,[2] [1]Socios en Salud - Partners In Health, Tuberculosis Program, Lima, Peru, [2]Harvard Medical School, Department of Global Health and Social Medicine, Boston, CT, United States of America, [3]University of South Florida, College of Behavioral and Community Sciences, Tampa, FL, United States of America, [4]Socios en Salud - Partners In Health, Direction, Lima, Peru. e-mail: dpuma_ses@pih.org

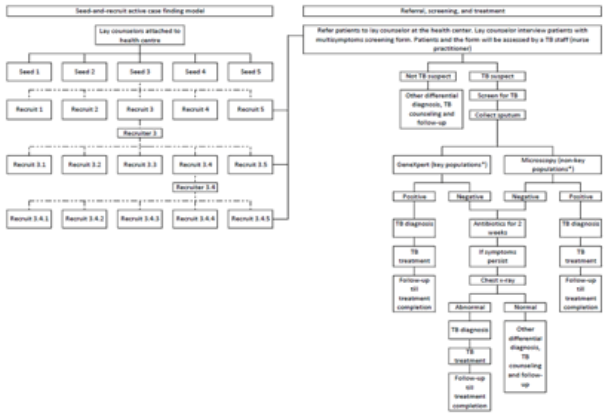
Background: In 2016, notified TB incidence in Peru was 86 per 100,000 people, and 124 per 100,000 people in northern Lima. Our objective was to determine if active case-finding in communities using mobile x-ray vans and Xpert can improve case detection.
Methods: Beginning in February 2019, we implemented mass community screenings in three districts of northern Lima using mobile x-ray vans equipped with the Cad4TB automated detection system. It was not necessary to report symptoms or risk factors to be eligible for screening. We requested sputum samples for Xpert MTB/RIF testing from participants >8 years old with abnormal radiographs, defined as a Cad4TB score >50. People diagnosed with TB were linked to treatment in public health facilities.
Results: During the first 50 days of implementation, we performed 2,944 radiographs, of which 589 (20%) were abnormal. Of people with abnormal chest radiographs, 397 (67%) were evaluated by Xpert. Of these, 20 (5%) were Xpert-positive, and 2 additional cases were diagnosed based on radiographic and clinical criteria; one case was rifampin-resistant.
Of the 22 people diagnosed with TB, 3 (14%) had a family member with a history of TB, and 16 (73%) reported cough in the last 14 days. The percentage of people diagnosed with TB via the intervention was around six times higher than the case notification rate in northern Lima. It was necessary to screen 134 people and conduct 27 Xpert tests to detect one case of TB.
Conclusions: Implementation of active case-finding using mass community screenings with a mobile x-ray van and Xpert identified more cases than would have been expected based on case notification rates. This strategy has the potential to improve case detection, helping to reduce ongoing transmission.

OA-01-301-31 Active case finding using a seed-and-recruit model: mobilising communities to find missing tuberculosis cases in Cambodia

S Tuot,[1,2] C Ly,[2] AKJ Teo,[3] S Ong,[2] D Cazabon,[4] MS Smelyanskaya,[5] SC Choub,[6] S Yi,[1,3,7] [1]KHANA, Center for Population Health Research, Phnom Penh, Cambodia, [2]KHANA, TB Reach Program, Phnom Penh, Cambodia, [3]National University of Singapore and National University Health System, Saw Swee Hock School of Public Health, Singapore, Singapore, [4]McGill University Health Centre, McGill International TB Centre, Montréal, QC, Canada, [5]Stop TB Partnership, Stop TB Partnership, Geneva, Switzerland, [6]KHANA, Executive Director Office, Phnom Penh, Cambodia, [7]Touro University California, Center for Global Health Research, Vallejo, CA, United States of America.
e-mail: tsovannary@khana.org.kh

Background and challenges to implementation: Globally, 36% of tuberculosis (TB) cases were undiagnosed in 2017, and a similar proportion of missing cases was documented in Cambodia. TB case finding remains a great challenge due to limited resources, geographical barriers, and social stigma.
Intervention or response: A community-led "seed-and-recruit" approach, shown to be effective in addressing HIV but previously untested for TB, was implemented in four operational health districts in Cambodia from July 2017 to June 2018. Representatives of TB key affected populations and TB survivors (seeds) verbally screened and referred other individuals in their social networks (recruits) for TB testing and treatment. The recruits of one "seed" in turn referred their contacts, thus facilitating a snowball effect. We describe the process and impact of the model on TB case detection and linkage to treatment.
Results and lessons learnt: During the intervention period, 6,275 individuals were screened for TB by the seeds and recruiters using a multi-symptom questionnaire. Ninety-percent of those screened were identified as presumptive for TB. All 5,620 individuals referred to the health centers were tested for TB and 29% were diagnosed with TB. More than 99% of people with TB enrolled in treatment.
In comparison with the 1-year historical baseline, there was an increase of 10% in new TB cases during the intervention period. At the end of the follow-up period, 97% of the patients were successfully treated.

Conclusions and key recommendations: The active case finding intervention using a seed-and-recruit model has empirically demonstrated an increase in TB diagnoses in underserved communities of Cambodia. Further research is required to confirm the cost-effectiveness of the model in comparison to other case-finding strategies. A social return on investment (SROI) would also need to explore.



[Figure 1-Active case finding with seed and recruit model]

OA-01-302-31 Defining novel TB risk groups for intensified case finding based on state-level case detection gaps in Nigeria

S Chang,[1] C Ogbudebe,[2] O Chijioke-Akaniro,[3] S-A Igbabul,[4] H Abdur-Razzaq,[5] O Okorie,[6] [1]Institute for Disease Modeling, HIV-TB, Bellevue, WA, United States of America, [2]KNCV Tuberculosis Foundation, Technical, Abuja, Nigeria, [3]Federal Ministry of Health, National TB and Leprosy Control Programme, Abuja, Nigeria, [4]Benue State Ministry of Health, TB and Leprosy Control Programme, Makurdi, Nigeria, [5]Lagos State Ministry of Health, Planning, Research and Statistics, Lagos, Nigeria, [6]Abia State Ministry of Health, TB and Leprosy Control Programme, Umuahia, Nigeria. e-mail: stchang@intven.com

Background: Nigeria has the lowest TB case detection rate among high TB burden countries and faces significant resource constraints. As a result, intensified case-finding activities should target risk groups expected to offer the highest case yield. In this study, we analyzed case notification data from admin1 (state) and admin2 (local government area, LGA) levels to identify novel risk groups based on case detection gaps that could be targeted to efficiently increase case detection rates.
Methods: Case notification and health facility data were provided by state TB programs and used to estimate notification rates at the LGA level. Prevalence data were obtained from the 2012 national prevalence survey, and covariate data (including urban/rural, poverty, age, and sex) from public databases. Case detection gaps were determined from covariate-stratified prevalence-to-notification ratios using non-parametric permutation tests, and statistical associations with case notification rates using multivariate regression.
Results: Age- and sex-specific case detection gaps were heterogeneous across states in Nigeria. In South West Nigeria, gaps were largest among males and ages 45-54 years (with relative gap sizes of 1.7 and 1.4 compared to females and other age groups, respectively). In South East Nigeria, gaps were largest among ages 15-24 years (with a relative gap size of 2.1 compared to other age groups) but similar by sex. Notification rates were more strongly associated with distance to health facility than other covariates, suggesting that placing facilities near population centres and screening location-specific demographic groups would efficiently increase case yields.
Conclusions: The "missing cases" in Nigeria differ in composition depending on geographic area. To maximize case yield, intensified case-finding activities should target groups informed by detection gaps at the admin1 level of the activity. Other national TB programmes may also benefit by developing strategies at the admin1 level rather than taking generalized "one size fits all" approaches.

OA-01-303-31 Cost analysis of community-based tuberculosis case finding and patient support in six urban districts of Ho Chi Minh City, Viet Nam

LNQ Vo,[1,2] RJ Forse,[3] AJ Codlin,[4] LMT Hoang,[5] M Caws,[6,7] K Lonnroth,[8] SB Squire,[9] HB Nguyen,[10] NV Nguyen,[10] N Teixeira De Siqueira-Filha,[6] [1]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [2]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [3]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [4]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [5]Ho Chi Minh City Public Health Association, Operations, Ho Chi Minh City, Viet Nam, [6]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom, [7]Birat Nepal Medical Trust, Operations, Kathmandu, Nepal, [8]Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden, [9]Liverpool School of Tropical Medicine, Clinical Tropical Medicine, Liverpool, United Kingdom, [10]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam. e-mail: luan.vo@tbhelp.org

Background: A higher proportion of the 'missing cases' must be found to end tuberculosis (TB) epidemic. Active case finding (ACF) has been shown to improve TB case detection and find sources of transmission earlier. However, more evidence on the investment requirements for ACF incremental to passive case finding (PCF) is needed prior to recommendation for programmatic implementation.
Methods: The study encompassed six intervention (ACF) districts and six control (PCF) districts of Ho Chi Minh City. ACF consisted of contact investigation and

systematic screening of vulnerable populations. Costs were collected from the health system perspective from 2017 and 2018 for the intervention arm only. Health system costs associated with programmatic PCF in both arms were excluded as sunk costs. We calculated one-time and recurrent costs associated with ACF using an ingredient approach. We calculated cost per additional bacteriologically-confirmed (Bac+) and all-form case detected. Additionality was based on the double-difference comparison of ACF notifications with the pre-intervention period and concurrent control area. Costs were collected in local currency and converted to US dollars (USD1=VND0.0000436).

Results: The total cost to implement ACF in six districts of HCMC was USD496,680.63 (19% one-time 81% recurrent costs). One-time costs consisted of Information/Communication equipment (USD38,573.64), diagnostic equipment (USD36,134.22), consensus-building meetings (USD13,336.97), and Trainings (USD7,371.07). 82% of recurring cost (USD329,863.21) were related to personnel and incentives. ACF activities resulted in an additionality of 630 Bac+ and 628 all-form cases, so that mean cost per additional case detected was USD788.38 for Bac(+) TB and USD790.89 for all forms of TB.

Conclusions: Scale-up of ACF will require extensive investment to expand population coverage of screening and testing activities. However, our parallel study on patient costs found that ACF could significantly reduce pre-treatment costs, so that the investment may be warranted to increase case finding and provide patient-centered care.

OA-01-304-31 Investigation of factors influencing cost effectiveness of a comprehensive active case finding strategy in Zambia

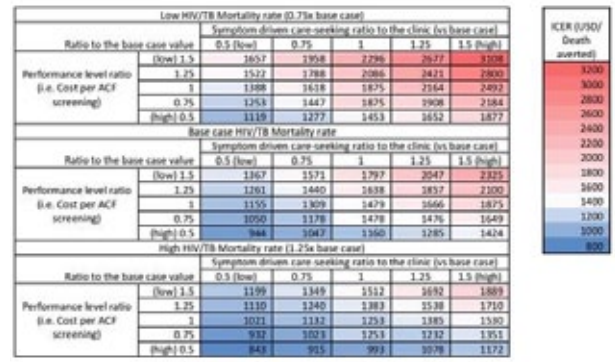
Y Jo,[1] H Sohn,[1] C Hanrahan,[1] P Hangoma,[2] M Kagujje,[3] M Muyoyeta,[3] D Dowdy,[1] [1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [2]University of Zambia, School of Public Health, Zambia, Zambia, [3]Centre for Infectious Disease Research in Zambia (CIDRZ), TB Program, Lusaka, Zambia. e-mail: yjo5@jhu.edu

Background: Active-case finding (ACF) programs play an important role in supplementing symptom-driven TB diagnosis and streamlining the TB care cascade. In designing ACF programs, it is important to consider resource constraints and local epidemiologic and operating factors in evaluating cost-effectiveness, scalability, and sustainability.

Methods: We developed a Markov state-transition model incorporating TB symptom status (TB-asymptomatic, non-TB-specific symptoms, and classical symptoms of TB) and associated care-seeking behavior. We used this model to evaluate the cost-effectiveness of a multi-component ACF program in Zambia that included both community-based outreach and facility-based programs. In this program, individuals with presumptive TB - identified through symptom screening and/or with the mobile chest X-ray - were asked to provide sputum for laboratory-based Xpert MTB/RIF testing. We collected empiric data on cost and performance based on time-and-motion studies and service volume statistics. From the health system perspective, we estimated the incremental cost effectiveness ratio (ICER, measured as cost per TB death averted) by simulating a population of 100,000 hypothetical individuals representative of Zambia's TB epidemiology and care cascade (over 5 year period).

Results: The ACF intervention incrementally diagnosed 479 (7157 versus 6678) cases of TB and averted 621 (719 versus 1340) TB deaths compared to the status quo (passive case-finding), at an incremental cost of $907,000. Thus, the ACF intervention cost an estimated $1460 per death averted. Key drivers of cost-effectiveness were the HIV/TB mortality rate, patients' symptom-associated TB care seeking probabilities, and the cost of ACF screening. Three-way sensitivity analyses revealed that care seeking behavior may be the primary determinant of ACF cost-effectiveness, especially when HIV/TB mortality is low (Figure).

Conclusions: Our results demonstrate that a comprehensive ACF program is highly cost-effective, with an estimated incremental cost of $1460 per death averted, when implemented in this setting with health system and social barriers that limit patient presentation to routine care.



[Figure: Cost per death averted through active TB case finding in Zambia]

OA-01-305-31 Role of community health workers and TB patient associations (Shuras) on TB case notification in Balkh province 2015-2018

N Tareen,[1] A Hamim,[1] GQ Qader,[1] BA Maseed,[1] SM Sayedi,[1] K Sediq,[2] MK Rashidi,[1] M Melese,[3] SP Guillermo,[3] [1]Management Sciences for Health (MSH), Challenge TB, Kabul, Afghanistan, [2]NTP, MoPH/NTP, Kabul, Afghanistan, [3]Management Sciences for Health (MSH), Challenge TB, Arlington, WA, United States of America.
e-mail: mrashidi@msh.org

Background and challenges to implementation: Due to lack of knowledge and awareness of tuberculosis (TB), many people with TB symptoms do not seek out care. This delay in diagnosis and treatment increases the risk of TB transmission within communities, which leaves many people undiagnosed and increasing mortality rates. Awareness creation and community level case finding in rural areas is a national priority.
Intervention or response: From 2015 to 2016, a total of 1,561 community health workers (CHWs) and 56 community health supervisors in the Balkh province were trained on conducting awareness raising events, identifying and referring presumptive TB patients (PTB), and observing TB treatment. In 2015 - 2018 regular awareness raising events were organized for communities and promoted through community gatherings, radio messages, and billboards. In addition to the CHWs, 150 associations (Shuras) consisting of TB patients who completed TB treatments, were created and trained to organize awareness raising events and conduct contact screening.
Results and lessons learnt: In 2015, CHWs/Shuras referred 817 PTB, which is 5% the overall PTBs identified in the Balkh province, and 50 (6.1%) were diagnosed with a form of TB. The number of patients who were notified of their TB status due to CHWs/Shuras referral steady increased from year, starting in 2015 with 50 (5%), in 2016 with 156 (13%), in 2017 with 400 (16%) and ending in 2018 with 433 (21%) (See Table 1).
Conclusions and key recommendations: The contribution of CHWs and Shura Associations was essential in identifying and notifying TB patients. The use of CHWs and Shura Associations in community-based DOTS in other rural provinces is recommended.

Year	Presumptive TB patients notified in province	Presumptive TB cases referred by CHWs/ Shura	All forms of TB notified in the province	All forms of TB notified among referred CHWs/ Shuras
2015	15,039	817 (5%)	1,032	50 (5%)
2016	21,308	2,504 (12%)	1,212	156 (13%)
2017	27,383	4,907(18%)	2,542	400 (16%)
2018	26,943	5,299 (20%)	2,109	433 (21%)
Total	90,547	13,401 (15%)	6,895	1039 (15%)

[Table 1: Engagement of community on CB DOTS activities]

OA-01-306-31 Cough screening is not enough: improving the sensitivity of systematic screening for active TB with chest X-ray

R Eneogu,[1] C Ogbudebe,[1] B Olaniyi,[2] M Tukur,[3] O Chukwuogo,[4] B Nsa,[1] A Lawanson,[5] M Gidado,[6] J Levy,[6] J Scholten,[6] [1]KNCV Nigeria / Challenge TB, Program, Abuja, Nigeria, [2]KNCV Nigeria / Challenge TB, ACF, Lagos, Nigeria, [3]KNCV Nigeria / Challenge TB, ACF, Kano, Nigeria, [4]KNCV Nigeria / Challenge TB, Program, Enugu, Nigeria, [5]National Tuberculosis and Leprosy Control Programme of Nigeria, Program, Abuja, Nigeria, [6]KNCV TB Foundation, Program, Hague, Netherlands.
e-mail: reneogu@gmail.com

Background and challenges to implementation: Systematic screening of high-risk groups is a key component of the End TB strategy. TB prevalence surveys show that a significant proportion of prevalent cases were asymptomatic. We explored the use of chest x-ray (CXR) aided with an automated interpretation software, computer-aided detection for tuberculosis (CAD4TB), to improve the screening sensitivity of high-risk groups for TB in Nigeria.
Intervention or response: Two mobile diagnostic trucks (MDTs), each fitted with a digital x-ray and Genexpert machines, were used to screen clients at high risk of TB for cough and with CXR interpreted with CAD4TB in southern and northern Nigeria. Clients who reported cough of ≥ 2 weeks and/or had a CAD4TB score greater than or equal to an established threshold (60 for MDT 1 and 56 for MDT 2) on CXR were classified as presumptive TB. Sputa from presumptive clients were tested with Xpert MTB/RIF and diagnosed patients were started on appropriate treatment. The sensitivity and positive predictive values (PPV) for CXR, cough ≥ 2 weeks and cough < 2 weeks were calculated.
Results and lessons learnt: After one year of implementation, 62,416 clients were screened for TB; with 6,062 (10%) identified as presumptive TB. Sputa from 5,755 (95%) clients were successfully tested with Xpert MTB/RIF, with 919 (16%) clients diagnosed with TB, including 37 (4%) RR-TB patients. The PPV for CXR, cough ≥ 2 weeks and cough < 2 weeks were similar; 18%, 17% and 19% respectively, but there was a wide variation in the sensitivity; 94%, 13% and 48% ($P < 0.001$) respectively. So, 87% and 39% of the patients did not report cough ≥ 2 weeks or cough of any duration respectively, compared to 6% who had CAD4TB scores lower than the threshold.
Conclusions and key recommendations: CXR improves the sensitivity of systematic screening for TB and should be considered as a routine screening tool for selected high-risk groups.

OA-01-307-31 Driving private sector notification from zero to four digits, JEET (The Joint Effort for Elimination of TB) experience in the province of Bihar, India

P Das,[1] G Kumar,[1] S Krishna Jha,[1] S Mannan,[2] [1]William J Clinton Foundation, TB Division, Patna, India, [2]William J Clinton Foundation, TB Division, New Delhi, India.
e-mail: pdas@clintonhealthaccess.org

Background and challenges to implementation: Of the targeted 1.4 million patients from private sector in 2018 by the National TB Programme (NTP), India reported 540,000 (38%) patients whereas the public sector reported 75% of the targeted numbers. Bihar reported 30% of the estimated private sector patients in the same period. Gap in notification by private providers is largely attributed to lack of clarity about the notification order and absence of systematic, consolidated efforts for sensitization of these providers.
Intervention or response: The Joint Effort for Elimination of TB (JEET) project, funded by Global Fund and supported by India's NTP, is being implemented across 23 provinces for effective and sustainable engagement with formal private providers to address the gaps of under reporting, non-standard diagnosis and treatment. A Patient Provider Support Agency (PPSA) model is being rolled-out for sensitization of providers through detailing in-clinic visits and Continuing Medical Education, providing support for notification, linking NTP GeneXpert and Fixed Dose Combination anti TB drugs along with treatment adherence support for private sector patients. Darbhanga in Bihar, with over 300 formal private providers, mostly in standalone clinics and small nursing homes, is being supported under the PPSA model.
Results and lessons learnt: Until June 2018, no patient was notified from private sector in Darbhanga. JEET team started engaging with providers from July 2018, yielding a total of 3355 private patient notifications in 2018 (of which 128 were diagnosed before the advent of the project) and 1201 patients in the first quarter of 2019. 139 formal private providers continue to notify TB patients. 1582 patients have been offered GeneXpert. All reported patients are on treatment and tracked for adherence to enable successful treatment completion.
Conclusions and key recommendations: Private sector needs to be systematically and sustainably engaged for TB control. PPSA-like engagement presents a potential to streamline diagnosis, reporting, treatment and adherence monitoring of the large number of private sector patients.

OA-02-D8 Modelling in the fight against TB

OA-02-308-31 Mathematical modelling of the epidemiological impact, budget impact and cost-effectiveness of novel tuberculosis vaccines on multidrug-resistant tuberculosis

C Weerasuriya,[1] R Harris,[1] F Bozzani,[1] G Gomez,[1] R White,[1] TB Modelling Group [1]London School of Hygiene and Tropical Medicine, Infectious Disease Epidemiology (IDE), London, United Kingdom.
e-mail: c.weerasuriya@lshtm.ac.uk

Background: The limited resources available for new TB control efforts, coupled with rising MDR-TB burden and costs warrant investigation into the role of vaccination in controlling TB drug resistance.
We model the potential impact of novel prophylactic vaccines on MDR-TB burden and identify vaccine characteristics likely to contribute most towards achieving the 2030 UN SDG and 2050 WHO End TB targets.
Methods: We constructed an age-stratified, deterministic, compartmental dynamic transmission model of TB, including treatment history, drug resistance and vaccination strata. We fitted "baseline" (no new vaccine) scenarios, to historic epidemiological and demographic data and projected (MDR-)TB epidemiology until 2050 in China, with and without scaled-up future programmatic MDR-TB management.
Into these baseline scenarios, we simulated introducing potential TB vaccines in 2027, with
(1) efficacy pre-infection, post-infection or pre- and post-infection,
(2) 5 years to lifelong duration of protection,
(3) and 30-90% prevention of disease efficacy.
We simulated routine vaccination of 9-year olds, with 10-yearly adult/adolescent mass campaigns. We estimated economic costs from a health service perspective to calculate incremental cost-effectiveness ratios as incremental costs per disability-adjusted life year.
Results: Vaccination will likely be effective in reducing MDR-TB burden, even alongside scaled-up programmatic management. Such scale up altered the primarily transmission-driven MDR-TB epidemic towards a mixed transmission-reactivation driven epidemic, improving the effectiveness of post-infection vaccines relative to pre-infection vaccines. Analysis of vaccine cost-effectiveness and budget impact in China and a multi-country comparison including India and Russia is underway.
Conclusions: Novel vaccines could contribute to reducing MDR-TB burden by 2030. Concurrent changes in programmatic management may alter the preferred characteristics of such vaccines.
We present the first dynamic model of TB which includes both vaccines and MDR-TB, whose results are

important for informing decisions in vaccine development, and programmatic considerations in efforts to end TB.

OA-02-309-31 Potential impact of new tuberculosis vaccines in China, South Africa and India and implications for vaccine development

RC Harris,[1] T Sumner,[1] GM Knight,[1] H Zhang,[2] RG White,[1] [1]London School of Hygiene & Tropical Medicine, TB Modelling Group, Department of Infectious Disease Epidemiology, London, United Kingdom, [2]Chinese Center for Disease Control and Prevention, National Center for Tuberculosis Control and Prevention, Beijing, China. e-mail: rebecca.harris@lshtm.ac.uk

Background: New tuberculosis vaccines are needed to help reach the WHO 2050 TB elimination goal. Insufficient evidence exists on the potential impact of new TB vaccines with varying characteristics and in different epidemiological settings. Two phase IIB trials reported positive efficacy results in 2018. To inform decision making, we estimated impact of new TB vaccines in three high-burden countries using mathematical models.

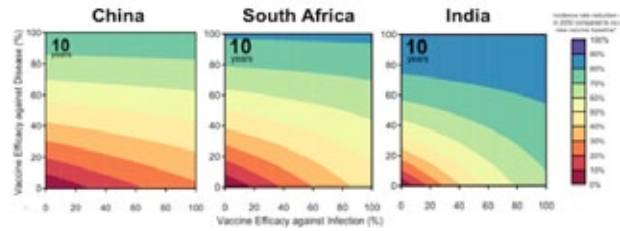
Methods: TB models were calibrated to age-stratified demographic and epidemiological data from China, South Africa and India. Vaccine efficacy to prevent infection and/or disease, effective in persons M.tb uninfected and/or infected, and duration of protection were varied. Routine early-adolescent vaccination and 10-yearly mass campaigns were introduced from 2025. Median population-level TB incidence rate reduction in 2050 compared to a no-new-vaccine scenario (% IRR) was estimated.

Results: In all settings, results suggest that vaccines preventing disease in M.tb-infected populations would have most impact by 2050(10-year, 70% efficacy against disease, IRR 51%, 51% and 54% in China, South Africa and India, respectively).

Vaccines preventing re-infection delivered lower impact(IRR 1%, 6% and 17%). Intermediate impact was predicted for vaccines effective only in uninfected populations, if preventing only infection(IRR 21%, 32% and 50%), or disease(IRR 19%, 26%, 51%), with greater impact in higher transmission settings.

Using phase IIB results, and assuming 10 years protection, predicted IRR for BCG revaccination 50% effective for preventing infection in uninfected populations was 16%, 19% and 39% for China, South Africa and India; and for M72/AS01$_E$ 50% effective for preventing disease in infected populations was 37%, 32% and 41%, respectively.

Conclusions: New TB vaccines could deliver substantial population-level impact. If prioritising impact by 2050, vaccine development should focus on preventing disease in M.tb-infected populations. Vaccines preventing infection or disease in uninfected populations may be useful in higher transmission settings. Impact depended upon epidemiological context, therefore different development strategies will be required.



[Median incidence rate reduction in 2050 compared to no new vaccine baseline for a pre- and post-infection vaccine with 10 years duration of protection, by percentage vaccine efficacy for prevention of infection (x-axes), and vaccine efficacy for prevention of disease (y-axis)]

OA-02-310-31 Impact of nutrition transition and ending hunger on the control of tuberculosis in high tuberculosis-burden countries

C-Y Wu,[1] M Ezzati,[2] K Lönnroth,[3] H-H Lin,[1] [1]National Taiwan University, Institute of Epidemiology and Preventive Medicine, College of Public Health, Taipei, Taiwan, [2]Imperial College London, Faculty of Medicine, School of Public Health, London, United Kingdom, [3]Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden. e-mail: jenny1004wu@gmail.com

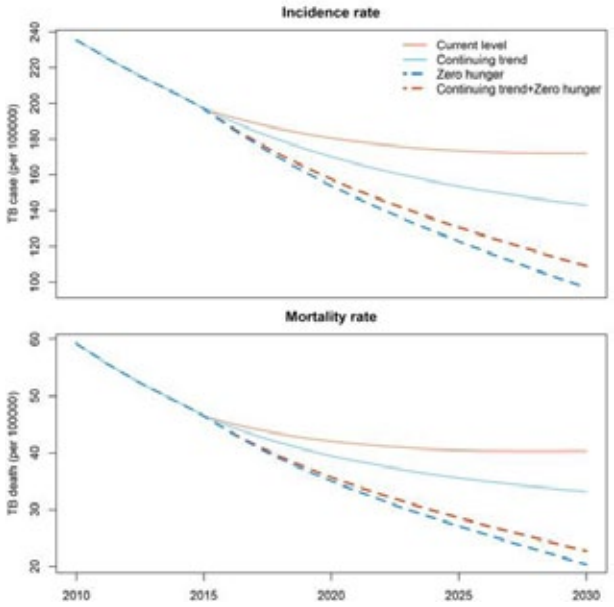
Background: Increasing epidemiological evidence revealed a strong and inverse relationship between body mass index (BMI) and tuberculosis incidence. Yet it is unclear how the global nutrition transition and the efforts of ending hunger in the SDGs would affect tuberculosis control in high burden countries.

Methods: We analyzed data from 12 high tuberculosis burden countries with low HIV prevalence. For each country a dynamic transmission model was constructed to account for the natural history of tuberculosis and the effects of BMI on tuberculosis risk. The association between BMI and tuberculosis risk (including the diabetes-mediated effect and the direct effect not mediated through diabetes) was obtained from a meta-analysis of cohort studies. The models were calibrated to the historical trend of tuberculosis epidemiology and BMI in each country. We estimated the cumulative reduction of tuberculosis incidence between 2015 and 2030 under different future scenarios of prevalence of underweight and overweight/obesity.

Results: If the mean BMI remained at the 2015 level and other factors remain unchanged, tuberculosis incidence and mortality would only decline by 12.9% (95% CrI:2.76-23.6%) and 14.0% (CrI:3.7-23.2%) from 2015 to 2030 ("Current level" in Figure). The continued increase in BMI would accelerate the decline in tuberculo-

sis incidence and mortality (additional decline of 14.7% (CrI:12.7-16.7%) and 15.6% (CrI:12.5-19.2%) respectively by 2030) ("Continuing trend"). Compared to the current BMI level, achieving the End Hunger target of SDGs ("Zero hunger") would bring an additional decline of tuberculosis incidence and mortality by 32.0% (CrI:20.0-43.8%) and 37.3% (CrI:26.1-49.6%) by 2030, equivalent to an avoidable 17.6 (CrI:5.5-30.4) million incident cases and 4.8 (CrI:1.2-11.0) million tuberculosis deaths.

Conclusions: Global nutrition transition and efforts to reduce hunger could have a major impact on future epidemiology of tuberculosis in high-burden countries. Our analysis highlights the potential impact of social and political solutions for TB in the SDG era.



[Weighted average of projections of TB incidence and mortality under four scenarios.]

OA-02-311-31 Identifying tuberculosis vulnerability clusters for targeted interventions

R Li,[1] F Nordio,[2] M Murray,[1,3] [1]Harvard T.H. Chan School of Public Health, Department of Epidemiology, Boston, MA, United States of America, [2]Brigham and Women's Hospital, Department of Medicine, Boston, MA, United States of America, [3]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America. e-mail: rul612@mail.harvard.edu

Background: Tuberculosis is sustained by persistent vulnerabilities in the population. Identifying vulnerable populations and disentangling the social and biological processes that lead to these vulnerabilities could inform prevention and control strategies.

Methods: Learning from the literature on market segmentation, a method often used in business settings for consumer profiling and targeted marketing, we developed a survey-weighted unsupervised learning technique that identifies distinct tuberculosis vulnerability clusters in the Indian population using data from the nationally representative National Family Health Survey in 2015-16. The method describes the joint distribution of epidemiologic risk factors that are known to have causal effect on tuberculosis transmission and progression. We validated this method by testing the spatial autocorrelation between identified clusters and self-reported tuberculosis within households. We further described the distribution of these vulnerability clusters across wealth quintiles.

Results: We extracted data on eight epidemiologic risk factors from 602,509 households representing 640 districts in India and identified three clusters of households with distinct underlying vulnerabilities to tuberculosis:
(1) a high-risk cluster characterized by undernutrition, crowding, young age, indoor air pollution and poorest access (32%),
(2) a high-risk cluster characterized by household smoking, drinking, indoor air pollution and poor access (26%), and
(3) a lower risk cluster but with a high prevalence of diabetes (42%).
High-risk clusters exhibit positive spatial autocorrelation with self-reported tuberculosis in neighboring districts (Moran's I $p< 0.02$). Even among households in the richest wealth quintile, over 30% belonged to one of the high-risk clusters.

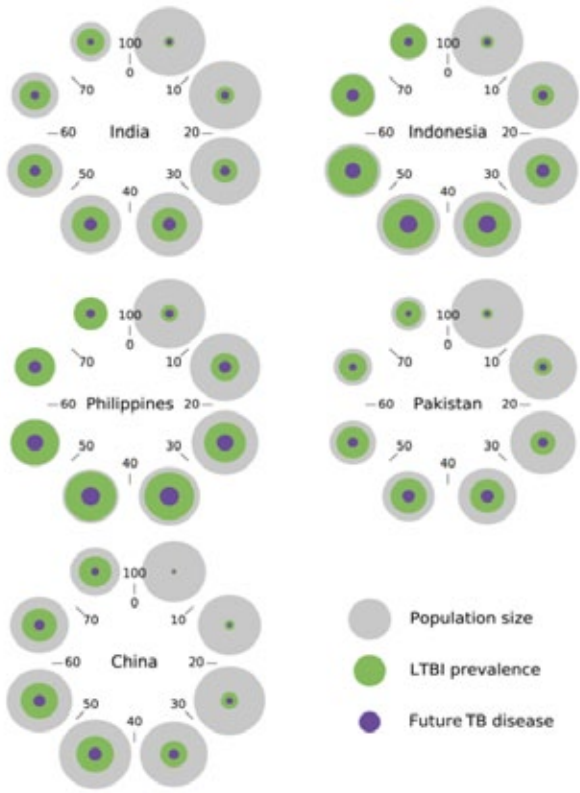
Conclusions: Preliminary analysis showed that in India, targeting active case finding or preventive therapy according to any single comorbidity or to the poorest households would not adequately address underlying vulnerabilities to tuberculosis. These results highlight the added value of examining the joint distribution of factors that lead to vulnerabilities for designing localized intervention strategies.

OA-02-312-31 Profiling Mycobacterium tuberculosis transmission and the resulting disease burden in the five highest tuberculosis burden countries

R Ragonnet,[1] J Trauer,[1] N Geard,[2] N Scott,[3] E McBryde,[4] Australian Tuberculosis Modelling Network [1]Monash University, School of Public Health and Preventive Medicine, Melbourne, VIC, Australia, [2]University of Melbourne, School of Computing and Information Systems, Melbourne, VIC, Australia, [3]Burnet Institute, Burnet Institute, Melbourne, VIC, Australia, [4]James Cook University, Australian Institute of Tropical Health & Medicine, Townsville, VIC, Australia. e-mail: romain.ragonnet@monash.edu

Background: Tuberculosis (TB) control efforts are hampered by imperfect understanding of TB epidemiology. The true age-distribution of disease is unknown because a large proportion of individuals with active TB remain undetected. Understanding of transmission is limited

by the asymptomatic nature of latent infection and the pathogen's capacity for late reactivation. A better understanding of TB epidemiology is critically needed to ensure effective use of existing and future control tools.
Methods: We use an agent-based model to simulate TB epidemiology in the five highest TB burden countries - India, Indonesia, China, the Philippines and Pakistan - providing unique insights into patterns of transmission and disease. Our model replicates demographically realistic populations, explicitly capturing social contacts between individuals based on local estimates of age-specific contact in household, school and workplace settings. Time-varying programmatic parameters are incorporated to account for the local history of TB control.
Results: We estimate that the 15-19 year-old age-group is responsible for more than 20% of transmission events in India, the Philippines and Pakistan, despite representing only 5% of the incident TB cases. Childhood TB represents around one-quarter of cases in these three countries, which is significantly higher than the proportions observed from notification data. In China, nearly three-quarters of incident TB occurs in the ≥45 year-old population. The calibrated per-contact transmission risk was found to be similar in each of the five countries despite their very different TB burdens.
Conclusions: Adolescents and young adults are a major driver of TB in high-incidence settings. Relying only on the observed distribution of disease to understand the age-profile of transmission is potentially misleading.

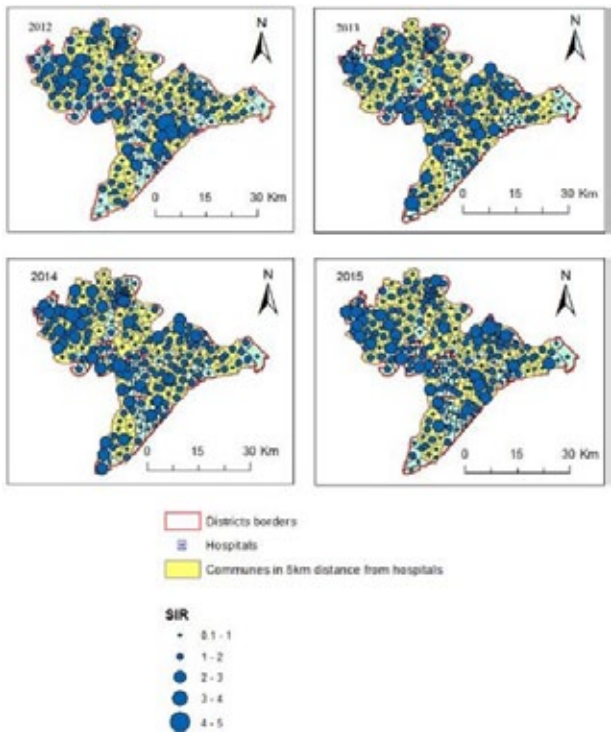


[Age-profile of the LTBI reservoir and proportion of current infections resulting in future TB]

OA-02-313-31 Use of geographically weighted Poisson regression to examine the effect of distance on tuberculosis incidence

L Bui,[1] Z Mor,[2] D Chemtob,[3,4] S Ha Thai,[5] H Levine,[4]
[1]Center for Research - Consulting and Support of Community Health, Monitoring and Evaluation, Ha Noi, Viet Nam, [2]Ashkelon Academic College, School of Health Sciences, Ashkelon, Israel, [3]Ministry of Health, Jerusalem, Department of Tuberculosis and AIDS, Tel Aviv, Israel, [4]Hebrew University of Jerusalem, Braun School of Public Health and Community Medicine, Jerusalem, Israel, [5]Ministry of Health, Administration of Medical Services, Ha Noi, Viet Nam. e-mail: longbv@rdh.org.vn

Background: The study described the geographical distribution of tuberculosis in Nam-Dinh province, Vietnam, by the Geographic Information System (GIS). It also compared Generalized Linear Model Poisson Regression (GLMPR) model with Geographically Weighted Poisson Regression (GWPR) model, which incorporate non-stationary spatial structures of data to determine the best fitting model to assess the association between tuberculosis age and sex standardized incidence ratio, distances from tuberculosis facilities and other social risk factors, such as population density, urban/rural status and household poverty rates.
Methods: All new and relapse tuberculosis patients aged ≥15 years in Nam-Dinh from 2012 to 2015 and data on social risk factors were combined into ArcGIS. Distances between communes to the nearest tuberculosis facilities were computed. Tuberculosis incidence was indirectly standardized by age and sex. GLMP and GWPR were performed to assess the association between the tuberculosis incidence and geographical distances as well as social risk factors.
Results: During the study period, 6,036 tuberculosis cases were recorded in the province. The average incidence was 82 cases per 100,000 population. In the GWPR model, social risk factors demonstrated spatially-varying effects on tuberculosis incidence in the different communes.
There was a negative association between tuberculosis incidence and the distance from the nearest clinic: age and sex standardized incidence ratio decreased by a factor of 0.87 for each 1km increased from the clinic.
The GWPR significantly removed spatial heterogeneity and minimized the residuals and spatial autocorrelation of the GLMPR, therefore fitted the finding better than GLMPR.
Conclusions: There was a negative association between the distance of the commune from the nearest tuberculosis clinic and tuberculosis incidence. GIS serves as an effective tool for tuberculosis programming in visually investigating trends of tuberculosis incidence and its relations to social and spatial factors. National tuberculosis programs should appropriate the distribution of tuberculosis clinics to the geographical incidence of disease.



[Geographical distribution of indirect age and sex standardized incidence ratios of 229 communes]

OA-02-314-31 TB from transmission in clinics in high HIV-burden settings may be far higher than suggested by contact data

N McCreesh,[1] A Grant,[2,3,4] RG White,[1] [1]London School of Hygiene & Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [2]London School of Hygiene & Tropical Medicine, Department of Clinical Research, London, United Kingdom, [3]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [4]University of KwaZulu-Natal, Africa Health Research Institute, Durban, South Africa.
e-mail: nicky.mccreesh@lshtm.ac.uk

Background: In high TB burden settings, only a small proportion of people's social contacts occurs in clinics. Estimates from South Africa range from 0.5-6%. Both people with infectious TB and people with increased susceptibility to disease progression may spend above average amounts of time in clinics however, potentially increasing the importance of transmission within clinics to overall disease incidence.
Methods: We developed an illustrative mathematical model of Mycobacterium tuberculosis transmission in clinics and other settings. We assumed that 1% of all contact time occurs in clinics.
We varied the ratio of clinic contact time of simulated HIV+ people compared to HIV- people, and of people with TB compared to people without TB, while keeping the overall proportion of contact time in clinics, and the amount of contact time of each person, constant. The model was fitted to data on TB and HIV in South Africa.
Results: With clinic contact time 10 times higher in HIV+ people, and five times higher in people with TB, 10.7% (plausible range: 8.5%-13.4%) of all TB and 16.3% (14.0%-19.2%) of TB in HIV+ people resulted from transmission in clinics. With contact rates in HIV+ people and people with TB five and two times higher respectively, 5.3% (4.3%-6.3%) of all TB disease and 7.7% (6.7%-8.8%) of TB in HIV+ people, was due to transmission in clinics.
Conclusions: The small amounts of contact time that occur in clinics may greatly underestimate their importance for TB disease in high TB/HIV burden settings.

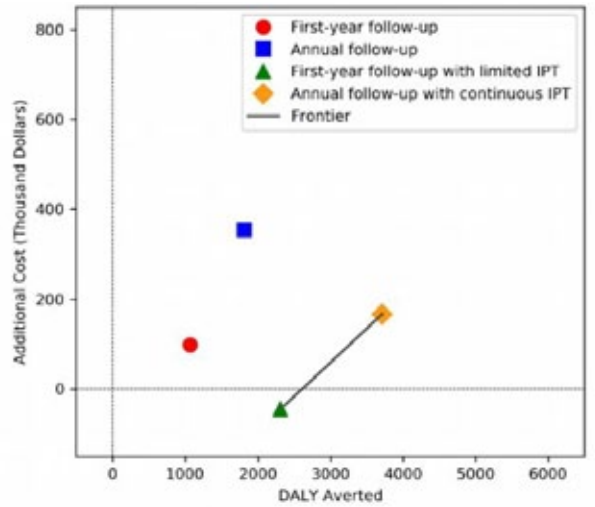
OA-02-315-31 Cost-effectiveness of post-treatment follow-up and secondary prevention of tuberculosis in a high-incidence setting: a model-based analysis

FM Marx,[1,2] T Cohen,[3] NA Menzies,[4] JA Salomon,[5] R Yaesoubi,[6] [1]DST-NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA), Stellenbosch University, Stellenbosch, South Africa, [2]Stellenbosch University, Department of Paediatrics and Child Health, Desmond Tutu TB Centre, Cape Town, South Africa, [3]Yale School of Public Health, Epidemiology of Microbial Diseases, New Haven, CT, United States of America, [4]Harvard School of Public Health, Department of Global Health and Population, Boston, MA, United States of America, [5]Stanford University School of Medicine, Department of Medicine, Standford, CA, United States of America, [6]Yale School of Public Health, Health Policy and Management, New Haven, CT, United States of America.
e-mail: fmarx@sun.ac.za

Background: In tuberculosis (TB) high-incidence settings, previously treated people remain at high risk of recurrent TB and contribute substantially to overall disease burden. Whether TB case-finding and preventive interventions among previously treated people are cost-effective has not been established.
Methods: We developed a dynamic mathematical model, and calibrated it to data from a setting of approximately 40,000 people with an estimated TB incidence exceeding 1.0% in suburban Cape Town, South Africa. We used the model to estimate the cost-effectiveness of follow-up examinations and secondary preventive therapy among individuals completing TB treatment. We investigated scenarios under which these interventions were limited to vs. extended beyond the first year post treatment.
Results: We estimate that a combination of follow-up examinations and secondary preventive therapy during the first-year post treatment would avert 2,109 (95% uncertainty interval [UI]: -1,609, 7,571) disability-adjusted life years (DALYs) over a 10-year period and would be cost saving compared to current control efforts. Sustained annual follow-up of previously treated individuals and continuous secondary preventive therapy would avert an additional 1,382 (95%UI 1,149; 1,615) DALYs

over 10 years at a cost of USD 162.2 per DALY averted. Strategies of follow-up without secondary preventive therapy were dominated (i.e. they had less health benefit at greater cost) (Figure).

Conclusions: In this high-incidence setting, post-treatment follow-up and secondary preventive therapy can accelerate declines in TB incidence and potentially save resources for TB control provided that a majority of individuals completing treatment can be reached. Feasibility of implementing these strategies should be considered given their potential to accelerate declines in TB incidence in settings most severely affected by the disease.



[Best estimates of incremental costs and DALY averted for each of the intervention scenarios]

OA-03-A1 The host and the pathogen in detail

OA-03-316-31 Gut microbiome dysbiosis and correlation with blood biomarkers in active tuberculosis in endemic setting

R Ravindran,[1] A Khaliq,[2] S Afzal,[3] P Jena,[1] M Waheed Akhtar,[2] K Malik,[3] Y-JY Wan,[1] M Irfan,[3] I Khan,[1]
[1]University of California Davis Medical Center, Pathology, Sacramento, CA, United States of America, [2]University of Punjab, School of Biological Sciences, Lahore, Pakistan, [3]Forman Christian College, Department of Biological Sciences, Lahore, Pakistan. e-mail: rravindran@ucdavis.edu

Background: The etiologic agent of tuberculosis (TB), Mycobacterium tuberculosis (M.tb.), infects over two billion people worldwide. Active-TB is an inflammatory disease and is increasingly viewed as an imbalance of immune responses to M. tb. infection. Understanding of the underlying mechanisms of a switch from latent infection to active disease is not well worked out but a shift in the immune responses is thought to be responsible. Increasingly, the role of gut microbiota has been described as a major influencer of the immune system. And because gut is the largest immune organ we aimed to analyze the gut microbiome in active-TB patients in a TB- endemic country, Pakistan.

Methods: A total of 90 participants (TB patients n=50, Healthy n=40) were included in this study. Analysis of bcoA gene copy number was performed by qPCR and 16S rRNA gene was sequenced using Illumina MiSeq from stool DNA. Multiplex analysis of plasma antibodies, against eleven M. tb. antigens, in active-TB patient was performed and correlation with microbiota was evaluated.

Results: The study revealed that gut microbial genera associated with chronic inflammatory diseases (e.g., Enterococcus, Fusobacterium, Psuedocitrobacter, Rothia, Vagococcus etc.) were the major genera associated with active-TB. Plasma antibody profile against several M. tb. antigens, that we have previously published as specific biomarkers for active-TB, correlated closely with the patient gut microbial profiles. In addition, bcoA gene copy number which is indicative of the level of butyrate production by the gut microbiome and critical for the maintenance of gut health, was five-fold lower in TB patients compared to healthy individuals.

Conclusions: These findings suggest that gut health in TB patients is compromised, with implications for disease morbidity (e.g., severe weight loss) as well as immune impairment, and in addition to the plasma antibodies, or in combination with, gut microbiota can be used as active-TB biomarkers.

OA-03-317-31 Tuberculosis treatment promotes a healthy sputum microbiome that, post-treatment, resembles that of contacts

C Naidoo,[1] G Nyawo,[1] S Moodley,[1] Z Palmer,[1] Y Li,[2] B Wu,[2] J Clemente,[3] R Warren,[1] L Segal,[2] G Theron,[1]
[1]Stellenbosch University, Department of Biomedical Sciences, Cape Town, South Africa, [2]New York University School of Medicine, Department of Medicine, New York, NY, United States of America, [3]Icahn School of Medicine at Mount Sinai, Genetics and Genomic Sciences, New York, NY, United States of America.
e-mail: cnaidoo15@gmail.com

Background: Tuberculosis (TB) treatment requires long-term use of multiple antibiotics (including broad-spectrum rifamycins), however, knowledge of the impact of treatment on the microbiome is limited. We characterised the sputum microbiome of cases before, during, and after treatment.

Methods: Persons with TB symptoms were recruited in Cape Town, South Africa. Induced sputa were collected from 72 culture-confirmed cases at pre-treatment, months 2 and 6 (both during treatment) and months 12 and 18 (both post-treatment). Up to two healthy close contacts (total n=118) per patient provided induced

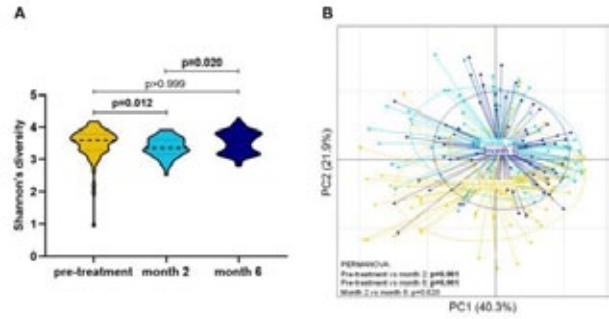
sputa at baseline, 6 and 18 months. After microbial DNA extraction, 16S rRNA sequencing was done using Illumina MiSeq and analyses with QIIME and R. Kruskal-Wallis testing and permutational multivariate analysis of variance (PERMANOVA) were used to compare groups.

Results: Cases had reduced microbial diversity (Shannon's index: 3.35 vs 3.59; p=0.012) and a distinct microbial composition (PERMAVOVA p=0.001) in sputum after 2 months of treatment vs. pre-treatment (Figure). At month 6, microbial diversity increased to pre-treatment levels, however, the overall composition remained altered (PERMAVOVA p=0.001), with Prevotella and respiratory pathogens Haemophilus and Neisseriaceae depleted at 2 and 6 months vs. pre-treatment, whereas healthy lung commensals Veillonella and Streptococcus were enriched. The post-treatment sputum microbiome (months 12, 18) was comparable to pre-treatment in microbial diversity (p=0.491) and composition (p=0.174). Moreover, at month 18, the sputum microbiome of treated patients resembled that of close contacts (Shannon's index: p=0.528; PERMANOVA p=0.175), whose microbiome remained stable throughout. Mycobacterial reads remained undetected in cases at all timepoints.

Conclusions: This work shows that:

1) first-line antibiotics decrease bacterial diversity and alters bacterial community structure in the airways (enriching for healthy lung commensals and depleting common respiratory pathogens), and

2) the sputum microbiome stabilises to its pre-antibiotic state within six months post-treatment completion.



[Figure. (A) Microbial diversty and (B) principal coordinate analysis based on weighted UniFrac distance.]

OA-03-318-31 Global transcriptomic investigation of the human macrophage response towards pathogenic/non-pathogenic Mycobacteria

A Madhvi,[1] H Mishra,[1] N Chegou,[1] G Tromp,[1] B Baker,[1]
[1]Stellenbosch University, Boimedical Sciences, Cape Town, South Africa. e-mail: abhilasha@sun.ac.za

Background: Tuberculosis (TB) is a major cause of infection related mortality. An estimated 1.3 million HIV negative individuals died of TB in 2017. An estimated 5-10% of infected individual develop TB during their lifetime, while rest 90% (of infected population) can counter the bacteria. Also, some of the close household contacts of TB patients remain uninfected and healthy throughout lifetime. Studying host immune response of healthy individuals towards M.tb can unfold the reason behind this enigma.

Methods: We measured in-vitro host response (from hMDMs) towards different detergent-free grown strains of mycobacteria including drug-resistant pathogenic strain (R179), non-pathogenic (M.smegmatis) and facultative pathogenic (BCG) mycobacteria. The host response was measured post-infection (at mRNA and protein levels) using Ampliseq, qPCR, Luminex, IPA, CFUs and Cytotoxicity assay. 19 differentially expressed genes (DEGs) were selected after applying stringent six fold criteria (strong p-value, FDR, log CPM, fold-changes, IPA and biological functions). Out of these 19 DEGs, we selected inter-related family of IFITs (IFIT1, IFIT2 and IFIT3) for knocking-up (via vector-based transfection) and knocking-down (via siRNA) experiments to evaluate their role in host immune response towards mycobacteria.

Results: Ampliseq analysis found 19 DEGs at 12 hours post-infection across all three strains. We observed lower number of CFUs and higher host response in hMDMs infected with M.smegmatis as compared to other two strains. Intra-cellular bacterial growth and survival measured through CFUs decreased significantly upon knocking up of IFITs, while increased significantly upon knocking down of IFIT1, IFIT2 and IFIT3 in the host macrophages. We confirmed mRNA expression though qPCR and protein expression through Western Blot.

Conclusions: Knock-up of IFITs are found to be strongly associated with reduced survival of pathogenic/non-pathogenic and drug-resistant mycobacteria. IFITs should be pursued for developing adjunct immuno-therapies against TB in future.

OA-03-319-31 Mycobacterium tuberculosis isolates from pulmonary tuberculosis patients during early treatment show differential response in human macrophages in vitro

S Vaswani,[1] A Shaikh,[1] K Sriraman,[1] V Pandey,[1] V Oswal,[2] N Mistry,[1] [1]The Foundation for Medical Research, TB Department, Mumbai, India, [2]Vikas Nursing Home, Pulmonary Medicine, Mumbai, India.
e-mail: kalpanasriraman@yahoo.com

Background: Minimal effective treatment reportedly abolishes infectiousness of tuberculosis patients long before sputum/culture conversion. Does treatment affect host-pathogen interaction in the early stages remains unclear. Hence the current study investigated initial changes brought about by drugs in patient isolates when infected in macrophages in vitro.
Methods: M. tuberculosis was isolated from sputum samples of three drug sensitive (DS) and one drug resistant (DR) TB patient recruited from private clinics in Mumbai. The samples were collected before and after first-line treatment initiation (first and third doses). Additionally, five DS and one DR pre-treatment sample, collected at diagnosis, were individually treated with Rifampicin (Rif; 1μg/ml), Isoniazid (Inh; 0.1μg/ml) and both drugs (Rif + Inh) for 24 hours, and compared with untreated control. THP-1 derived macrophages were infected with all isolates. Intracellular growth rate, macrophage apoptosis, and TNFα levels were measured.
Results: Patient samples demonstrated a longer generation time in THP-1 macrophages (52.63h Vs. 32h) and showed 7.3-fold (1.5-13.04) decline in TNFα levels post one dose of treatment and 36.8-fold decline (1.5-72.18) ($p< 0.05$) post three doses of treatment. The increase in apoptotic activity - 1.6 fold (0.61-2.72) was observed only after three doses. When individual drug effect was compared in clinical isolates after 24h, Rif and Rif + Inh treatment but not Inh alone showed longer generation time, decreased TNFα levels and increased apoptosis with respect to untreated control. DR Mtb from patients or in vitro drug treatment did not show a similar pattern.
Conclusions: Initial doses of first-line drugs received by patients may reduce the infectivity of Mtb by reducing its ability to grow, and modulate macrophage response. In vitro, a 24h treatment of clinical isolates corroborated the trend with Rif, but not with Inh, indicating that Rifampicin may play a primary role in preventing disease transmission from DS TB patients post minimal effective treatment.

OA-03-320-31 In people with latent TB, HIV-infection results in a cytotoxic and dysregulated CD8+ T-cell infiltrate in the bronchoalveolar compartment

B Xulu,[1] D Muema,[1] A Schiff,[2] T Basset,[1] M Suleman,[3,4] P Baijnath,[3,4] K Nyamande,[3,4] D Kwon,[5,6] T Ndung'u,[1,7,8] E Wong,[1,9] [1]Africa Health Research Institute, Laboratory, Durban, South Africa, [2]Ragon Institute of MGH, MIT and Harvard, Department of Pulmonology, Cambridge, MA, United States of America, [3]Inkosi Albert Luthuli Central Hospital, Department of Pulmonology, Durban, South Africa, [4]Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Department of Pulmonology, Durban, South Africa, [5]Ragon Institute of MGH, MIT and Harvard, Laboratory, Cambridge, MA, United States of America, [6]Massachusetts General Hospital, Division of Infectious Diseases, Cambridge, MA, United States of America, [7]Ragon Institute of MGH, MIT and Harvard, Division of Infectious Diseases, Cambridge, MA, United States of America, [8]HIV Pathogenesis Program, Laboratory, Durban, South Africa, [9]Massachusetts General Hospital, Division of Infectious Diseases, Boston, MA, United States of America.
e-mail: bongiwe.xulu@ahri.org

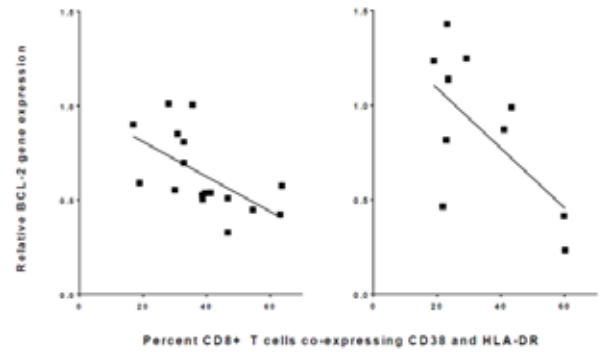
Background: Mechanisms by which HIV causes increased susceptibility to tuberculosis are incompletely understood. Genome-wide transcriptomics may provide novel insights into the impact of HIV-infection at the lung's mucosal surface.
Methods: Paired bronchoalveolar lavage (BAL) and peripheral blood mononuclear cells (PBMC) from 31 human participants with well-defined states of untreated HIV and latent Mtb infection were subjected to differential cell count and phenotyped by flow cytometry. A subset were stimulated and subjected to intra-cellular protein staining for cytokines and cytolytic products. Mann-Whitney tests were used for comparisons. Whole BAL and PBMC pellets and FACS-sorted immune subsets were subjected to mRNA isolation, RNAseq library preparation and Illumina sequencing. Transcriptomic data were analyzed for significantly differentially expressed genes (DEGs) and enrichment of gene ontology (GO) pathways.
Results: HIV infection did not significantly alter the differential cell counts of either whole BAL or PBMC. In both compartments, HIV infection was associated with CD4+ T cell depletion and CD8+ T cell expansion. The large majority of HIV-induced DEGs were compartment-specific (1307/1404, 93%). DEGs in the HIV-infected peripheral blood were enriched for interferon alpha/beta signaling ($q = 8.04e-4$) and in the BAL for lymphocyte activation ($q=2.14e-4$), regulation of the immune response ($q=0.032$), and cytolysis ($q=0.029$). Higher expression of representative transcripts and proteins, including INFG (IFN-g) GZMB (Granzyme B) and PDCD1 (PD-1), on BAL CD8+ T cells was confirmed by cell-type specific transcriptional analysis and flow cytometry.

Conclusions: Transcriptomic and protein-level analysis revealed that HIV induced a strong type 1 interferon response in blood and an infiltration of cytolytic and dysregulated CD8+ T cells at the lung's mucosal surface. Tissue-specific effects of HIV infection, including the impact of BAL CD8+ T cells on immune milieu and alveolar macrophage function, may provide novel targets to improve TB immunity in people living with HIV.

OA-03-321-31 Immune activation and NAT2 genotype are independently associated with BCL-2 gene expression in PBMCs of TB-HIV patients

I Zentner,[1] S Ravimohan,[2] C Modongo,[3] N Zetola,[4] J Pasipanodya,[5] S Srivastava,[5] V Ivaturi,[6] T Gumbo,[5] G Bisson,[7] C Vinnard,[1] [1]Rutgers University, Public Health Research Institute, Newark, NJ, United States of America, [2]Bristol-Myers Squibb, Immunology, Lawrenceville, NJ, United States of America, [3]University of Pennsylvania, Perelman School of Medicine, Pennsylvania Botswana-UPenn Partnership, Gaborone, Botswana, [4]University of Pennsylvania, Perelman School of Medicine, Radiation Oncology, Philadelphia, PA, United States of America, [5]Baylor University Medical Center, Center for Infectious Diseases Research and Experimental Therapeutics, Baylor Research Institute, Dallas, TX, United States of America, [6]University of Maryland School of Pharmacy, Center for Translational Medicine, Baltimore, MD, United States of America, [7]University of Pennsylvania, Perelman School of Medicine, Medicine, Philadelphia, PA, United States of America. e-mail: christopher.vinnard@njms.rutgers.edu

Background: Redox imbalance is one potential mechanism of isoniazid toxicity. Tuberculosis (TB) patients with slow NAT2 genotype have increased risk for hepatotoxicity. The relationship between NAT2 genotype and other types of cellular toxicity are not well understood. High levels of oxidative stress can trigger intrinsic apoptosis leading to down-regulation of anti-apoptotic BCL-2 proteins. We sought to determine the relationship of NAT2 genotype and BCL-2 expression in peripheral blood mononuclear cells (PBMCs) of HIV/TB patients.
Methods: We conducted a prospective study of HIV/TB patients in Botswana during first-line TB treatment, obtaining blood samples before and after initiation of ART. The gene expression of BCL-2 in PBMCs was measured by real-time PCR relative to β-actin. NAT2 genotype was determined by whole exome sequencing, and HIV-associated immune activation was defined as the co-expression of CD38 and HLA-DR on CD8+ T cells. In a linear mixed model framework, we evaluated the independent associations of immune activation and NAT2 genotype on BCL-2 gene expression in PBMCs.
Results: PBMCs from 28 subjects were available for analysis, including 17 pre- and 11 post-ART. Increasing levels of immune activation were associated with greater BCL-2 downregulation among PBMCs (Figure). In a linear mixed model analysis, with random effects at the individual level, immune activation ($p < 0.001$)), NAT2 genotype ($p=0.009$), and receipt of ART ($p=0.011$) were related to BCL-2 gene expression on PBMCs. Downregulation of BCL-2 (signifying pro-apoptosis) was greatest among HIV/TB patients with slow NAT2 genotype and high levels of immune activation, pre-ART initiation.
Conclusions: Expression of BCL-2 in PBMCs is downregulated among HIV/TB patients with slow NAT2 genotype, consistent with pro-apoptotic effects. Further work will examine the functional consequences of INH and hydrazine metabolite exposures in immune cells.



[BCL-2 gene expression and CD8+ T cell immune activation. Left panel: pre-ART; right panel: post-ART.]

OA-03-322-31 Delamanid primary resistance: myth or reality?

J Jaffré,[1,2] W Sougakoff,[1,2] F Brossier,[1,2] A Aubry,[1,2] N Veziris,[1,2,3] on behalf of the CNR MyRMA [1]APHP, Hôpital Pitié-Salpêtrière, Centre National de Référence des Mycobactéries et de la Résistance des Mycobactéries aux Antituberculeux, Paris, France, [2]Sorbonne Université, INSERM, U 1135, Centre d'Immunologie et des Maladies Infectieuses, Paris, France, [3]APHP, Hôpitaux Universitaires de l'Est Parisien, Département de Bactériologie, Paris, France. e-mail: alexandra.aubry@sorbonne-universite.fr

Background: Delamanid (DLM) is the last marketed antituberculous drug recommended for the treatment of multidrug resistant tuberculosis (MDR TB). As illustrated by the bedaquiline, analyzing the prevalence of primary resistance is crucial. Therefore, we aim at measuring the prevalence of DLM resistance in M. tuberculosis complex strains isolated from patients that have not been previously treated by DLM.
Methods: DLM resistance was evaluated on M. tuberculosis complex clinical strains received at the French National Reference Centre for Mycobacteria by phenotypic or genotypic method. The phenotypic method was performed on 113 strains by the proportion method in solid medium (7H11) containing 0.06 µg/mL DLM (EUCAST guidelines). The genotypic method was performed on 291 strains by whole genome sequencing (WGS) with

a focus on Single Nucleotide Polymorphism (SNPs) detected on the 5 genes involved in DLM resistance: ddn, fgd1, fbiA, fbiB and fbiC.

Results: Among the 113 strains tested phenotypically (108 M. tuberculosis, 3 M. africanum, 1 M. bovis, 1 M. bovis BCG), 4 (3,5%) were primarily resistant to DLM and the average proportion of DLM resistant mutants was 10^{-5} for susceptible strains. From the 291 available genomes, 182 harbored at least one SNP in one of the 5 analyzed genes with a total of 208 SNPs detected. Among them, 194 were silent mutations or lineage markers. Among the 12 different non synonymous SNPs, 1 were known to be involved in DLM resistance (ddn-W88Stop; mutation detected in 2 different strains), 3 would not confer resistance (ddn-V148A, fbiC-T273A and fbiC-W678G; the last mutation was detected in 2 different strains) and 8 were possibly involved in DLM resistance (Table).

Conclusions: The prevalence of primary DLM resistance among the M. tuberculosis complex strains is alarmingly high (3,5% by phenotypic and genotypic method) underlying the need to implement DLM susceptibility testing.

Number of mutated strains	Mutations known to be involved in DLM resistance	Mutations potentially involved in DLM resistance	Mutations not conferring DLM resistance
2	ddn-W88Stop		
8		ddn-L109F, fgd1-27 T>G, fbiA-D74E, fbiA-A199T, fbiB-9 A>C, fbiB-A171S, fbiC-32 A>G, fbiC-T850A	
4			ddn-V148A, fbiC-T273A, fbiC-W678G

[Results of DLM genotypic susceptibility testing]

OA-03-323-31 Tuberculosis infection and Inflammation among HIV-infected adults in India

V Kulkarni,[1] S Sangle,[1,2] A Chavan,[1] P Deshpande,[1] I Marbaniang,[1] S Salvi,[2] D Shere,[1] N Gupte,[1,3] A Gupta,[1,3] V Mave,[1,3] [1]Byramjee-Jeejeebhoy Government Medical College-Johns Hopkins University Clinical Research Site, Clinical Trial Unit, Pune, India, [2]Byramjee-Jeejeebhoy Government Medical College, Medicine, Pune, India, [3]Johns Hopkins University School of Medicine, Medicine, Baltimore, MD, United States of America.
e-mail: vandanakulkarni_5@hotmail.com

Background: Tuberculosis (TB) disease in people living with HIV (PLHIV) contributes to increased immune activation however limited data are available on the impact of TB infection (TBI) on immune activation. We sought to assess the impact of TBI on soluble and inflammatory biomarkers in PLHIV.

Methods: Antiretroviral therapy (ART)-naïve and experienced PLHIV >18 years of age, without TB disease, were enrolled from large public sector ART centre in Pune, India. TBI was defined using QuantiFERON-TB Gold In-Tube test (QFT-GIT) of >0.35 IU/ml. Inflammatory biomarkers IL-6, TNF-α, IL-10 and sCD163 were tested using multiplex immunoassays, sCD14 levels by ELISA, D-dimer and C-reactive protein (hs-CRP) by turbidimetric assay. Immune activation/ inflammation was defined as marker value of highest quartile. The effect of TBI inflammation was assessed using logistic regression.

Results: Of 261 enrolled, 103 (39%) had TBI (QFT-GIT 1.71(IQR, 0.7-5.71); 35 (35%) were males, and 78(42%) were on HAART (log viral load 1.60 (IQR, 1.60-1.78). Overall, median CD4 count was 479 (IQR, 262-661) cells/ul, and viral load was 44 (IQR, 40-4064) copies/ ml. In multivariable analysis adjusted for age, sex, HAART, CD4 count and viral load, TBI had more inflammation than no TBI and was associated with two-fold increased risk of elevated TNF-α levels (adjusted odds ratio (aOR, 2.04; 95% CI: 1.01 - 4.12, p=0.045) (**Table 1**). Furthermore, we found a trend for hs-CRP with TBI (aOR, 1.74; 0.96 - 3.14, p=0.07). All p-values were two-sided with statistical significance evaluated at the 0.1alpha level.

Table 1. Effect of Tuberculosis Infection (TBI) on inflammatory markers in HIV-infected individuals in India.

Markers	N	Overall	TBI	No TBI	uOR (95% CI)	aOR* (95% CI)
IL-6 (pg/mL)						
Median, IQR	197	1.93 (0.78 – 4.74)	1.93 (0.78 – 5.02)	1.93 (0.78 – 4.74)	-	-
< Q3		148 (75%)	56 (75%)	92 (75%)	Reference	Reference
> Q3		49 (25%)	19 (25%)	30 (25%)	1.04 (0.54 – 2.02)	1.05 (0.53 – 2.10)
TNF-alpha (pg/mL)						
Median, IQR	182	1.85 (0.47 – 4.35)	3.11 (0.47 – 5.63)	1.57 (0.47 – 4.01)	-	-
< Q3		137 (75%)	46 (68%)	91 (80%)	Reference	Reference
> Q3		45 (25%)	22 (32%)	23 (20%)	1.89 (0.96 – 3.75)	2.04 (1.01 – 4.12)
IL-10 (pg/mL)						
Median, IQR	201	2.61 (1.44 – 4.56)	2.29 (1.38 – 3.19)	3.09 (1.63 – 5.61)	-	-
< Q3		151 (75%)	66 (80%)	85 (71%)	Reference	Reference
> Q3		50 (25%)	16 (20%)	34 (29%)	0.61 (0.31 – 1.19)	0.63 (0.31 – 1.24)
sCD14 (ng/mL)						
Median, IQR	260	8919 (6455 – 13180)	8562 (6976 – 112648)	9085 (6100 – 13287)	-	-
< Q3		195 (75%)	78 (76%)	117 (75%)	Reference	Reference
> Q3		65 (25%)	25 (24%)	40 (25%)	0.94 (0.53 – 1.67)	0.96 (0.54 – 1.71)
sCD163 (pg/mL)						
Median, IQR	248	2167 (1451 – 3495)	1900 (1324 – 3294)	2362 (1665 – 3600)	-	-
< Q3		186 (75%)	77 (79%)	109 (73%)	Reference	Reference
> Q3		62 (25%)	21 (21%)	41 (27%)	0.73 (0.40 – 1.32)	0.80 (0.42 – 1.52)
D-Dimer (ug/mL)						
Median, IQR	261	0.24 (0.16 – 0.41)	0.22 (0.15 – 0.42)	0.27 (0.17 – 0.41)	-	-
< Q3		197 (75%)	77 (75%)	120 (76%)	Reference	Reference
> Q3		64 (25%)	26 (25%)	38 (24%)	1.07 (0.60 – 1.90)	1.34 (0.67 – 2.71)
hs-CRP (mg/dL)						
Median, IQR	261	0.16 (0.05 – 0.47)	0.20 (0.06 – 0.57)	0.12 (0.04 – 0.39)	-	-
< Q3		197 (75%)	72 (70%)	125 (79%)	Reference	Reference
> Q3		64 (25%)	31 (30%)	33 (21%)	1.63 (0.92 – 2.88)	1.74 (0.96 – 3.14)

uOR= unadjusted odds ratio; CI=confidence interval; aOR= adjusted OR
* adjusted for age, sex, HAART, CD4 count and viral load
** The selected inflammatory biomarkers have shown contribution in prediction to progression of AIDS and mortality, monocyte activation and severity of MTb infection.

[Effect on Tuberculosis Infection(TBI) on inflammatory markers in HIV -infected individuals in India]

Conclusions: Pro -inflammatory markers, TNF-α and hs-CRP levels were elevated in HIV-infected individuals with TBI, suggesting the presence of persistent, low-grade inflammatory state likely due to low level of TB

pathogen replication. Future studies should address the need for anti-inflammatory agents- in addition to TBI prophylaxis- to suppress immune activation, known to be associated with suboptimal response to ART.

OA-04-D3 Addressing the lung health emergency in adults and children: from epidemiology to intervention

OA-04-324-31 The prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis from the Global Burden of Disease Study 2017

P Kendrick,[1] V Gupta,[1] J Soriano,[2] GBD 2017 Chronic Respiratory Disease Collaborators [1]University of Washington, Global Health, Seattle, WA, United States of America, [2]Hospital Universitario La Princesa, Pneumology, Madrid, Spain. e-mail: parkesk@uw.edu

Background: A systematic summary on the global burden of chronic respiratory diseases (CRDs) and their trends over time is not yet available. In this study, we characterize the burden of CRDs globally, highlighting geographic and time trends from 1990 to 2017.
Methods: Using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, we estimate prevalence and attributable morbidity and mortality from CRDs through an analysis of deaths, disability-adjusted life-years (DALYs), and years of life lost (YLLs) over the same period. Specific diseases analyzed as a CRD include: chronic obstructive pulmonary disease (COPD), asthma, interstitial lung diseases and pulmonary sarcoidosis, and pneumoconiosis.
Results: The geographical distribution of CRD prevalence demonstrated wide variability across GBD super regions, with the highest prevalence observed across both genders in the high-income region, while the lowest prevalence was observed in Latin America. The age and sex-specific prevalence of each CRD in 2017 was also highly variable. Deaths due to CRDs increased by 17.77% between 1990 and 2017, while DALYs increased by 13.33%. The majority of CRD-attributable DALYs and deaths were due to COPD across both sexes. In regional analysis, mortality rates from CRDs are greatest in South Asia and lowest in Sub-Saharan Africa, also across both sexes. Notably, though absolute prevalence is lower in the South Asia region, attributable years of life lost (YLLs) from CRDs across the subcontinent are overwhelmingly the highest worldwide.
Conclusions: Our study reveals that chronic respiratory diseases remain a leading and growing cause of death and disability worldwide. The greater share of YLLs observed in South Asia versus the High-income region suggests that premature mortality from CRD is highest in regions with less-resourced health systems on a per-capita basis.

OA-04-326-31 Pulmonary function testing and predictive equations in adult population in Maputo, Mozambique

O Ivanova,[1] C Khosa,[2] A Bakuli,[1] E Sathoff,[1] N Bhat,[2] M Hoelscher,[1] A Rachow,[1] [1]Medical Centre of the University of Munich (LMU), Division of Infectious Diseases and Tropical Medicine, Munich, Germany, [2]Ministry of Health, Instituto Nacional de Saúde (INS), Maputo, Mozambique.
e-mail: olena.ivanova@lrz.uni-muenchen.de

Background: The increased use of pulmonary function testing in research as well as in diagnosing and managing of lung diseases has led to the need for locally derived reference equations in African settings. These local data are important for interpreting pulmonary function test results and deciding on the management strategies of respiratory diseases.
This study aimed at establishing lung function values and predictive equations for adult population living in Maputo, Mozambique.
Methods: We applied a cross-sectional design. Eligible participants who provided informed consent have undergone anthropometric measurements, e.g. height, weight, answered questionnaire with demographic and behavioural components, and performed lung function testing using hand-hold spirometer. Data were double-entered, coded and analysed using descriptive statistics and logistic regression to develop predictive equations.
Results: A total of 212 males and females took part in the study. From them, a total of 155 participants had usable spirometry results, after rigorous quality control procedures were employed. Mean age of participants was 35.2 (18.46, 65.58) with 63 males and 92 females. Mean FVC in litres was 3.28 (1.86, 5.26) and mean FEV1 in litres was 2.71 (1.45, 4.67). We constructed the predictive Mozambican equations and compared them to the South African and GLI equations. The South African and GLI equations overestimate the spirometry values for the given sex, age and height in our studied population.
Conclusions: To our knowledge, this was a first study to obtain local population spirometric equations in Maputo, Mozambique and compare them to other widely-used standards such as GLI and South African equations. The established equations and references will be used in the analysis of the TB Sequel Project spirometry data.

OA-04-327-31 Clinical features and treatment outcomes of Mycobacterium chimaera lung disease

J-Y Chien,[1] L-C Chen,[1] P-R Hsueh,[2] [1]National Taiwan University Hospital, Internal Medicine, Taipei, Taiwan, [2]National Taiwan University Hospital, Laboratory Medicine, Taipei, Taiwan. e-mail: jychien@ntu.edu.tw

Background: Mycobacterium chimaera is a new species of the Mycobacterium avium complex (MAC) that was identified using modern gene sequencing analysis. We investigated the clinical features, antimicrobial susceptibilities, and treatment outcomes of lung disease caused by M. chimaera.

Methods: This study was conducted in a medical center from December 2012 to July 2015. Patients who fulfilled the 2007 American Thoracic Society and the Infectious Diseases Society of America diagnostic criteria for nontuberculous mycobacterial lung disease were enrolled in the study. M. chimaera isolates were identified based on the findings of sequencing of rpoB gene, the internal transcribed spacer region of the 16S-23S rRNA gene, and the heat-shock protein 65 gene (hsp65). Minimum inhibitory concentrations (MICs) of 13 antimicrobial agents against M. chimaera isolates causing lung disease were determined.

Results: During the study period, 158 patients with MAC lung disease were identified, and 17.7% (28/158) of the patients had lung disease caused by M. chimaera. Among these patients, 17 (60.7%) were female, and their median age was 72.5 (40-100) years. All M. chimaera isolates were susceptible to clarithromycin and rifabutin, but only 10 (35.7%) were susceptible to amikacin. Of the nine patients who received macrolide-based regimens, more achieved radiographic resolution than those treated with non-macrolide-based regimens (66.7% vs 15.8%, P = .013), and they tended to have better survival (P = .10).

Conclusions: A substantial portion (17.7%) of MAC lung disease cases were caused by M. chimaera, and treatment with macrolide-based regimens resulted in better clinical outcomes.

OA-04-328-31 Access to healthcare for patients with chronic lung disease is sub-optimal in sub-Saharan Africa: findings from a health systems analysis in Sudan and Tanzania

U Egere,[1] E Shayo,[2] S Mpagama,[3] NE Ntinginya,[4] H Ibrahim,[5] A Elsony,[5] B Squire,[6] R Tolhurst,[1] M Taegtmeyer,[1] [1]Liverpool School of Tropical Medicine, International Public Health, Liverpool, United Kingdom, [2]National Institute for Medical Research, Policy Analysis and Advocacy, Dar es Salaam, Tanzania, United Rep., [3]Kibong'oto Infectious Diseases Hospital, Infectious Diseases, Kilimanjaro, Tanzania, United Rep., [4]National Institute for Medical Research (NIMR), Tuberculosis and Emerging Diseases, Mbeya, Tanzania, United Rep., [5]Epidemiological Laboratory (Epi-Lab) for Public Health and Research, Epidemiology, Khartoum, Sudan, [6]Liverpool School of Tropical Medicine, Clinical Sciences, Liverpool, United Kingdom. e-mail: uzochukwu.egere@lstmed.ac.uk

Background: Chronic lung diseases (CLD) are responsible for over 4 million deaths per year globally, yet they are not prioritized in low- and middle-income countries where their impact is greatest. In these countries, the health systems are largely under-resourced and there is a disproportionate focus on single disease "vertical" health programs. As a result, potential CLD patients with chronic cough investigated within the TB platform are lost in the cascade of care if they are TB negative, and therefore fail to access appropriate health services. There is therefore limited visibility of the burden of chronic lung disease.

We aimed at generating evidence to inform development of integrated lung health services in Sudan and Tanzania by exploring perspectives of Health systems and community stakeholders and assessing readiness of health facilities for CLD services.

Methods: We used a mixed-methods, four-phased, action research design, that involved ministry of health officials early on. Qualitative key informant interviews, in-depth interviews and focus group discussions explored perceptions, experiences, expectations and priorities of stakeholders at all levels of the health system and the community. Complementary quantitative assessment of health system readiness characterized existing care platforms and infrastructure.

Results: Overall, CLD was poorly recognized among informants and the health systems response was inadequate. Human resource capacity was limited, data management was inadequate, and diagnostic equipment and drugs for management of CLD were lacking at all levels of the health system.

Respondents accepted integration of CLD services into existing health services as a potential intervention but identified limited funding and lack of training as barriers.

Conclusions: There are health system gaps in provision of CLD services in Tanzania and Sudan which, in turn, may negatively impact effectiveness of TB servic-

es. These findings provide a strong basis for addressing identified challenges of CLD integration into health systems in these settings.

OA-04-329-31 Improving childhood pneumonia case management by patent medicine vendors (PMVs) through an integrated community case management (iCCM) approach

O Onuoha,[1] J Anyanti,[2] [1]Society for Family Health (SFH), Programmes, Lugbe, Nigeria, [2]Society for Family Health (SFH), Programmes, Abuja, Nigeria.
e-mail: oonuoha@sfhnigeria.org

Background and challenges to implementation: To determine whether improving competency of PMVs to deliver quality case management of common childhood illnesses through training and routine supervision could lead to improved health outcomes in two local government areas (LGAs) in Ebonyi State, without the use of subsidies for medications. Malaria, diarrhea, and pneumonia are leading causes of child deaths accounting for 14%, 15%, and 10% of deaths respectively. 2013 Nigeria Demographic Health Survey (DHS), indicates just 37% of children with pneumonia received antibiotics, 34% with diarrhea received ORS, 2% received zinc and 18% with malaria received an ACT.
Intervention or response: The intervention targeted PMVs already utilized by the community. 325 PMVs were enlisted but only 295 met all eligibility criteria and were trained, mentored and supervised to conduct community case management and follow up on children managed. Case management lasted 9 months in the two LGAs - Ikwo and Onicha.
Results and lessons learnt: In 9 months, 26,847 cases were treated across three illness areas with any one child showing symptoms for up to three illnesses. Proportion of PMVs who know the best method to diagnose pneumonia at endline was 80% in intervention LGA and 13% in control LGA. 63% of PMVs at endline in intervention LGAs correctly identified amoxicillin and the dosing instructions as the recommended treatment for pneumonia as compared to both the intervention arm at baseline (< 1%) and the control arm at endline (11%). Proportion of PMVs who could correctly identify all three recommended treatments at endline was 88% in intervention LGAs compared to 2% at baseline, while it was only 15% in the control LGA at endline. PMVs followed up with 22,515 cases- an estimated 85% of treated cases. 22,317 cases (99%) of cases followed-up recovered, 178 (0.8%) were referred, and 20 (0.1%) died.
Conclusions and key recommendations: Evaluation demonstrated PMVs increased knowledge of childhood case management following training and supervision.

OA-04-330-31 Household air pollution exposure is associated with alterations of the upper respiratory microbiome

SM Patel,[1] RR Young,[2] M Vincent Allende,[3] S Boiditswe,[4] KA Feemster,[5,6] T Arscott-Mills,[4,5,6] SS Shah,[7] CK Cunningham,[2] PC Seed,[3] MS Kelly,[2,4]
[1]Duke University, Division of Pulmonary, Allergy, and Critical Care Medicine, Durham, NC, United States of America, [2]Duke University, Division of Pediatric Infectious Diseases, Durham, NC, United States of America, [3]Ann & Robert H. Lurie Children's Hospital, Divison of Pediatric Infectious Diseases, Chicago, IL, United States of America, [4]Botswana - University of Pennsylvania Partnership, N/A, Gaborone, Botswana, [5]Children's Hospital of Philadelphia, Global Health Center, Philadelphia, PA, United States of America, [6]Children's Hospital of Philadelphia, Division of Pediatric Infectious Diseases, Philadelphia, PA, United States of America, [7]Cincinnati Children's Hospital Medical Center, Divisions of Hospital Medicine and Infectious Diseases, Cincinnati, OH, United States of America.
e-mail: sweta.patel@duke.edu

Background: Nasopharyngeal colonization precedes pneumonia caused by Streptococcus pneumoniae and other bacterial respiratory pathogens. The nasopharyngeal microbiome may serve as a barrier to colonization and invasion by such pathogens. In particular, certain Corynebacterium species inhibit growth of Streptococcus pneumoniae and can eradicate Staphylococcus aureus nasopharyngeal carriage. We sought to identify factors that affect the abundance of Corynebacterium within the upper respiratory microbiome of infants.
Methods: We conducted a prospective cohort study of mother-infant dyads in Gaborone, Botswana. We enrolled subjects within 72 hours of delivery and followed them every 1-2 months until the infant was 12 months of age. We collected nasopharyngeal swabs at each visit and sequenced the V4 region of the bacterial 16S ribosomal RNA gene to characterize the microbiome. We used mixed effect longitudinal models to identify factors predictive of changes in relative abundance of Corynebacterium. We included age, sex, breastfeeding, maternal HIV infection, low-birth-weight status, season, household use of solid fuels, antibiotic exposures, and Corynebacterium relative abundance at the previous time point in the adjusted model.
Results: Of 75 mother-infant dyads analyzed to date, 11% were low birth weight (< 2500g), 65% lived in homes using wood for cooking or heating, and 32% were HIV-exposed, uninfected. Exposure to wood smoke (P = 0.01) and receipt of antibiotics (P = 0.01) were associated with a lower relative abundance of Corynebacterium in the nasopharyngeal microbiome over time
(Table 1).
Conclusions: Wood smoke exposure is associated with a decreased relative abundance of Corynebacterium species within the nasopharyngeal microbiome. Given the importance of Corynebacterium species for resistance to colonization by bacterial respiratory pathogens, this

suggests that household air pollution exposure may increase pneumonia risk in part through alteration of the nasopharyngeal microbiome. Further research is needed to evaluate the impact of air pollutants on respiratory microbiome composition and pathogen colonization.

	Univariable		Multivariable	
Predictor	Mean Difference* (95% CI)	*P*	Mean Difference* (95% CI)	*P*
Female sex	0.01 (-0.03, 0.05)	0.51	0.02 (-0.02, 0.06)	0.28
Low birth weight	-0.05 (-0.12, 0.01)	0.30	-0.05 (-0.12, 0.01)	0.14
Maternal HIV infection	0.02 (-0.02, 0.06)	0.37	-0.01 (-0.06, 0.05)	0.75
Wood smoke exposure	-0.05 (-0.09, -0.01)	0.01	-0.05 (-0.10, -0.01)	0.01
Antibiotic exposure	-0.06 (-0.10, -0.01)	0.02	-0.06 (-0.10, -0.01)	0.01
Breastfeeding	0.08 (0.03, 0.14)	0.003	0.04 (-0.01, 0.09)	0.17
Rainy season	-0.03 (-0.07, 0.01)	0.10	-0.03 (-0.07, 0.01)	0.23

*Refers to the change in the relative abundance of Corynebacterium over the entire follow-up period in exposed subjects compared to unexposed subjects.

[Table 1. Associations between clinical factors and the relative abundance of Corynebacterium within the upper respiratory microbiome of infants]

OA-04-331-31 Evaluation of a public health programme for chronic airway diseases as compared with the existing care in primary health centres, South Kerala, India

G Soumya,[1] MS Manu,[2] B K Gopal,[3] M J Valamparampil,[4] S Nair,[5] R Kamala,[5]
[1]Government Medical College, Community Medicine, Kottayam, India, [2]Directorate of Health Services, State Tuberculosis Training and Demonstration Centre & State TB Cell Kerala, Thiruvananthapuram, India, [3]Directorate of Health Services, Health Services, Thiruvananthapuram, India, [4]Directorate of Health Services, State Tuberculosis Cell, Thiruvananthapuram, India, [5]Government Medical College, Department of Pulmonary Medicine, Thiruvananthapuram, India.
e-mail: soumyagopakumar83@gmail.com

Background: Kerala, a state in south India, is the first state in India to implement a public health programme called SWAAS (Step Wise Approach to Airway diseaseS) to address Chronic Obstructive Pulmonary Disease -COPD and asthma. The present study aimed to evaluate the SWAAS programme, to determine whether there is a difference in treatment plan and characteristics of patients with obstructive airway diseases in PHCs implementing SWAAS as compared to those not implementing and providing usual care.
Methods: A cross sectional study was conducted among patients with COPD and asthma getting treatment from PHCs implementing SWAAS and not implementing during October 2018 to February 2018. The required number of study subjects from each PHC implementing SWAAS was selected using simple random sampling. The PHCs in the comparator group of FHC were randomly selected and study subjects recruited from the outpatient clinic. Analysis included proportions, Chi square test and Odds ratio with 95% confidence interval.
Results: A total of 97 patients from SWAAS and 85 patients from PHC were studied. Spiromerty was used for the diagnosis in 98 % of the COPD and 100 % of the asthma patients in the SWAAS PHCs. In the PHCs 23% of COPD and 25% of asthma patients underwent spirometry. Among patients on treatment (n-113), guideline appropriate management was present in 54 (47.7% (95 % CI 38.3 - 57.4)). A higher number of patients in SWAAS PHCs were managed as per standard guidelines than in the comparator PHCs. The proportion of patients who had to buy inhaled medicines on their own reduced from 46 % before the SWAAS clinic was started to 9 % after the starting of clinic, while it was 15 % for those getting treated in the PHCs.
Conclusions: The number of visits for injections and nebulisations was reduced significantly in the SWAAS PHCs than PHCs.

OA-05-A3 TB tests for TRIAGE and MONITORING

OA-05-332-31 Tuberculosis detection in chest X-rays: the effects of image preprocessing on deep learning classifier performance

K Kantipudi,[1] Z Yaniv,[1] [1]National Institutes of Health, NIAID/OCICB/BCBB, Bethesda, MD, United States of America. e-mail: karthik.kantipudi@nih.gov

Background: A variety of convolutional neural network (CNN), deep learning, models for classifying whether chest X-rays (CXR) contain tuberculosis have been published. Image inputs to these classification models usually undergo intensity modifications with the intent of enhancing contrast, potentially leading to improved performance. These modifications include non-linear intensity mappings such as sigmoid and linear mapping within a sub-range of the intensities (window-leveling), and most commonly histogram equalization. We evaluate the effect of intensity modifications on the performance of three pre-trained CNN architectures.
Methods: We apply a transfer learning approach with the following pretrained CNNs: VGG16, Xception, and NASNet mobile. All networks are trained using a balanced dataset of 2312 CXRs, with intensity values in [0,4095]. Data was divided into 1618 images for training, 347 for validation, and 347 for testing. All images were resized to the common image size used by these CNNs, 224x224. Each pretrained CNN was truncated prior to their best performing layers and four new layers:

pooling, two fully connected and dropout layers were appended. Each network was trained using five image sets as follows: (1) no intensity modification; (2) window-leveling that accounts for outlying intensity values by using (2a) an interval of [0.08,0.92] of the histogram values and (2b) an interval of [Q1-1.5IQR,Q3+1.5IQR] where Q1 and Q3 are the first and third quartiles and IQR=Q3-Q1; (3) sigmoid mapping; and (4) histogram equalization.

Results: Accuracy of all networks was stable or improved by intensity modifications with the best results obtained for sigmoid mapping. Accuracy results for no (sigmoid) modifications were: VGG16 92.2 (92.2)%; Xception 87.9 (91.0)%; NASNet 65.9 (88.1)%. See Table 1 for corresponding area under curve results.

Conclusions: Intensity modifications have a measurable effect on the performance of deep learning models with sigmoid mapping leading to the most improvement for the models evaluated in this study.

	No Modification	Best (sigmoid)
VGG16	0.955	0.971
Xception	0.936	0.962
NASNet	0.706	0.923

[Table 1. Area Under Curve results when using original intensity values and the best AUC corresponding to sigmoid intensity mapping.]

OA-05-333-31 Development and validation of a novel, fast and low-cost point-of-care triage test for tuberculosis

JL Nuno,[1] A Nuno,[1] P Lugo,[1] G Rubio,[2] I Thior,[3] C Puta,[4] A Kinter,[5] M Moore,[6] [1]Unima Inc, Research and Development, Zapopan, Mexico, [2]Instituto Nacional de Ciencias Médicas y de Nutrición Salvador Zubirán, Translational Medicine and Innovation Unit, Ciudad de Mexico, Mexico, [3]PATH, AIDSFree Project, Washington DC, DC, United States of America, [4]PATH, BID Project, Lusaka, Zambia, [5]PATH, HIV/TB Program, Washington DC, DC, United States of America, [6]PATH, Global Program, Seattle, WA, United States of America.
e-mail: jose.nuno@unima.com.mx

Background: According to High Priority Target Product Profile published by the WHO in 2014, there is a high priority need for a point-of-care triage test which should be a simple, low-cost test that can be used by first-contact health care providers to rule out Tuberculosis cases and identify those who need further testing. Serological tests could be suitable for use at the point of care because they have less intensive laboratory requirements.

Methods: A new triage test for Tuberculosis was developed using heat resistant chimeric recombinant proteins capable of binding three biomarkers in whole blood samples. These proteins are printed in paper microfluidic devices which generates a visual reaction in patients with active Tuberculosis. The result of the test is evaluated in a smartphone application which runs an image analysis process and an artificial intelligence algorithm. This technology has been tested in three validation protocols: first, in a clinical validation in the Tijuana region in Mexico with a 225 patient cohort. A second study was run by the Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran (INCMNSZ) in Mexico City with a sera bank of 96 patients previously diagnosed. A third study was run in Zambia by PATH on a 595 patient cohort.

Results: In the first validation study in Baja California, results shown a pooled sensitivity of 98.3% and a specificity of 92.7%. In the INCMNSZ study results shown a pooled sensitivity of 96% and a specificity of 93%. Results from the Zambia study are still in process to this date and will be presented during the session.

Conclusions: Current results shown a sensitivity and specificity levels above those specified as optimal in the WHO´s 2014 TPP. This test represents a promissory triage technology to optimize case detection at community level and above with lower costs for Tuberculosis programmes.

OA-05-334-31 Optimising parsimonious gene signatures defining the spectrum of tuberculosis infection

WE Johnson,[1] S Knudsen,[2] N Hochberg,[2] N Joseph,[3] G Roy,[4] S Sarkar,[4] J Ellner,[5] P Salgame,[5] [1]Boston University, Computational Biomedicine, Boston, MA, United States of America, [2]Boston Medical Center, Division of Infectious Disease, Boston, MA, United States of America, [3]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Microbiology, Pondicherry, India, [4]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Preventive and Social Medicine, Pondicherry, India, [5]Rutgers University, Center for Emerging Pathogens, Newark, NJ, United States of America. e-mail: wej@bu.edu

Background: Blood-based gene expression signatures have been developed to predict TB-related outcomes such as including distinguishing between disease and controls, predicting progression to disease, and monitoring treatment resposne. These have been developed using multiple technologies (microarray, RNA-sequencing, rt-PCR) and using a diverse set of computational and machine learning prediction algorithms. These existing signatures have variable performance across different conditions including comorbidities such as diabetes, malnutrition, and pregnancy. However, there has not previously been a comprehensive evaluation, a single resource of compiled signatures, or a uniform platform for profiling multiple signatures or algorithms at the same time in the same patients.

Methods: Here we present a customized 107 gene Nanostring panel and computational/analytics platform [PTB107 profiler] that includes genes from 10 existing

TB disease and risk of progression to disease signatures. We have profiled whole blood-derived RNA from 100 patients with TB, 80 LTBI individuals without comorbidities, and 120 additional LTBI with comorbidities including malnutrition, pregnancy, alcoholism, diabetes, and parasites.

Results: Individual gene signatures produce AUCs as high as 0.895 (0.850, 0.937) in selected subsets of the patients, and the full panel of genes discriminates TB and LTBI with an AUC of 0.899 (0.852, 0.934). We will also present efforts to develop parsimonious Nanostring-based signatures that will segregate infected individuals into those with high risk of progression to TB disease and those with incipient, subclinical or active disease for appropriate targeted therapy.

Conclusions: We develop and present the PTB107 profiler, a Nanostring panel and computational platform for efficiently profiling multiple TB-related pathways simultaneously. The results show promise that the PTB107 profiler can be used to efficiently profile TB outcomes in an efficient way. Importantly, instruments are currently in development to translate nCounter technology to the point-of-care stage.

OA-05-335-31 Variability of interferon gamma release assay over six months of anti-tubercular therapy in children

A Mukherjee,[1] S Saini,[1] A Tripathi,[1] V Singh,[2] H Grewal,[3] R Lodha,[1] SK Kabra,[1] [1]All India Institute of Medical Sciences, Pediatrics, New Delhi, India, [2]Lady Hardinge Medical College, Pediatrics, New Delhi, India, [3]University of Bergen, Microbiology and Global Health, Bergen, Norway. e-mail: aparna.sinha.deb@gmail.com

Background: The changes in levels of interferon gamma as measured by the interferon gamma release assay (IGRA) with treatment of tuberculosis can give us some insight into the immune status of the patient against Mycobacterium tuberculosis. Our objective was to study the changes in Quantiferon (QFT) positivity over six months of anti-tubercular therapy (ATT) in children with intrathoracic tuberculosis.

Methods: As part of a randomized controlled trial to study the effect of micronutrients as an adjunctive therapy in children with intrathoracic tuberculosis, QFT and tuberculin skin testing (TST) was performed at baseline, 2 month and 6 months of ATT. Kappa statistic was calculated to check the agreement between two tests.

Results: A total of 336 children [mean (SD) age: 106.9 (43.7) months; girls: 55.4%] were enrolled. At baseline, 93.7% and 82.4% were TST and QFT positive, respectively; kappa = 0.14. At the end of six months of therapy, 92.3 % and 63.1% of children were TST and QFT positive, respectively; kappa=0.05. There were 87 (out of 227 positive tests, 37.4%) children whose QFT changed from positive to negative at the end of 6 months of treatment; in 22 children a negative QFT response (of 59 negative results, 37.3%) converted to positive at 6 months and for 190 children there was no change. There was significant quantitative fall in median (IQR) interferon gamma levels- baseline: 6.63 (1.39,10) IU/mL, 2 months: 2.59 (0.55, 10) IU/mL and 6 months: 0.87 (0.29, 2.54) IU/mL.

Conclusions: There is considerable variability in QFT results after anti-tubercular therapy. A sizeable proportion of the children became negative on QFT after ATT. Studies with longer post-therapy follow-up period are required to observe the difference in course and probability of relapse in children in whom QFT remained positive and those in whom QFT reverted to negative.

OA-05-336-31 Successful molecular detection of trans-renal DNA in urine: new tool for treatment response monitoring?

MF Franke,[1] R Holmberg,[2] R Calderon,[3] A Mesman,[1] J Coit,[1] M Soto,[4] M Murray,[1] M Mendoza,[5] L Lecca,[6] N Pollock,[7] [1]Harvard Medical School, Global Health & Social Medicine, Boston, MA, United States of America, [2]Akonni Biosystems, Diagnostics, Frederick, MD, United States of America, [3]Socios en Salud Sucursal Peru, Laboratory, Lima, Peru, [4]Socios en Salud Sucursal Perú, Laboratory, Lima, Peru, [5]Socios en Salud Sucursal Perú, Field, Lima, Peru, [6]Socios en Salud Sucursal Perú, Management, Lima, Peru, [7]Boston Children's Hospital, Infectious Diseases Diagnostic Laboratory, Boston, MA, United States of America.
e-mail: molly.f.franke@gmail.com

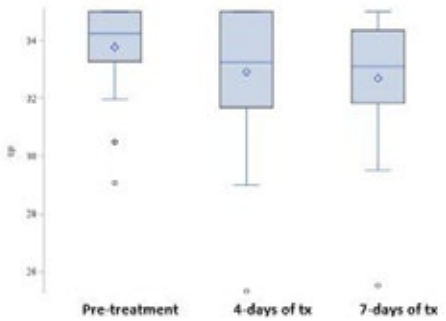
Background: Transrenal Mycobacterium tuberculosis (Mtb) DNA has been detected in the urine of patients with active tuberculosis (TB); however, sensitivity has been variable, and factors influencing detection are unknown. Among adults with TB, we examined within-person changes in cell-free DNA during the first week of TB treatment. We hypothesized that a greater quantity of DNA would be excreted following treatment initiation, relative to pre-treatment samples, due to increased treatment-related Mtb cell death.

Methods: We analyzed trios of urine samples from 31 HIV-negative adults with culture-confirmed pulmonary TB (23 smear-positive, 8 smear-negative) in Lima, Peru. Samples were collected prior to and four and seven days following treatment initiation. Single urine samples were collected from 10 control patients in whom TB had been ruled out. EDTA was added to urine samples upon collection to prevent DNA degradation. We extracted DNA from 20mL of urine using a positively charged resin followed by spin column purification, optimized to isolate short fragments. The extracted Mtb DNA was amplified using a 45 base IS6110 target. We conducted paired statistical tests to examine changes in PCR cycle threshold (Ct) values at days four and seven, relative to baseline.

Results: Median Ct values were 34.25, 33.24, and 33.01 for pre-treatment, 4-day, and 7-day samples, respectively (Figure 1). Corresponding median fluorescence values

were 4.20, 6.88, and 6.38, respectively. Within-person changes in Ct value were -0.135 and -0.405 at days four and seven (paired-test p-values=0.13 and 0.02, respectively). We found no evidence of Mtb DNA in the samples from ten controls.

Conclusions: We observed increased Mtb DNA detection following treatment initiation, suggesting increased shedding of DNA over time. Changes in cell-free TB DNA may be an indicator of early treatment response. These findings should be reproduced in a larger cohort, including stratified analyses based on smear and HIV status.



[Figure 1. Decreases in cycle threshold (CT) values and increasing fluorescence values in 31 adults during the first week of TB treatment, relative to pre-treatment samples, suggest increased shedding of trDNA in the early days of TB treatment (p-value testing for within-person change: 0.13 and 0.02 for CP change at days 4 and 7, respectively; 0.04 and 0.02 for fluorescence change at days 4 and 7 respectively.)]

OA-05-337-31 Association between long non-coding RNAs (lncRNAs) of the MAPK signal pathway and pulmonary tuberculosis

Y Li,[1] H Song,[1] L Zhu,[1] [1]Jiangsu Provincial Center for Disease Prevention and Control, Department of Chronic Communicable Disease, Nanjing, China.
e-mail: liyan.nju@163.com

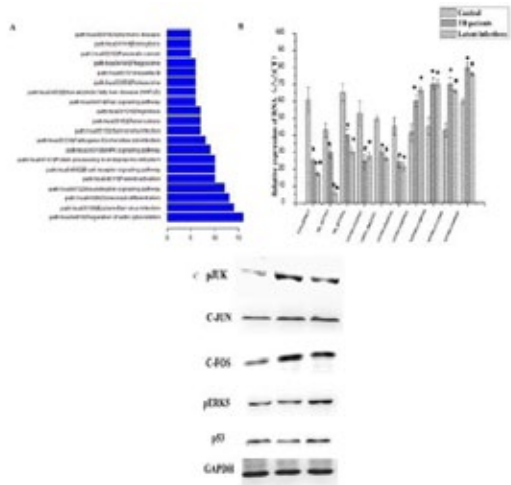
Background: Tuberculosis (TB) still a major threat for human health. The MAPK signal pathway plays an important role in the immune response of Mycobacterium Tuberculosis after infection. Furthermore,increasing evidence suggests that lncRNAs have multiple important roles in immune responses. However, their roles in response to TB infection remain to be elucidated.

Methods: LncRNAs expression profiles were analyzed by microarray in paired pathogenic positive TB patients and noninfectious healthy control models(Hco). GO and KEGG biological pathway analysis of the differentially expressed lncRNAs was applied to research the potential functions and pathways related to the pathogenesis of TB, and to screen specific lncRNAs of the MAPK signal pathway associated with TB patients. Real-time PCR (qRT-PCR) was used to validate the selected specific lncRNAs in TB patients and latent infections(LTBI). Western-blotting (WB) was used to detect the expression of proteins in the MAPK pathway among different groups.

Results: Our results revealed that many lncRNAs in the MAPK signal pathways were differentially expressed in TB patients. Furthermore, ten lncRNAs were selected and examined in TB patients and latent infections, followed by qRT-PCR evaluation. We found LINC02502:7, NR_103718.1, NR_027335.2, NONHSAT129417, TCONS_00023421 and NONHSAT016311 down-regulated significantly in TB patients and latent infections; whereas NONHSAT055923, NONHSAT081163, NONHSAT113004 and NONHSAT098107 up-regulated significantly in TB patients and latent infections.

WB results proved proteins pJUK、C-JUN and C-FOS significantly increased in the LTBI and TB patient groups, while pERK5 and p53 increased in the TB patient group only. Finally, these ten lncRNAs were identified as novel candidate molecular markers for Tuberculosis infection diagnosis.

Conclusions: We reveal a new insight into the mechanisms of the TB infection and TB patients, and also suggest that the ten-MAPK pathway-lncRNAs signature is a new biomarker for early diagnosis and a potential target for treatment of Tuberculosis.



[Study of lncRNA expression in MAPK Signal Pathway of Tuberculosis]

OA-05-338-31 Developing a blood-based active TB diagnostic using multiplexed microbeads with flow cytometry

M Mehrpouyan,[1] M Suni,[1] O Guryev,[1] R Ravindran,[2] W Huang,[1] A Khaliq,[3] MW Akhtar,[4] I Khan,[2] S Bornheimer,[5] E Goldberg,[6] [1]BD Biosciences, Application Development, San Jose, CA, United States of America, [2]UC Davis, Pathology & Laboratory Medicine, Sacramento, CA, United States of America, [3]University of the Punjab, College of Earth and Environmental Sciences, Lahore, Pakistan, [4]University of the Punjab, School of Biological Sciences, Lahore, Pakistan, [5]BD Biosciences, Scientific Affairs, San Jose, CA, United States of America, [6]BD Biosciences, Advanced Technology Group, San Jose, CA, United States of America.
e-mail: scott_bornheimer@bd.com

Background: Blood-based diagnosis of active TB could enable wider implementation of TB diagnostics and screening programs in resource limited settings as blood is easier to obtain than sputum and readily available in many settings. There is an urgent need to improve upon the low sensitivity of sputum smear microscopy and chest x-ray, the delay in culture results, and the cost of molecular methods. We are investigating a blood-based test of patient-specific immune responses to TB antigens. Previous testing led to selection of ~10 TB antigens providing ~90% sensitivity and ~95% specificity. We translated this method to a quantitative multiplex immunoassay based on commercialized cytometric bead array flow cytometry technology from BD.
Methods: A series of microbeads have been coated with components of specific TB surface proteins. Antibodies in plasma from TB-infected patients bind to one or more of these proteins and a fluorescent secondary antibody binds to human IgG. The bead fluorescence intensities are then measured by flow cytometry in a 96-well plate format. The method is designed to process ~180 samples/day and was tested with 90 TB positive specimens (all culture positive, 73 sputum smear positive and 17 negative) and 90 negative specimens.
Results: TB-positive intensity thresholds were set using a subset of TB negative specimens and the remaining specimens (excluding one unevaluable specimen) were used to assess specificity (91%, std error 3%) and sensitivity (91%, std error 3%). A subset of TB positive specimens was run 3 times over 4 months to test reproducibility, yielding consistent fluorescent signal intensities and identical positive/negative results for each antigen.
Conclusions: These data demonstrate feasibility of blood-based TB testing using available flow cytometry technology. Data are being accumulated on additional populations, including non-pulmonary TB, pediatric, and other negative controls. The test is configured in a laboratory format but may be adapted to point of care.

OA-06-C10 Mycobacterial genotype and drug susceptibility

OA-06-340-31 Towards XDR-TB: evolution and adaptation of a multidrug-resistant M. tuberculosis outbreak over three decades

M Merker,[1] M Barbier,[2] J-P Rasigade,[2] E Shitikov,[3] K Klaos,[4] P Supply,[5] S Niemann,[1] T Wirth,[2] [1]Research Center Borstel, Priority Area Infection, Borstel, Germany, [2]Laboratoire Biologie Intégrative des Populations, Evolution Moléculaire, Paris, France, [3]Federal Research and Clinical Centre of Physical-Chemical Medicine, Moscow, Russian Federation, [4]SA TUH United Laboratories, Mycobacteriology, Tartu, Estonia, [5]Université Lille Nord de France, Center for Infection and Immunity of Lille, Lille, France. e-mail: mmerker@fz-borstel.de

Background: Multidrug- and extensively drug-resistant (M/XDR) Mycobacterium tuberculosis complex (MTBC) strains are responsible for one third of all deaths caused by drug resistant pathogens globally. Previous studies indicate that MDR-TB is mainly caused by recent infections with resistant strains and that certain MDR-MTBC lineages go through unprecedented waves of propagation. Spatial and temporal dimensions of these epidemics are poorly understood but of outmost importance for the successful implementation for new treatment guidelines.
Methods: We leveraged a collection comprising 720 lineage 2 isolates (W148 Russian/European clade) from 22 Eurasian countries. A combination of whole genome sequencing and Bayesian statistics was employed to unravel the evolutionary history and adaptation to drug resistances through space and time.
Results: The onset of the W148 epidemic most likely occurred in Central Asia dating back to the early 1980s, followed by geographic westward spread. Early ancestor strains were already naturally resistant to isoniazid and streptomycin at that time.
After the breakdown of the former Soviet health system bacterial population size increased in the early 1990s along with the acquisition of rifampicin resistance, and thus MDR, in over 50 independent events. This was accompanied by mutations mediating resistance to ethambutol, ethionamide, kanamycin, para-aminosalicylic acid, and putative fitness compensating mutations.
A second population increase around the year 2000 is coinciding with the selection of multiple pyrazinamide resistance conferring mutations rendering these strains now fully first-line resistant. XDR-strains emerged on average 20 years after acquisition of an MDR-genotype in multiple countries and with traceable transmission events.
Conclusions: Our findings demonstrate that MDR and pre-XDR strains are transmissible in Eurasia. The genetic background, exhibiting intrinsic resistances to first and second-line drugs, evolves rapidly towards XDR-

TB and jeopardizes the success of newly endorsed drug combinations in the absence of routine resistance tests for M/XDR drugs such as bedaquiline and clofazimine.

OA-06-341-31 Identifying gaps in universal drug susceptibility testing through a bottom-up approach: a prospective observational study in Telangana State, India

S Chittiboyina,[1] S Shukla,[2] J Kurada,[2] M Zameer,[1] R Adepu,[1] M Parmar,[3] R Ramachandran,[3] S Mase,[3] K Sachdeva,[4] [1]Directorate of Public Health Telangana, State TB Cell, Hyderabad, India, [2]WHO India, RNTCP Technical Assistance Project, Hyderabad, India, [3]World Health Organisation Country Office for India, Tuberculosis, New Delhi, India, [4]Ministry of Health & Family Welfare, Govt. of India, Central TB Division, New Delhi, India. e-mail: stdcepidemiologist@gmail.com

Background and challenges to implementation: Early diagnosis of Multidrug-Resistant tuberculosis (MDR TB) has been a challenge under the National Tuberculosis Program (NTP) in India. To improve the diagnosis of MDR TB, Universal Drug Susceptibility testing (U-DST) was initiated on 1st April 2018 in the State using the Xpert MTB/RIF assay for every bacteriologically confirmed specimen.

If rifampicin resistance (RR), which is predictive of MDR TB, is confirmed, the specimen is sent for second-line Line Probe Assay (SL-LPA) to detect resistance to fluoroquinolones and injectable agents;

If rifampicin susceptibility is confirmed, the specimen is sent for first-line Line Probe Assay (FL-LPA) to detect Isoniazid resistance.

During implementation of U-DST, the following operational challenges were noted-

1.Timely transportation of samples from a Primary Health Center (PHC) to the lab performing the Xpert MTB/RIF assay.

2. Absence of a strong courier service from interior field to District headquarters

3. Difficulty in collecting pediatric/ extra pulmonary samples at PHC level

4. Out of pocket expenditure for health staff/ delay in bills reimbursement.

Intervention or response: U-DST was offered free of cost for patients, using the 31 Xpert MTB/RIF assay public laboratories in the State.

Results and lessons learnt: Data for 2018 reference period revealed that 23924/52010 (46%) bacteriologically positive TB patients received U-DST. Further, only 57% (10717/18514) of RIF susceptible and 40% (756/1886) of RR specimens respectively, reached the State Laboratory for LPA. To complement the limited existing specimen transportation mechanism in State, a formal partnership between State Health Department & Postal Department was devised. The presumptive pediatric & extra-pulmonary cases were referred to District hospitals for superior specimen collection aids.

Conclusions and key recommendations: The uptake of U-DST despite being a National policy, offered free of cost, is sub-optimal in the reference period. Prior situational analysis of logistics, resources and specimen transport mechanisms should be done for better identification and timely resolution of barriers in U-DST implementation.

OA-06-342-31 Expanded drug susceptibility testing to accompany fluoroquinolone-containing universal regimens: the setting dependence of optimal Xpert XDR use

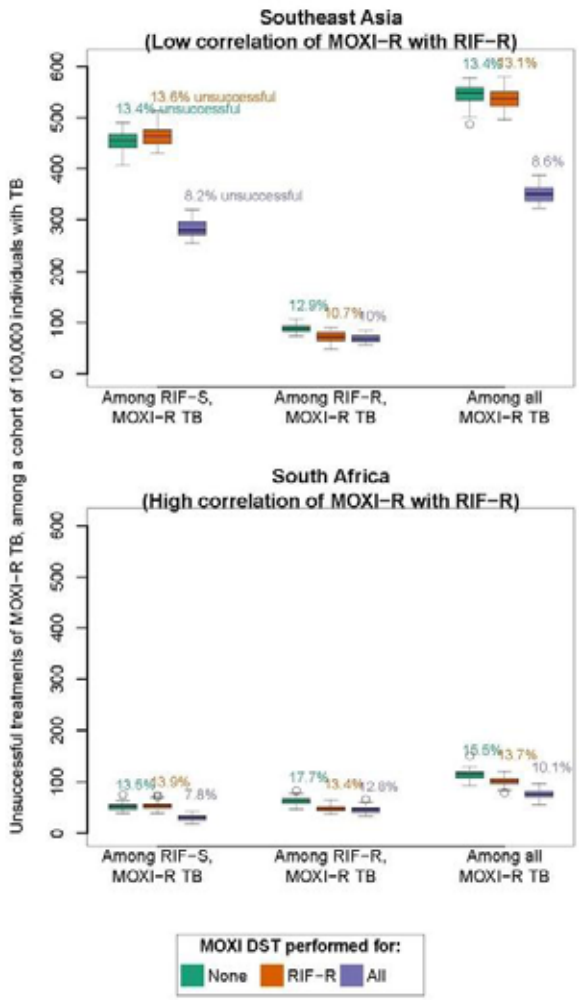
E Kendall,[1] S Malhotra,[2] S Cook-Scalise,[2] C Denkinger,[3,4] D Dowdy,[5] [1]Johns Hopkins School of Medicine, Infectious Diseases, Baltimore, MD, United States of America, [2]Global Alliance for TB Drug Development, Market Access/External Affairs, New York, NY, United States of America, [3]University of Heidelberg, Center for Infectious Disease, Heidelberg, Germany, [4]FIND, TB Program, Geneva, Switzerland, [5]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America. e-mail: ekendal2@jhmi.edu

Background: Clinical trials are currently underway to evaluate rifampin (RIF)-free drug regimens for tuberculosis (TB) that combine novel agents with existing drugs such as pyrazinamide (PZA) and fluoroquinolones - to which nontrivial resistance already exists. The forthcoming Xpert XDR assay could allow for rapid drug susceptibility testing (DST) for fluoroquinolones including moxifloxacin (MOXI) before using such regimens.

Methods: We developed a Markov state-transition model of 100,000 adults with TB undergoing diagnosis and treatment with the regimen BPaMZ (bedaquline, pretomanid, MOXI, and PZA) in two epidemiologic settings: South Africa, where MOXI and PZA resistance are strongly correlated with RIF-R, and Southeast Asia, where the prevalence of MOXI-R among RIF-S TB is also substantial. We evaluated cure and utilization outcomes using no MOXI DST, "stepwise" MOXI DST after RIF-R TB was detected, or MOXI DST for all patients.

Results: Without MOXI DST, BPaMZ cured 89.5±0.1% of patients with TB in both settings, but of patients with MOXI-R TB, it cured only 79.3±1.6% in South Africa and 82.5±0.6% in Southeast Asia. With stepwise MOXI DST, MOXI-R TB cure rates rose to 82.4±1.5% in South Africa and 83.1±0.7% in Southeast Asia (Figure), with similar DST efficiency in each setting: median 130 (interquartile range 90-230) tests per incremental cure in South Africa, and 170 (110-240) in Southeast Asia. MOXI DST for all patients facilitated cure in 86.2 ±1.4% of patients with MOXI-R TB in South Africa and 88.8±0.6% in Southeast Asia while also preventing acquired novel-drug resistance; however, expanding MOXI DST to all TB was far more efficient in Southeast Asia where the prevalence of MOXI-R among RIF-S TB was higher (320±40 additional tests per additional cure, compared to 4300±400 in South Africa).

Conclusions: Xpert XDR could improve outcomes when used with a novel regimen such as BPaMZ, but the optimal implementation approach will depend heavily on local epidemiology.



[MOXI DST enhances BPaMZ cure, but the efficiency of universal DST depends on RIF-S MOXI-R prevalence]

OA-06-343-31 Prevalence and dynamics of genetic heteroresistance in KwaZulu-Natal, South Africa

C Nimmo,[1,2] J Millard,[2,3,4] K Brien,[5] M O'Donnell,[6] A Grant,[7] F Balloux,[8] A Pym,[2] [1]University College London, Infection and Immunity, London, United Kingdom, [2]Africa Health Research Institute, Steyn Lab, Durban, South Africa, [3]Wellcome Trust Liverpool Glasgow Centre for Global Health Research, Clinical PhD Programme, Liverpool, United Kingdom, [4]University of Liverpool, Institute of Infection and Global Health, Liverpool, United Kingdom, [5]Africa Health Research Institute, Microbiology Core, Durban, South Africa, [6]Columbia University College of Physicians and Surgeons, Division of Pulmonary, Allergy and Critical Care Medicine, New York, NY, United States of America, [7]London School of Hygiene & Tropical Medicine, Department of Clinical Research, London, United Kingdom, [8]University College London, UCL Genetics Institute, London, United Kingdom. e-mail: c.nimmo@ucl.ac.uk

Background: Genetic heteroresistance, where >1 allele is present at a resistance-associated variant (RAV) site, can be caused by mixed infection or more commonly within-patient evolution and has been implicated in resistance acquired during treatment although its prevalence remains unclear. Heteroresistance is not quantified by rapid molecular tests or phenotypic drug susceptibility testing (pDST). This prompted us to use whole genome sequencing (WGS) to assess the prevalence of heterozygous RAVs (hetRAVs) in patients initiating therapy for tuberculosis (TB) in South Africa. We primarily selected patients enrolled into observational studies of drug-resistant (DR)-TB.

Methods: Patients newly diagnosed with TB in KwaZulu-Natal, South Africa. Most had rifampicin resistant-TB diagnosed programmatically (292/347, 84.1%) while the remainder had drug susceptible-TB. Sputum was taken for culture at baseline and then at 2-4 week intervals for 6 months. Variants present at < 95% frequency were designated heterozygous. Heterozygous lineage-specific variants were used to identify mixed infections. RAVs were determined according to a modified version of publicly available lists.

Results: After exclusion of nine cases of mixed-strain infections, the majority of hetRAVs identified were present at intermediate frequencies (mean 45.6%). As shown in the table, genetic heteroresistance (i.e. hetRAVs in the absence of any fixed RAVs) was most common for bedaquiline (42.9% of all resistance) and fluoroquinolones (12.9%). Of the 16 hetRAVs that were assessed again at a later timepoint, half had either reached fixation (8/16) or remained present as a hetRAV (5/16), with the remaining 3/16 resistances being lost during treatment.

Drug	Genetic heteroresistance as a proportion of all genetic resistance	hetRAV presence in further sample(s) in those with later sequenced cultures		
		Becomes fixed (homozygous)	Persists as hetRAV	Disappears
Rifampicin	14/292 (4.8%)	4/7	2/7	1/7
Isoniazid	3/229 (1.3%)	1/2	0/2	1/2
Pyrazinamide	0/128 (0.0%)	-	-	-
Ethambutol	3/197 (1.5%)	1/2	0/2	1/2
Fluoroquinolones	8/62 (12.9%)	2/3	1/3	0/3
Injectables	1/41 (2.4%)	-	-	-
Clofazamine	0/23 (0.0%)	-	-	-
Bedaquiline	3/7 (42.9%)	0/2	2/2	0/2

[Frequency and outcomes of genetic heteroresistance by drug]

Conclusions: In South African patients starting treatment for DR-TB, hetRAVs identified by WGS contribute a significant proportion of genetic resistance for some drugs. It is important that future diagnostics are tested for their ability to identify and report hetRAVs, especially given their high frequency at bedaquiline resistance-conferring sites.

OA-06-344-31 Molecular basis of Mycobacterium tuberculosis resistance to new drugs acquired during treatment of MDR/XDR-TB patients

I Mokrousov,[1] A Vyazovaya,[1] G Akhmedova,[2] D Polev,[3] V Molchanov,[1] V Zhuravlev,[4] [1]St. Petersburg Pasteur Institute, Laboratory of Molecular Epidemiology and Evolutionary Genetics, St. Petersburg, Russian Federation, [2]Kaliningrad Regional Anti-Tuberculosis Dispensary, Bacteriology Laboratory, Kaliningrad, Russian Federation, [3]St. Petersburg State University, Biobank, St. Petersburg, Russian Federation, [4]St. Petersburg Research Institute of Phthisiopulmonology, Etiological Diagnostics, St. Petersburg, Russian Federation.
e-mail: imokrousov@mail.ru

Background: Emergence of MDR/XDR Mycobacterium tuberculosis strains requires use of new or repurposed compounds with longer treatment regimens. We aimed to gain insight into genetic variation underlying development of M. tuberculosis resistance to these drugs in the country with a high burden of MDR-TB, Russia.
Methods: We conducted this study as part of an ongoing molecular surveillance study of M. tuberculosis in the Kaliningrad region of Northwest Russia where bedaquiline, perchlozone, and linezolid are used to treat XDR-TB patients. M. tuberculosis isolates were recovered from sputum at the 1-3 months intervals and DST was done using the method of absolute concentrations or Bactec MGIT 960 system. All samples used in this study were blinded. Whole genome sequencing (WGS) was performed at the MiSeq platform (Illumina). The fastq files were analysed using Geneious 9 program (Biomatters, New Zealand) and PHYRESSE.org tool. Protein structures were predicted using Phyre2 web portal and visualized using UCSF Chimera tool.
Results: In total, 34 serial isolates from 12 patients (2-4 per patient) were included. Multiple mutations associated with bedaquiline resistance (stepwise acquired, fluctuating heteroresistance at Rv0678 [MmpR5] efflux pump gene) were observed in the Beijing CAO-cluster isolate. A mutation associated with perchlozone resistance was found in the Beijing B0/W148-cluster isolate (heteroresistance at ethA gene that encodes prodrug activating monooxygenase).
Conclusions: At present, the prevalence of resistance to novel anti-TB drugs in M. tuberculosis in the westernmost Russian province of Kaliningrad appears low but may emerge during treatment. WGS using sufficiently long 300 bp reads was especially useful to detect not only heterogeneous alleles but also co-segregated mutations hence to more adequately monitor development of resistance. In BDQ-resistant isolate, dynamic changes in the Rv0678 mutational profile may speculatively correlate with M. tuberculosis adaptation to the host via biofilm formation.
Acknowledgement. Russian Science Foundation (grant 19-15-00028).

OA-06-345-31 Whole genome sequencing (WGS) is more accurate in predicting drug susceptibility than phenotypic testing by MGIT: a population-based study

R Jajou,[1] T van der Laan,[2] R de Zwaan,[2] M Kamst,[2] A Mulder,[2] A de Neeling,[2] R Anthony,[2] D van Soolingen,[2] [1]National Institute for Public Health and the Environment (RIVM) in the Netherlands, Center of Epidemiology and Surveillance of Infectious Diseases, Bilthoven, Netherlands, [2]National Institute for Public Health and the Environment (RIVM) in the Netherlands, Center for Infectious Diseases Research, Diagnostics and Laboratory Surveillance (IDS), Bilthoven, Netherlands.
e-mail: rana.jajou@rivm.nl

Background: WGS is increasingly used in many countries to detect resistance and predict susceptibility. We investigated the accuracy of WGS to predict susceptibility to the first-line anti-TB drugs and analysed the discrepancies between WGS and phenotypic drug susceptibility testing (DST) by the Mycobacteria Growth Indicator Tube (MGIT) method.
Methods: A population-based study was performed and included in total 1,121 M. tuberculosis complex samples isolated in 2016/2017 in the Netherlands. Nine genes and/or their promotor regions were screened by WGS for resistance-associated mutations. All isolates that were discrepant in their WGS/MGIT results and an additional control group with concordant results, were re-tested in the MGIT at the critical concentration, one concentration lower, and incubated up to 45 days.

Results: In total, 53 discrepancies were re-tested in the MGIT, of which 37/53 (70%) were resolved. The majority of discrepant isolates for isoniazid and ethambutol were explained by growth at one concentration below the critical concentration, and for rifampicin by prolonged incubation (max 26 days) in the MGIT; both indicators of low-level resistance. For pyrazinamide, many results were not reproducible, even not for the standard critical concentration. The negative predictive value of WGS to predict susceptibility was ≥ 99.3% for all four drugs, but positive predictive values (PPV) varied significantly by mutation. When WGS was compared to a composite reference standard, the PPV increased considerably, highlighting the shortcoming of the MGIT to detect low-level resistance. This was confirmed when the MGIT was compared with the composite reference standard and showed low sensitivity for some mutations.
Conclusions: WGS is a more reliable tool in predicting drug susceptibility and especially low-level resistance, which is sometimes missed in the MGIT. Implementing WGS in a country like the Netherlands with a low prevalence of resistance will prevent approximately 90% of phenotypic MGIT DST for isolates that are susceptible.

OA-06-346-31 Sequencing of discrepant rifampicin results between Xpert MTB/RIF and phenotypic drug susceptibility testing on Mycobacterium tuberculosis isolates

M Ninan,[1] E Shalini,[1] D Murugan,[1] P Rupali,[2] V Balaji,[1] J Michael,[1] [1]Christian Medical College Vellore, Clinical Microbiology, Vellore, India, [2]Christian Medical College Vellore, Infectious Diseases, Vellore, India.
e-mail: marilyn@cmcvellore.ac.in

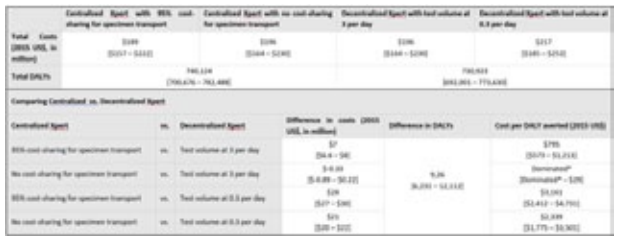
Background: Although WHO recommended probe based methods such as the Xpert MTB/Rif are available for the diagnosis of multi drug resistant tuberculosis, they do not have the discriminatory power to define the mutations that are found. This however, is essential, as silent or disputed mutations do occur. The automated Xpert MTB/RIF assay detects resistance to rifampicin, but occasionally demonstrates false-positive rifampicin resistance.
Therefore we used Sanger sequencing of the Rifampicin Resistance Determining Region (RRDR), in order to resolve discordant Rifampicin results between Xpert-MTB/Rif and phenotypic drug susceptibility testing (Mycobacteria Growth Indicator Tube, MGIT DST) for Mycobacterium tuberculosis(MTB).
Methods: Of all cases of rifampicin resistant tuberculosis diagnosed from January 2017 to December 2018 at the Department of Clinical Microbiology, CMC Vellore, by the Xpert MTB/Rif assay, 25 isolates were discordant between Xpert MTB/Rif and phenotypic DST by MGIT. Sequencing of the RRDR was carried out on 15 retrievable isolates.
Results: Of 15 isolates that underwent sequencing, 3 were susceptible by Xpert MTB/Rif but resistant by the MGIT DST and 12 were Xpert MTB/Rif resistant (probe A-3, probe B-3, probe C-0, probe D-1, probe E-5) but susceptible by MGIT DST.
Sequencing of the RRDR showed all 3 isolates with a mutation in the probe A region by Xpert MTB/Rif had L430P mutation, of those that had a mutation in the probe B region, 2/3 had a D435Y mutation, though all five were susceptible phenotypically. One isolate which was susceptible by Xpert MTB/Rif had an H445D mutation by sequencing, and was also resistant phenotypically. The remaining nine isolates had no mutations by sequencing, including two that were resistant by the MGIT DST method.
Conclusions: In case of discordant results, the clinician is left in a quandary. Sanger sequencing can be used to resolve this and tailor anti tuberculous therapy for such disputed mutations.

OA-06-347-31 Informing decision-making for universal access to quality tuberculosis diagnosis in India: an economic-epidemic model of rapid molecular testing placement strategies

H Sohn,[1] P Kasaie,[1] E Kendall,[2] G Gomez,[3] A Vassall,[3] M Pai,[4] D Dowdy,[1] [1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America, [2]Johns Hopkins School of Medicine, Infectious Disease, Baltimore, MD, United States of America, [3]London School of Hygiene and Tropical Medicine, Global Health and Development, London, United Kingdom, [4]McGill University, Epidemiology and Biostatistics, Montreal, QC, Canada. e-mail: dhjsohn@gmail.com

Background: Many high-burden countries have committed to providing universal access to high-quality rapid diagnosis for tuberculosis (TB), but the most cost-effective strategy to achieve this goal remains uncertain. Centralized testing can generate economies of scale but requires establishment of an efficient specimen transport network. Decentralization can provide faster diagnosis and reduce losses to follow-up (LTFU) but is likely associated with higher operating costs.
Methods: We generated functions to evaluate the costs of centralized and decentralized molecular testing for tuberculosis with Xpert MTB/RIF (Xpert), under different operating assumptions reflecting a range of mean daily testing volume and costs of specimen transport.
We merged the cost estimates with an agent-based simulation model of TB transmission incorporating health system components and patient care-seeking behavior in the three distinct sectors (informal private, formal private, and public).
We constructed this population in a hypothetical emblematic region in India to assess the impact and cost-effectiveness of decentralized versus centralized Xpert testing.

Results: Decentralization was more cost-effective when testing volumes at decentralized facilities and pre-treatment LTFU were high, or when centralized testing relied on a specimen transport network established exclusively for TB. Assuming that centralized and decentralized testing could be performed with equivalent quality, decentralization saved a median $338,000 (interquartile simulation range [IQR]: -$222,000; $889,000) per 20 million people over ten years in the most cost-favorable scenario. In the most cost-unfavorable scenario, decentralized testing would cost a median $3,161 [IQR: $2,412; $4,731] per disability-adjusted life year averted relative to centralized testing.
Conclusions: Assuming that high quality can be assured, decentralized Xpert testing is likely to be cost-saving or cost-effective, particularly in settings with moderate-to-high peripheral testing volumes, high existing clinical LTFU, inability to share specimen transport costs with other disease entities, and/or high willingness to pay. Decision makers should assess these factors when deciding whether to decentralize molecular testing for tuberculosis.



[Incremental Cost-Effectiveness of Decentralized Versus Centralized Xpert Testing]

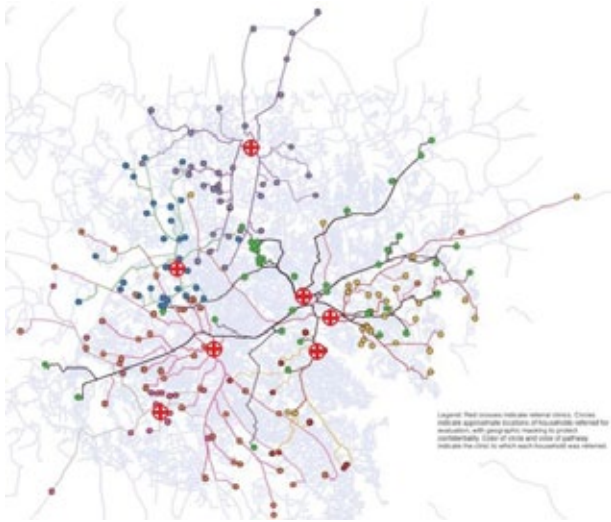
OA-07-C8 Contact management: a neglected approach to active TB case finding?

OA-07-348-31 Geospatial predictors of evaluation for TB among household contacts of confirmed pulmonary TB patients

M Armstrong-Hough,[1,2] E Coker,[3] Y Pan,[4] A Katamba,[5] JL Davis,[1] [1]Yale School of Public Health, Epidemiology of Microbial Diseases, New Haven, CT, United States of America, [2]New York University, College of Global Public Health, New York, NY, United States of America, [3]University of Florida, Environmental and Global Health, Gainesville, FL, United States of America, [4]Yale School of Public Health, Biostatistics, New Haven, CT, United States of America, [5]Makerere University College of Health Sciences, Clinical Epidemiology Unit, Kampala, Uganda.
e-mail: mari.armstrong-hough@yale.edu

Background: The World Health Organization recommends household contact investigation as an active case-finding strategy for tuberculosis (TB). Individuals screened during household contact investigation typically must travel to clinics to complete microbiologic and/or clinical evaluation for TB. Cost or inconvenience of travel to clinic may impede completion of TB evaluation. However, geospatial analyses have been limited to studies of patients who already received a diagnosis or initiated treatment. To increase evaluation among close contacts of TB patients, it is critical to understand potential spatial contributors to evaluation completion.
Methods: We carried out network analyses of spatial data collected from households and clinics during a pragmatic, household-randomized trial in seven public-sector TB units and surrounding communities in Kampala, Uganda. We estimated pathway to referral clinic and transportation distance. We evaluated the association of travel distance to clinic in kilometers with completion of TB evaluation among adults ≥15 years in a logistic regression model, using robust standard errors to account for clustering.
Results: 130 adults from 107 households with complete spatial data were referred for evaluation. Some pathways bypassed nearer clinics (Figure 1) to reach the clinic where the index patient sought treatment (mean distance to referral clinic 4.4km, range 0.05-15.47km). In bivariate analyses, total travel distance to clinic was associated with decreased likelihood of completing evaluation (OR 0.82, 95%CI 0.69-0.98, p=0.03). In adjusted analyses, total distance (aOR 0.82, 95%CI 0.67-0.99, p=0.04) and being male (aOR 3.71, 95%CI 1.67-8.25, p=0.001) were associated with completion of evaluation.
Conclusions: Some index patients sought treatment for TB far from their homes. Among adult contacts, longer distance to referral clinic decreased likelihood of completing TB evaluation. When contacts are referred to the same clinic as index patients, they may be asked to trav-

el unnecessarily long distances for evaluation, passing more convenient clinics and decreasing likelihood that TB evaluation will be completed.



[Figure 1. Estimated pathways to referral clinic]

OA-07-349-31 Lay health worker motivation to perform household contact tuberculosis investigation in a high-burden metropolitan district in South Africa

G Kigozi,[1] C Heunis,[1] M Engelbrecht,[1] [1]University of the Free State, Centre for Health Systems Research & Development, Bloemfontein, South Africa.
e-mail: heunisj@ufs.ac.za

Background: In South Africa, lay health workers (LHWs) are entrusted with a range of crucial TB, HIV/AIDS and maternal health services, including facilitating linkages between communities and primary health care (PHC) facilities. As increased access to quality service delivery hinges upon their motivation, this study investigated LHWs' motivation to deliver systematic TB household contact investigation (SHCI).
Methods: A cross-sectional survey was conducted among all 235 available LHWs in the Mangaung Metropolitan District in late 2017. Descriptive, exploratory factor analysis and multiple linear regression were conducted to establish the dimensions, levels and determinants of LHW motivation. Statistical significance was determined at $p \leq 0.05$.
Results: Participants' median age was 39 years. Job satisfaction, burnout and team commitment characterised LHW motivation or lack thereof, together explaining 56.04% of the total variance. The mean motivation score was 51.59 (± 5.14) out of 64. LHW cadre (community health workers [CHWs] vs. community care givers [CCGs]), TB contact investigation knowledge and training statistically significantly influenced LHW motivation. CHWs (permanent members with formal training) scored twice higher ($\beta = 2.020$; $p = 0.009$) than CCGs (temporary members with less formal training) on the motivation scale. Motivation scores increased by 0.841 ($p = 0.007$) times with every unit increase in LHW TB contact investigation knowledge. Scores were more than twice lower ($\beta = -2.289$; $p = 0.003$) among LHWs who did not attend TB contact investigation training than those who did.
Conclusions: The high mean score implies that overall, the LHWs were motivated to perform SHCI. In the context of PHC re-engineering in South Africa where LHWs perform generalist as opposed to specialist tasks, it is important to ensure sustained LHW motivation to effect improved access to quality TB service provision. The TB programme should pay attention to the CHW cadre's knowledge and training.

OA-07-351-31 Cost-effectiveness of home visits as part of contact investigations to improve tuberculosis preventive treatment uptake in children under five in Benin

M Adjobimey,[1] JR Campbell,[2] O Oxlade,[2] D Menzies,[2] [1]Centre National Hospitalier Universitaire de Pneumo-Pthisiologie, Prevention, Cotonou, Benin, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada.
e-mail: menoladjobi@yahoo.fr

Background: Household contacts (HHC) under-five years of age are highly susceptible to developing tuberculosis (TB). Identification of symptomatic HHC and providing young children with tuberculosis preventative treatment (TPT) can reduce this risk. As part of the ACT4 (NCT02810678) randomized trial, a home visit by nurses during contact investigations was proposed as an intervention to improve TPT uptake in children under-five and TB diagnosis among all HHC in Porto Novo, Benin. In this study we evaluate the cost-effectiveness of this approach.
Methods: A decision analytic model was developed using TreeAge. In the standard of care scenario, TB patients were assumed to bring some high-risk contacts (HHC under-five years and symptomatic HHC) to the clinic for further evaluation. In the intervention scenario, a nurse went to the home to identify contacts, thereby increasing the probability that HHC would report to the clinic. Where possible, probabilities (such as the likelihood of HHC reporting to the clinic in the absence of the intervention) were obtained from trial data, otherwise values from the literature were used. Health system costs (2017 USD) were collected from the setting during the trial. Outcomes evaluated were health system costs and number of children under-five years completing TPT and TB cases detected per 100 contact investigations.
Results: Per 100 contact investigations, 39.2 more children under-five years completed TPT and 1.9 more TB cases were detected with a home visit (**Table**). Relative to standard of care, the cost per additional child under-

five completing TPT was $99.88 and per additional TB case detected was $2060.57 with a home visit.

	Health System Cost (Per 100 Contact Investigations)	TB Detected (Per 100 Contact Investigations)	Children Under-Five Completing TPT (Per 100 Contact Investigations)
Standard of Care Scenario	$2165.80	1.3	29.4
Home Visits Scenario	$6080.90	3.2	68.6
Incremental cost and effectiveness (Home Visits - Standard of Care)	$3915.10	1.9	39.2

[Health system costs and outcomes for standard care and home visit scenarios]

Conclusions: Adding home visits to contact investigations is expected to substantially increase to the number of children completing TPT at very low cost. This intervention is likely to be cost effective in the setting of Benin.

OA-07-352-31 The impact of intensified TB screening at health facilities and via contact tracing in central Mozambique

B José,[1] I Manhiça,[1] J Jones,[1] C Mutaquiha,[1] I Eduardo,[2] J Creswell,[3] ZZ Qin,[3] I Ramiro,[4] M Chidacua,[5] J Cowan,[5,6] [1]Mozambique Ministry of Health, National TB Program, Maputo, Mozambique, [2]Mozambique Ministry of Health, National TB Program, Chimoio, Mozambique, [3]Stop TB Partnership, TB REACH, Geneva, Switzerland, [4]Health Alliance International, Mozambique Office, Maputo, Mozambique, [5]Health Alliance International, TB, Maputo, Mozambique, [6]University of Washington, Department of Global Health, Seattle, WA, United States of America.
e-mail: beneditahjose@gmail.com

Background: Mozambique has one of the highest rates of both TB (551 cases per 100,000) and HIV (national prevalence: 13.2%) in the world and an estimated TB treatment coverage of 54% in 2017 per WHO estimates. As part of a TB REACH Wave 5 project the Mozambican National TB Program (NTP) and Health Alliance International (HAI) supported 30 Community Healthcare Workers (CHWs) across five districts in Manica province who were tasked with increasing TB notifications by performing facility-based active TB screening of all patients and TB contact tracing.
Methods: Using routine NTP data we analyzed trends in TB notifications in five intervention districts and seven control districts in the year before this project and during a one-year intervention period. We also compared this to monthly reports summarizing the activities of each individual CHWs.
Results: In the year before this intervention started (Q4 2016 to Q3 2017) the five intervention districts notified 5,219 cases of all forms of TB, and the seven other districts in Manica province (control area) notified 2,248 cases of all forms of TB. In the first year of this project (Q4 2017 through Q3 2018) the 5 intervention districts notified 5,982 cases of all forms of TB, an increase of 14.6% over the prior year, whereas the control districts notified 1,877 cases, a decrease of 16.5%. Overall these 30 CHWs referred 9,969 presumptive TB cases for laboratory testing and clinical evaluation, of these 1,791 (30% of total cases notified in these provinces) were notified and 979 (55%) had bacteriological confirmation.
Conclusions: This project demonstrated that CHWs who focus on facility-based TB screening and household contact tracing in Mozambique can lead to overall increases in TB notifications. The case-finding strategy and daily registries for CHWs developed for this project are in the process of being scaled up nationally.

OA-07-353-31 Chain referral of "out-of-household contacts" is an effective contact tracing and patient-reaching strategy: initial lessons from East-Central Uganda

R Nyinoburyo,[1] B Nsangi,[1] C Wandira,[1] N Tumwesigye,[2] J Isabirye,[3] B Oduya,[4] [1]University Research Co., LLC, USAID RHITES EC Project, TB/HIV, Jinja, Uganda, [2]University Research Co., LLC, USAID RHITES EC Project, Chief of Party, Jinja, Uganda, [3]Kamuli Hospital, TB/HIV, Kamuli, Uganda, [4]Busia Health Centre, TB/HIV, Busia, Uganda.
e-mail: rnyinoburyo@urc-chs.com

Background and challenges to implementation: In 2018, Uganda notified only 60% of the estimated 80,000 annual TB incident cases, mainly through passive case finding strategies. To achieve the End TB strategy goals, high yielding case finding interventions like contact tracing must be intensified. Implementation of contact tracing currently focuses on household (HH) contacts a practice that misses other social contacts of TB index cases. The Uganda TB prevalence survey also showed that most missed TB is 4 times more prevalent among men.
Intervention or response: The USAID Regional Health Integration to Enhance services in East-Central Uganda (RHITES-EC) project supported two high-volume health facilities (Kamuli hospital and Busia Health center IV) to conduct "chain referral of out-of-household contacts (OHC) by index TB clients" alongside household contact tracing to improve case finding. TB index case referred their OHC social contacts who had similar symptoms, using a referral form or by accompanying them at their next clinic visit. We reviewed program data for January to March 2019 for the two facilities and compared the yield of TB among OHC and HH contact tracing.
Results and lessons learnt: 73 index TB patients at the intervention sites referred a total of 221(159 male:62 female; zero children < 5) symptomatic OHCs These were tested with Xpert MTB/Rif; out of whom 23 were diag-

nosed with TB and started treatment. This represented a TB yield of 10.4% and Number Needed to Test (NNT) of 10 among OHCs. Routine HH contact tracing identified 221 symptomatic contacts who were also tested with Xpert MTB/Rif, yielding 17 TB cases, a yield of 7.7% (NNT 13).
Males among OHC symptomatics were 72% while the HH contactts only consisted of only 32% males.
Conclusions and key recommendations: The Chain referral of OHC by index TB patients model is an effective strategy for contact tracing and for reaching men and should complement household contact investigation for improved TB case finding.

OA-07-354-31 Comparison of effectiveness of door-to-door and contact tracing: tuberculosis case finding strategies in the Kingdom of Eswatini

T Mkhabela,[1,2] H Chomutare,[3] K Shumba,[4] T Dlamini,[5] J Sibanda,[5,6] [1]Ministry of Health National Eswatini, National TB Control Programme, Manzini, Eswatini, [2]Monash University, Public Health, Johannesburg, South Africa, [3]Pretoria Unversity, Public Health, Pretoria, South Africa, [4]University of Kwazulu Natal, Psychology, Durban, South Africa, [5]Eswatini/Swaziland MOH National TB Control Programme (NTCP), National TB Control Programme, Manzini, Eswatini, [6]University of South Africa, Health Sciences, Pretoria, South Africa.
e-mail: khonamkhabela@yahoo.com

Background: The Kingdom of Eswatini is one the TB/HIV high burdened countries. TB incidence is 308/10000 population and a TB/ HIV co- infection rate of 69%. In 2016 the country adopted a two pronged community TB case finding strategy to scale up case detection following a general decline in TB cases from 2010. The first prong of the strategy was door to door where active case finders visit homesteads randomly to educate, screen for TB, collect sputum samples from presumptive for diagnosis and link TB cases for treatment. Complementary they conduct TB screening to household members of index cases. Scientific evidence has shown that door to door screening is less effective than contact tracing hence this study seeks to compare the two strategies in the context of Eswatini.
Methods: All community identified TB cases recorded in paper based facility registers were delineated using two codes, one for contact tracing and door to door. A physical count of cases from June 2016 to December 2018 in 130 health facilities was done. A comparison of the two approaches was made to understand the proportion of clients diagnosed through door to door versus contact tracing. Data was analyzed using descriptive statistics.
Results: For door to door 678 124 people were screened for TB and 1821 cases diagnosed, number needed to screen was 372, yield 269/100 000. For contact tracing 14 828 were screened and 86 TB cases identified number needed to screen 172, yield 580 /100 000.
Conclusions: Although contact tracing had a higher yield than door to door, the proportion of TB cases identified through door to door were 21 times higher. The two approaches need to be implemented complementary because 1821 cases would have been missed if only one approach was used.

OA-07-355-31 Effectiveness of contact tracing mechanism for improving TB case detection in India

P Ambule,[1] R Rao,[1] M Mathew,[2] A Shafie,[1] KS Sachdeva,[1] [1]Ministry of Health & Family Welfare, Central TB Division, New Delhi, India, [2]WHO India, Central TB Division, New Delhi, India. e-mail: ambulep@rntcp.org

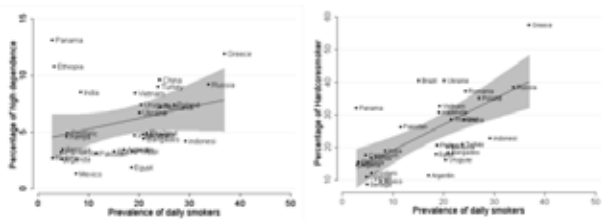
Background: Under the Revised National Tuberculosis Control Program (RNTCP), contact screening has been a clinical function with cursory programmatic monitoring. The National Strategic Plan 2017-2025 addresses the need for contact tracing to be more rigorous, expansive and accountable so that contacts of TB patients are systematically screened with early detection and treatment of secondary cases. The objective of this study is to determine the contribution contact tracing mechanism in TB case detection across the country.
Methods: We analyzed contact tracing data in public and private sectors during January - December 2018, notified in the national notification portal Nikshay.
Results: From January to December 2018, total 2155647 (1613414 from public + 543322 private) TB cases were notified. About 1,211,362 household contacts of index cases were identified in public sector, of which 789,116 (65%) were screened; among the screened, 24,173 (3.1%) were symptomatic, of which 12,292 (51%) were evaluated and 5770 cases (47%) reported positive.
In private sector, 6972 household contacts were identified, of which 6038 (87%) were screened, 272 cases (4.5%) were evaluated and 87 cases (32%) were reported positive.
This mechanism identified additional 5857 TB positive cases with case notification rate of 476/100,000 among contacts in public sector and 1248/100,000 in private sector. For every one case in public sector, there are about three cases in private sector among the household contacts.
Conclusions: A standard procedure for conducting household contact investigation is an extremely high yield activity for active case finding in both the public and private sectors. By ensuring proper implementation of this mechanism, several missing cases can be identified, contributing to the program's goals to end TB.

OA-08-C12 All hands on deck: tools to advance tobacco control

OA-08-356-31 The Heaviness of Smoking Index (HSI) as a measure of nicotine dependence: estimates of dependence from Global Adult Tobacco Surveys (GATS) in 30 countries

C Sreeramareddy,[1] [1]International Medical University, Community Medicine, Kuala Lumpur, Malaysia. e-mail: chandrashekharats@yahoo.com

Background: Hardening′ occurs when smoking prevalence decreases among a subgroup of smokers who are unable to quit. We studied the relationship between country-level daily smoking prevalence and the proportion of highly dependent smokers and hardcore smokers among daily smokers. We further assessed determinants of high dependence and hardcore smoking among daily smokers.
Methods: We reanalyzed 30 GATS country data. Heaviness of smoking index (HSI) measures nicotine dependence based on cigarettes per day (CPD) and time-to-first-cigarette(TTFC). HSI score range is 0-6 and score of 5-6 was high dependence. Hardcore smokers are daily smokers who smoke within 30 minutes after waking up, smoke ≥10 cigarettes per day, have not made any quit attempts during previous 12 months or have no intention to quit at all or during next 12 months. Spearman′s rank-correlation was done to assess the relationship of daily smoking prevalence with high dependence and hardcore smoking among daily smokers. A multi-level linear regression analyses was fitted with HSI score was dependent variable and socio-demographic and smoking characteristics as dependent variables.



[Scatter plot of prevalence of daily smoking with high dependence and hardcore smoking]

Results: The range for the prevalence of daily smoking was 2.8% (Panama) - 36.9% (Greece). Among daily smokers, high dependence ranged from 1.3% (Mexico) to 13.1% (Panama) and hardcore smoking was 8.7% (Senegal) and 57.4% (Greece). Daily smoking was positively correlated with both HSI (r_{sp} = 0.384 , p= 0.04) and HCS) (r_{sp} = 0.615, p< 0.01). HSI score was associated with older age, male sex, lower wealth, lack of attempts and wish to quit smoking and young age at initiation but not associated education, occupation and knowledge about harms of smoking. HCS was associated with age, sex, age at initiation and knowledge about smoking harms.
Conclusions: Daily smoking varied widely among GATS countries but its has positive relationship with HSI and HCS contrary to "**hardening hypothesis**" suggesting that "**Tobacco Endgame**" maybe feasible.

OA-08-357-31 Digit bias in cigarette per day (CPD) and age frequency data: evidence from 28 national tobacco surveys

A Singh,[1] P Jena,[1] P Mohanty,[1] [1]Kiit Deemed to be University, School of Public Health, Bhubaneswar, India. e-mail: drparimalamohanty@gmail.com

Background: Cigarette-per-day is a global tobacco surveillance system monitoring indicator for tobacco use. Being self-reported, digit preference is expected. This study explores and compares the extent of digit bias in cigarette-per-day and age frequency using adapted Whipple Index and explores other indicator to predict digit bias.
Methods: The self-reported cigarette-per-day and age frequency data collected from the daily users of manufactured cigarette by Global Adult Tobacco Survey in 28 countries were analyzed to estimate digit preference for '0' and '5'in cigarette-per-day frequency data and compare the adapted original Whipple Index for cigarette-per-day and age frequency. Use of mode as an indicator of digit bias was explored.
Results: The digit preference in cigarette-per-day frequency data for '0' digit (range: 4.7%,in India to 91.2% in Egypt) was significantly higher than digit preference for '5'digit (range: 2.6% in Egypt to 24.5% in Panama) except in India and Uganda. The adapted Whipple Index for the self-reported cigarette-per-day frequency was ranged from 175.6 to 486.5 indicating very rough quality data. The Whipple Index for age was ranged between 0 and 289.5. Comparing age and cigarette-per-day frequency, the concurrence for digit preference for '5' (range: 0% Indonesia to 45.9% in Panama) was significantly lower than that of '0' (range: 0% in Indonesia to 100% in Malaysia). The correlation between Whipple Index for CPD and age was negative (r=0.46) but non-significant. Most preferred mode was 20(64%) followed by 10(29%), 5(4%) and 2(4%) for cigarette-per day frequency data.
Conclusions: Very rough quality of cigarette frequency in comparison to age frequency is a concern and may be due to various contextual factors including pack size which need to be explored. The Modes for cigarette frequency matches with pack size and can be a rough guide for cigarette-per-day data quality for digit bias.

OA-08-358-31 Community-driven tobacco surveillance system: engaging communities to monitor tobacco industry using a mobile application

C Perera,[1] S Lakmal,[1,2] H Wijesuriya,[1] I Fernando,[1,2] P Dineshkumar,[1,3] S Kandeepan,[1] M Perera,[1,4] M Rajasuriya,[1,5] [1]Centre for Combating Tobacco (CCT), Faculty of Medicine, University of Colombo, Colombo, Sri Lanka, [2]Alcohol and Drug Information Centre (ADIC) Sri Lanka, Strategic Intervention Program, Colombo, Sri Lanka, [3]Alcohol and Drug Information Centre (ADIC) Sri Lanka, North and East Program, Colombo, Sri Lanka, [4]Department of Public Health, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka, [5]Department of Psychiatry, Faculty of Medicine, University of Colombo, Colombo, Sri Lanka. e-mail: chinthi29@yahoo.com

Background and challenges to implementation: Centre for Combating Tobacco (CCT) is the tobacco observatory in Sri Lanka established under the WHO FCTC article 5.3. Resource-efficient methods to engage public in monitoring tobacco industry interference and activities (TIIA) in low-resource settings are needed. Sri Lanka, a developing lower-middle-income country, reports user-rates closer to 100% for smart mobile devices.
Intervention or response: The "Tobacco Unmasked Hot Spots"(TU-HotSpots) mobile application was developed and launched in two stages.The preliminary launch, in May 2018, was to pilot the app for feasibility and acceptability. In March 2019, Community Driven Tobacco Surveillance System (CDTSS), a community network to monitor TIIA using the now-upgraded app following the piloting,was launched.
Freely downloadable from any mobile app store, TU-HotSpots enables registered users to report TIIA under three categories:"Report-a-HotSpot" (geographical location of TIIA circa FCTC articles 5.3, 6, 12, 13, 15, 16), "Interference-through-Media" (FCTC article 13) and "Tobacco-Industry-contacted-me" (FCTC article 5.3).
Data thus reported is approved following review by the CCT team, and is displayed on the TU-HotSpots Map, a website with an interactive map of Sri Lanka,and on its dash board with interactive graphs and charts.
Results and lessons learnt: In an evaluation following the launch of CDTSS, 91.4% (n=54) of participants, when questioned on the feasibility and acceptability, stated that TU-HotSpots would be useful in tobacco control, while 82.8% (n=48) stated the public would accept it. Inadequate technological knowledge and suboptimal online connectivity were the stated perceived challenges for implementation.
Active promotion using organised training sessions among youth and government field officers were the main suggestions for way forward.
As at April 2019, 178 registrants have reported 416 incidents; with 165 approved-Report-a-HotSpot and 92 approved-Interference-through-Media reports, and one approved-Tobacco-Industry-contacted-me report.
Conclusions and key recommendations: A mobile application coupled with an active functional community network constitutes an effective strategy to engage public in monitoring TIIA.

OA-08-359-31 Online surveillance of point of sale for tobacco products to monitor incidences of violation of tobacco advertisement, promotion and sponsorship (TAPS) ban in Bangladesh

H Rahman,[1] AKM Maksud,[2] K Reaz Hossain,[3] MY Abdullah,[4] [1]Datasearch, Data Management, Dhaka, Bangladesh, [2]Grambangla Unnayan Committee, Management, Dhaka, Bangladesh, [3]Grambangla Unnayan Committee, Program, Dhaka, Bangladesh, [4]Grambangla Unnayan Committee, Data Management, Dhaka, Bangladesh. e-mail: grambangla@yahoo.com

Background and challenges to implementation: Grambangla Unnayan Committee has developed an online surveillance software to document and monitor incidences of violation of TAPS ban at the Point of Sales (POS). This activities were under "Implementation of Bans on Tobacco Advertising, Promotion and Sponsorship of Tobacco Control Laws of Bangladesh in Barisal Division" project and supported by The Union and The Bloomberg Initiative To Reduce Tobacco Use.
Intervention or response: Tool of data collection was an online software system with GPS. The method of data collection was census i.e. complete count of all POS of Tobacco at 12 district and sub-district towns of Barisal division in Bangladesh.
Results and lessons learnt: The online surveillance identified 3972 POS at 12 project locations. Types of POS were grocery store (30.5%), kiosk (15.0%), tea stall (42.8%), street open-sky static tobacco vendor (3.8%), tobacco wholesale store (1.4%), tobacco retail shop (1.5%), mobile tobacco vendor (1.0%) etc.
Types of tobacco products were Cigarette (93.9%), Bidi (68.2%), Gul (35.6%), Jorda (90.8%), Cigar (8.3%) etc.34 types of incidences of TAPS ban violations were found at POS level. Recorded types of TAPS ban violations were sticker (59.6%), signage (50.3%), cash box with tobacco sign (28.1%), use of brand name or similar images at POS (27.9%), cigarette packs places on the same shelf as other products in a grocery store (24.7%), showcase with tobacco sign (21.1%), big dummy packet of tobacco product (19.0%), leaflet (18.2%), attractive cigarette display with easy access to children (18.2%), advertising on windows at POS (2.8%) etc.
Conclusions and key recommendations: Online surveillance data made it easy for the District and sub-district Task Force Committees to enforce provisions of Tobacco Control Law since data indicate GPS of the POS and incidences of TAPS ban violations at the POS. This online surveillance system of POS of tobacco products has established a system for enforcement of tobacco control law.

OA-08-360-31 Two for the price of one: purchase price of chewing tobacco and pan masala twin packs in five states in India

M Iacobelli,[1] S Saraf,[1] K Welding,[1] K Smith,[2] J Cohen,[1]
[1]Johns Hopkins Bloomberg School of Public Health, Institute for Global Tobacco Control, Baltimore, MD, United States of America, [2]Johns Hopkins Bloomberg School of Public Health, Department of Health Behavior and Society, Baltimore, MD, United States of America.
e-mail: ssaraf3@jhmi.edu

Background and challenges to implementation: Nearly 200 million individuals use smokeless tobacco (SLT) products in India. Gutkha, a popular type of SLT that combined chewing tobacco and pan masala spices in one packet, was banned in 2013. Although gutkha is banned, the sale of individual packets of chewing tobacco and pan masala spices, often known as "twin packs" is still allowed in most states, effectively circumventing the ban.
Intervention or response: In November 2017, systematic data collection was conducted to capture a breadth of SLT products and any accompanying spice packets vendors sold to consumers in towns (< 50,000 people) in five states (Assam, Maharashtra, Uttar Pradesh, Rajasthan, and Karnataka). Within each state, five towns were selected for data collection. All packs were recorded for price paid to the retailer, price printed on the package, and visually inspected and double coded for product type and presence of spice packet.
Results and lessons learnt: In total, 240 unique SLT products were purchased. Of those, 91 unique chewing tobacco products were purchased, with a range of prices (2-300 Indian Rupees) with an average of 17.59 Rupees. The purchase price of chewing tobacco products purchased with pan masala or pan supari, or twin packs (n=65) ranged from 2-25 Rupees and averaged 5.65 Rupees. Chewing tobacco purchased alone (n=26) ranged in price from 2-300 Rupees and averaged 47.46 Rupees. Nearly a third of twin packs were sold for less than the price printed on the combined packages.
Conclusions and key recommendations: Despite the gutkha ban, consumers are still able to recreate gutkha using chewing tobacco and pan masala or pan supari packets in every state where SLT was purchased. The purchase price paid to the vendor was oftentimes not the amount marked on the package, as required by law. These results should be considered as state governments consider strengthening existing bans or proposing new SLT control policies.

OA-08-361-31 Involving media for tobacco tax advocacy in Bangladesh

A Zubair,[1] MS Alam,[2] [1]PROGGA, Tobacco Control and other Programs, Dhaka, Bangladesh, [2]PROGGA, Tobacco Control Program, Dhaka, Bangladesh.
e-mail: basharzubair@hotmail.com

Background and challenges to implementation: Tobacco taxation was a minor issue for media in Bangladesh. It was one of the least attended issues related to national budget through which all taxes are determined. But things changed recently due to strategic media-focused initiatives for creating interest and increasing capacity on tobacco tax reporting in the media. As a result, the quantity and quality of media coverage on tobacco taxation before and after the declaration of national budget has been remarkable. Informed reporting highlighting demands of tobacco control groups for higher tobacco taxes before budget and critical reaction of tax measures proposed in budget are both widely visible during the few months around budget declaration. Strategic and continuous capacity building of journalists since 2010 has made this change possible. The analysis demonstrates trend of quantitative increase and qualitative enhancement of tobacco tax reporting in Bangladesh media.
Intervention or response: Initially over 350 journalists were trained in general tobacco control issues including at least one session on tobacco taxation. Based on demand, follow-up capacity buildings were done with smaller groups focusing on tobacco taxation. PROGGA organizes at least two annual workshops - before and after budget- to equip journalists with information regarding demands for tobacco taxes that year and with critical analysis of tax measures.
Results and lessons learnt: Increased quantity (4221 in 2016-17 from 1281 in 2014-15) and enhanced quality of media reporting on tobacco taxation was achieved which ultimately made the government consider higher tax measures on tobacco in budget.
Conclusions and key recommendations: Trend of quantitative increase and qualitative enhancement of tobacco tax reporting in Bangladesh media is seen in the last few years.

OA-08-362-31 Coordinated use of earned media campaign to expose, de-normalize and counter influence of tobacco industry in policymaking

M Hossein,[1] AK Azad,[1] [1]PROGGA, Tobacco Control Program, Dhaka, Bangladesh.
e-mail: mukte.mandal@gmail.com

Background and challenges to implementation: Tobacco industry has long been a strategic and aggressive influential factor in Bangladesh's policymaking, undermining tobacco control legislation and thwarting adoption of any stronger tobacco control tools and ef-

fective taxation measures. An effective way to counter industry interference has been the strategic use of media. The present study was conducted with the objective to review the strategy critically and identify what PROGGA has achieved through Anti-Tobacco Media Alliance (ATMA).

Intervention or response: Regular thorough monitoring is conducted to find any attempt of interference from tobacco industry and to promptly share an alert with tobacco control groups and sensitized journalists about the possible implications. A series of journalists' workshops is also conducted on a regular basis to disseminate the fundamental knowledge of tobacco industry, its detrimental effects and effective tobacco control measures. Along with other mechanisms, a yearly Tobacco Control Journalism Award is also awarded to journalists whose impactful media stories have contributed to tobacco control of the country.

Results and lessons learnt: Tobacco industry interferences in policy formulation are being counteracted in Bangladesh through the strategic use of media. The Anti-tobacco Media Alliance - ATMA, a journalists' network of over 350 trained journalists, has been formed to work on tobacco control issues working across the country. The number of media stories on tobacco control rose from 2483 in 2010-11 to 10993 in 2016-17.

Conclusions and key recommendations: The strategic counteraction of media to fight industry interference requires consistent supply of inputs (i.e. information support) to the media and regular follow-up with individual journalists for taking up investigative reporting.

OA-09-E1 Community engagement and advocacy for better lung health

OA-09-364-31 Photovoice: empowering communities to construct knowledge and mobilise collective action for tobacco control in India

M Pant,[1] V Mallik,[1] N Murukutla,[1] A Nagara Gadde,[2] N Mukherjee,[3] S Mullin,[4] N Singh Negi,[1] A Karnik,[5] B Mathew,[6] D Mohanta,[7] [1]Vital Strategies, Policy, Advocacy and Communications, Gurgaon, India, [2]MAYA, Advocacy, Bengaluru, India, [3]MANT, Tobacco Control, Kolkata, India, [4]Vital Strategies, Policy, Advocacy and Communications, New York, NY, United States of America, [5]IPR Media Solutions, Public Relations, Bengaluru, India, [6]Voluntary Health Association of India (VHAI), Public Relations, Delhi, India, [7]Voluntary Health Association of India (VHAI), Tobacco Control, Bhubaneshwar, India.
e-mail: mpant@vitalstrategies.org

Background and challenges to implementation: The problem of tobacco is complex and deeply rooted among many communities in India. For any successful public health intervention, it is imperative to cater to the community perspectives. 'Photovoice' is a qualitative action research method that enables community participation to reflect upon their issues, document their stories through photographs and narratives, and helps generate shared responsibility to take action and provide recommendations to policy makers.

Intervention or response: A rapid photovoice project was conducted in Karnataka, West Bengal, and Odisha. The focus was to highlight two key issues- 'Livelihood and health issues of tobacco farmers and beedi workers' and 'Enforcement of tobacco control laws'. The photovoice project entailed capacity building workshop for civil society participants, representatives from tobacco farmers, beedi workers, doctors, and victims of tobacco, for understanding the technique to express collective voices. It was followed by community group formations, group discussions, documenting photographs, perspectives and narratives, and exhibition of photovoice stories and recommendation to policy makers and program managers.

Results and lessons learnt: The project generated 18 photos with narratives under the focus issues, which were displayed along with a set of recommendations. Key issues under 'Livelihood' were disparity in share from tobacco farming, poor healthcare due to tobacco storage and gaps in accessing education for beedi rollers. Under 'Enforcement', effect of second hand smoke on children, poor implementation of smoke free laws, and flouting of laws at point of sale were some of the issues.

Conclusions and key recommendations: The result of the photovoice highlights the importance of community engagement and participation and reaches out to policy makers with the problems as well as solutions. Some of

the recommendations from both issues were provision of alternative livelihood and farming options, awareness on social schemes, strict enforcement of smoke-free and tobacco-free laws, campaigns to create awareness on health harms of tobacco use as well as for farmers/beedi rollers.

OA-09-365-31 Use of "iMonitor+ ATM Kenya" an alert system to strengthen social accountability around TB, HIV and malaria in Kenya

T Kiptai,[1] N Kimono,[2] N Were,[3] E Omondi,[1] C Mwamsidu,[1] M Mungai,[4] B Ulo,[5] [1]Amref Health Africa in Kenya, Global Fund TB Project, Nairobi, Kenya, [2]NEPHAK, Global Fund TB Project, Nairobi, Kenya, [3]TAC Health Africa, Global Fund TB Project, Nairobi, Kenya, [4]Amref Health Africa in Kenya, HIV/AIDs, TB, Malaria and NCDs, Nairobi, Kenya, [5]Amref Health Africa in Kenya, TB Programme, Nairobi, Kenya.
e-mail: titus.kiptai@amref.org

Background and challenges to implementation: Kenya is among countries with high burden of Tuberculosis (TB), Human Immunodeficiency Virus (HIV) and Malaria. According to WHO 2018 report, accountability can be strengthened by reinforcing monitoring and reporting, review and action. Accountability on commitments made or actions taken is key in improving health systems.

Through Global Fund support, Amref in collaboration with national and county governments, TAC and NEPHAK are implementing integrated TB, HIV and Malaria activities in three counties. Imonitor+ ATM alert system, promotes patient-centered care, prevention and accountability. The System leverages on technology and enable users to share feedback on health services as experienced for improvement in the health systems and promote ownership. Resolution of issues is real time.

Intervention or response: Between Jan 2017 and March 2019, national and county health management teams were sensitized on use of imonitor. 30 Civil Society Organizations and 60 Community Health Volunteers were trained as users and provided with smart phones installed with imonitor+. Users raised issues as experienced by patients and community for action within five thematic areas namely; Commodities, Human Rights, Service Delivery, Social Support and Treatment Literacy. Issues raised, were analyzed and reported immediately to the relevant departments at county and national levels for action. Follow up on resolution of issues and documentation of successes was done.

Results and lessons learnt: A total 866 issues on Commodities (46%), Service Delivery (23%), Treatment Literacy (11%), Social Support (10%) and Human Rights (10%)) were raised. Key issues raised on commodities were unavailability of medicine 30% and mosquito nets 15% while services delivery were on quality of services (46%), human resource (27%) among other services. The issues were resolved within 14 days. Gender based violence and human rights issues took longer time due to their complexities.

Conclusions and key recommendations: Alert system technology helps key stakeholders to timely identify and resolve bottlenecks experienced by the communities thereby promoting social accountability.

OA-09-366-31 Not deaf or dead!: evidence-based advocacy towards a third choice for all people with DR-TB

A von Delft,[1,2] I Schoeman,[1] D von Delft,[1] P Tisile,[1] H-M van der Westhuizen,[1,3] M Galloway,[1] W Human,[1] Z Sifumba,[1] T Mosidi,[1,2] R Nathavitharana,[1,4] [1]TB Proof, TB Advocacy, Cape Town, South Africa, [2]University of Cape Town, School of Public Health and Family Medicine, Faculty of Health Sciences, Cape Town, South Africa, [3]Oxford University, Department of Primary Care Health Sciences, Oxford, United Kingdom, [4]Harvard Medical School, Division of Infectious Diseases, Boston, MA, United States of America.
e-mail: vuzumsi@gmail.com

Background and challenges to implementation: Treatment outcomes for drug-resistant tuberculosis (DR-TB) are poor with high treatment-related morbidity, including irreversible hearing loss in 50% of people receiving injectable aminoglycosides. A 2017 review highlighted the lack of evidence for injectable aminoglycosides and their high toxicity, compared to growing programmatic evidence supporting the efficacy and safety of novel drugs, such as bedaquiline and delamanid.

Intervention or response: A coalition of TB survivors, activists and care providers, coordinated by TB Proof, co-launched the Jolene Samuels #MyPatientsChoice Pledge, calling for all people with DR-TB to be offered an informed choice between regimens including a safer and more effective novel drug or a toxic injectable drug. Activists leveraged international advocacy events, collective civil society organisation (CSO) initiatives and existing relationships with global, national and local healthcare stakeholders, researchers and journalists to gain support (Figure 1).

Results and lessons learnt: Affected DR-TB survivors led the push for policy change in South Africa (SA) with powerful personal testimonies, supported by a growing body of evidence. Media coverage included 23 online articles and six publications in SA newspapers and magazines. The pledge was signed by 13 organisations and 188 individuals, including the SA DR-TB Director. In June 2018, SA made the landmark announcement that bedaquiline would replace routine injectable use, representing a collective advocacy success for patients, CSOs, academic and healthcare partners. The WHO subsequently released new guidelines that also prioritise the use of bedaquiline and linezolid over injectable drugs in DR-TB regimens.

Conclusions and key recommendations: Evidence-based civil society action has played a key role in driving national and global policy and guideline changes, drawing on lessons learned and support from the HIV movement.
Advocacy campaigns underpinned by strong partnerships between TB affected communities, National TB programme managers, talismanic political TB champions, the media and researchers can improve the quality of TB care for all.

[Figure 1: #MyPatientsChoice Pledge Timeline]

OA-09-367-31 Building a unified and informed political leadership to engender policy change in India

D Singh,[1] [1]Global Coalition Against TB, TB, New Delhi, India. e-mail: majordalbirsingh@hotmail.com

Background and challenges to implementation: TB is one of India's most critical public health challenges. Recognizing the role of political leaders as social and policy influencers, interventions needed to be created to inform and encourage their participation in TB policy development and implementation.
Intervention or response: In 2012, the Global Coalition against TB (GCAT) (formerly the National Forum on TB) was convened to create an informed group of political leaders that were advised by public health experts and engaged health ministry officials on TB. Today with 41 motivated political leaders, and 19 technical experts as members, the GCAT meets regularly to discuss relevant challenges and derive recommendations that are shared with the Indian health ministry's leadership. Members also raise issues at different international and national platforms, through public statements and media articles, and support the TB program in their constituencies.
Results and lessons learnt: Regular policy deliberations by an independent, bi-partisan body like GCAT with senior government officials contributed to a series of landmark developments including making TB a 'notifiable' disease, banning of the inaccurate serology test, greater engagement of private sector, and the provision of nutrition support for all TB patients. Additionally, this has resulted in committed political leaders monitoring the progress of the TB program in their constituencies.
Conclusions and key recommendations: The Moscow Declaration 2017 and the UN Political Declaration on TB, both reiterate that leadership, governance and multi-stakeholder ownership is imperative to end TB. GCAT's model of elected leaders guided by technical experts and evidence has proven successful in presenting a unified multi-stakeholder, multi-partisan front for advancing policies to end TB. This model can be duplicated as interested leaders equipped with the right information and tools, can galvanize support and contribute to change at multiple levels.

OA-09-368-31 How to organise a successful advocacy campaign to further necessary TB progress: the new Romanian TB Law

CF Enache,[1] P Rusu,[2] S Radut,[3] [1]Romanian Angel Appeal Foundation, Advocacy, Bucharest, Romania, [2]Romanian Angel Appeal Foundation, Communication, Bucharest, Romania, [3]Association for Supporting MDR-TB Patients, (ASPTMR), Bucharest, Romania. e-mail: cristina.enache@raa.ro

Background and challenges to implementation: Every year Romania has the highest number of new and relapsed TB cases in the European Union. Unfortunately, quality people-centred TB care remains out of reach for the majority of the population. In order to further at least some of the principles of the quality people-centred care, the Romanian Angel Appeal Foundation (RAA) and the Association for Supporting MDR-TB Patients (ASPTMR) developed a legislative proposal in 2016, endorsing provision of social, psychological and financial support for people with TB. Unfortunately, due to initial disapproval by the Ministry of Health (MoH) and the National TB Programme (NTP), the Senate rejected the bill.
Intervention or response: To ensure that the proposal does not disappear in administrative "black hole" following rejection, RAA developed and carried out a comprehensive advocacy campaign in 2017-2018.
The advocacy campaign included three strands of action: 1) online mobilization campaigns aimed at the general public, including an online petition signed by more than 8500 people; 2) national level advocacy, including regular meetings with MPs, Health Minister and NTP Coordinator; 3) international advocacy, including contribution to the Universal Periodic Review and meetings with Embassies.
Results and lessons learnt: The advocacy campaign succeeded and on November 14th, the TB Bill was voted in the Parliament and became a law on December 15th 2018. The success of the campaign was noted and RAA received an award in the Public Participation Awards Gala 2019.

Conclusions and key recommendations: As the result of the law, people with TB are entitled to a monthly food allowance and sick leave and indemnity for temporary work incapacity, regardless of contribution period, for the whole period of treatment until being cured. The law ensures a free, correct, comprehensive quality treatment and psychosocial support within their community. The impact of the law is both budgetary and programmatic, and the MoH and the NTP will have to revise the guidelines accordingly.

OA-09-369-31 Community engagement to motivate participation in a mobile TB screening programme in Lima, Peru: a theory-driven approach

DV Puma Abarca,[1] H Valdivia,[1] LV Carrillo Montenegro,[2] J Jimenez Guevara,[1] CM Yuen,[3] MB Brooks,[3] L Lecca,[2] MC Becerra,[3] SA Keshavjee,[3] JT Galea,[4] [1]Socios en Salud - Partners In Health, Tuberculosis Program, Lima, Peru, [2]Socios en Salud - Partners In Health, Direction, Lima, Peru, [3]Harvard Medical School, Department of Global Health and Social Medicine, Boston, CT, United States of America, [4]University of South Florida, College of Behavioral and Community Sciences, Tampa, FL, United States of America.
e-mail: dpuma_ses@pih.org

Background and challenges to implementation: As part of the HALT TB initiative, Socios En Salud launched the "TB MOVIL" program in Lima, Peru aiming to screen 100,000 persons for TB. Concerned with reaching our recruitment targets, especially people less likely to be screened for TB (men; healthy individuals with no known contact with TB cases), we designed a multifaceted Community Engagement Plan (CEP) prior to the project launch.
Intervention or response: Informed by the Theory of Diffusion of Innovations, the CEP included:
1. Identification of key social networks and their leaders (called "community popular opinion leaders" (CPOLS)) and congregation venues;
2. Identification of barriers/facilitators to TB screening;
3. Logo creation, street murals, and messages addressing TB screening barriers and diffused verbally by CPOLs and,
4. The deployment of staff to both invite/direct people walking past the mobile unit and visit individual homes to invite and accompany residents to the mobile unit.
Results and lessons learnt: TB MOVIL launched in February, 2019. By April 15, 2019, we had screened 5,248 people (approximately 95 per day), 43.7% were men.
The CEP's multimodal messaging has penetrated the community, reaching people less likely to get screened for TB. Home visits have significantly boosted the recruitment of the most difficult to reach people and provided real-time information about events (eg, funerals, sporting events, political campaigns) that affect screening operations.
Of the 974 people with abnormal radiography, 510 (52%) had heard of the HALT TB initiative before reaching the campaign.
Conclusions and key recommendations: A theory-informed recruitment tailor-made for TB screening in our target community has proven successful in meeting our ambitious recruitment goals thus far. Crucially, our CEP reaches individuals who interact less with the health system and may normally forgo TB screening. Though crafted specifically for our project, a similar approach could be followed for the development of CEPs at the TB Program level.

[Community Engagement Plan]

OA-09-370-31 Survivor-led networks in Bihar and Jharkhand: empowering TB champions for a rights-based response to TB

S Kumar,[1] A Srinivasan,[1] A Panda,[2] P Mishra,[2] P Singh Baghel,[3] D Sharma,[4] S Singh,[5] R Verma,[6] R Ananthakrishnan,[7] A Goswami,[8] [1]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, Chennai, India, [2]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, New Delhi, India, [3]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, Patna, India, [4]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, Ranchi, India, [5]TB Mukt Vahini, Network, Patna, India, [6]TEJ, Network, Giridih, India, [7]REACH (Resource Group for Education and Advocacy for Community Health), Organisation, Chennai, India, [8]USAID India, Health Office, New Delhi, India. e-mail: smrity.reach@gmail.com

Background and challenges to implementation: In India, survivor-led networks for TB are relatively nascent. An effective network can build the knowledge of communities and act as advocates for rights-based care for people with TB.

Intervention or response: In Bihar and Jharkhand, survivor-led networks were formed in 2018 as an outcome of capacity-building workshops for TB survivors organized by REACH under Call to Action project supported by USAID. TB Mukt Vahini (TMV) was formed with 13 TB Champions from 7 districts of Bihar and TEJ (TB Elimination in Jharkhand) with 14 Champions from 9 districts. The networks defined their mandate as supporting people with TB, raising awareness among communities and advocating for high-quality services.

Results and lessons learnt: In 14 months, TMV has grown from 13 to 243 members from across 16 districts of Bihar. TEJ has 355 members from 21 districts in Jharkhand. Membership is restricted to TB survivors and in exceptional cases, family members of people affected by TB. Network members organized simultaneous padyatras (TB-walk) across several districts to sensitize communities. TEJ members supported frontline workers to counsel people with TB from tribal communities. Using social media, TEJ highlighted gaps at the facility level for swift action by authorities. TMV members provided psychosocial support to people with TB and help identify those with TB symptoms, linking them to the nearest facility. 13 members of TEJ and 11 from TMV are part of national, state and district TB Forums. TMV is now registered as an independent legal entity.

Conclusions and key recommendations: The steady expansion of TMV and TEJ has demonstrated that survivors can come together in a structured manner, and advocate with a unified voice for better services for people with TB. This process can be replicated across the country at national, regional and local levels to ensure voices of affected communities are heard.

OA-09-371-31 Generational awareness and acceptance of the National Comprehensive Tobacco Control Law in Iran

A Nazari,[1] S Ghafari,[1] S Hamzeh ali,[2] [1]Iranian Anti Tobacco Association, Tobacco Control Research Center, Tehran, Iran, Islamic Rep. Of, [2]Tobacco Control Research Center(Iranian Anti Tobacco Association), Tobacco Control Research Center, Tehran, Iran, Islamic Rep. Of. e-mail: sanaz.hamzehei@gmail.com

Background: According to the results of the STEPS studies in 2016, the prevalence of tobacco use in Iran is 14.3%. About 6.4 million adult smokers in Iran use about 50 billion cigarettes each year. The National Comprehensive Tobacco Control Law was ratified by the Iranian parliament in 2006.

Methods: This study was carried out during the 32nd Tehran International Book Fair in Tehran. Data collecting was executed through the field research with a sample consisted of 1,100 exhibitors. The method of research was simple random sampling.

Results: According to the present study, 33.8% of respondents were aware of the existence of the National Comprehensive Tobacco Control Law. Among them, 54.8% were properly informed of the details of the law, especially the prohibition of tobacco sale to people under the age of 18. Moreover, 69.4% of respondents reported their acceptance of restrictions and control of smoking in public places. However, the rate of acceptance varied among generations. For example, respondents born in the 1970s and earlier had the lowest acceptance rate (9.4%), while respondents born in the 1980s had the highest acceptance rate (41.9%). The rate of acceptance in respondents born in the 1990s and later was 31.1%.

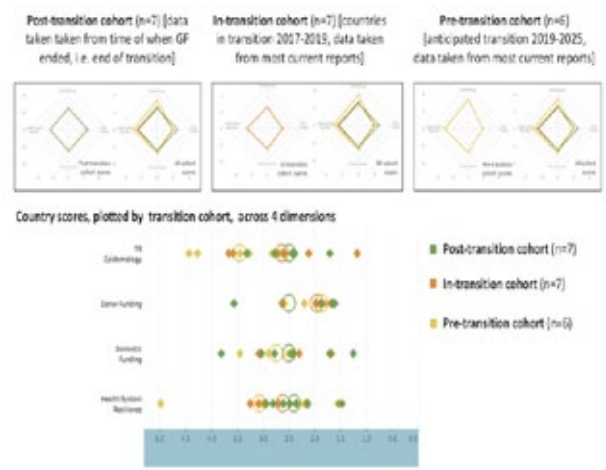
Conclusions: More than a decade after the ratification of the National Comprehensive Tobacco Control Law in Iran, less than one-third of the cultural strata of the community are aware of it. On the other hand, the two-third of these people agree to apply restrictions on tobacco use in public places. The rate of acceptance in young generations is significantly higher. Therefore, policymakers and the civil society should focus more than ever on improving the information dissemination, utilizing the generational capacities, and creating the sense of demanding in citizens.

OA-10-C9 National policymaking to achieve HLM & end TB goals

OA-10-372-31 A new tool for assessing country readiness for transition from Global Fund financing for Tuberculosis

M Reid,[1] G Roberts,[2] P Wesson,[3] N Beyeler,[4] S Fewer,[4] E Goosby,[1] [1]UCSF, Medicine, San Francisco, CA, United States of America, [2]N/A, N/A, New York, NY, United States of America, [3]UCSF, Epi & Biostats, San Francisco, CA, United States of America, [4]UCSF, Institute of Global Health Sciences, San Francisco, CA, United States of America.
e-mail: michael.reid2@ucsf.edu

Background: There is pressing need for validated tools to assess readiness for donor financing transition in high TB burden countries that will soon be ineligible for GF financing for TB.
Methods: We developed an assessment tool to evaluate country-level transition-readiness across four TB-related dimensions; (1) TB disease burden [measured as TB effective treatment coverage for drug-susceptible and drug-resistant TB], (2) domestic financing of TB services [measured as percentage domestic TB budget unfunded and domestic funding for TB per incident case] , (3) current GF financing for TB [as a percentage of each countries' total TB budget], and (4) health system resilience [documented as health workforce density and indicator of essential medicine costs]. Countries categorized as being in-transition, or pre-transition, were compared to a cohort of countries that had already successfully transitioned out of GF TB-specific aid. For each indicator, country-specific Z-scores were calculated, based on distribution of standard deviations derived from the post-transition cohort at the time of their GF-transition. Z-scores were then scaled (0=best, 5=worst) across each dimension and ANOVA used to compare cohorts across each dimension.
Results: The analysis included 6 pre-transition, 7 in-transition and 7 post-transition countries. There were no significant differences between the cohorts across 3 of 4 domains, but post-transition countries had achieved higher rates of TB treatment coverage at time of transition compared to the other cohorts (p=0.048). Notably, several pre-transition countries (e.g. Kazakhstan, Armenia and Albania) had much higher (e.g. worse) scores on all 4 dimensions compared to the post-transition cohort). Radar visualization (figure 1) highlights average differences between the three cohorts.
Conclusions: This simple transition-readiness tool can highlight countries where transition would be high-risk compared to countries that have successfully transitioned. Furthermore, the results demonstrate that the cohort of countries currently in transition appear to have strong capacity to manage this 'donor transition.'



[Figure 1. Radar visualization of transition cohorts across 4 scored dimensions (0=best, 5=worst)]

OA-10-373-31 Post-Global Fund household financial burden due to multidrug-resistant tuberculosis in Guizhou province, China

Y Wang,[1] E McNeil,[2] Z Huang,[3] L Chen,[4] H Chen,[5] X Lu,[1] C Wang,[4] V Chongsuvivatwong,[2] [1]Guizhou Medical University, School of Medicine and Health Management, Guiyang, China, [2]Prince of Songkla University, Epidemiology Unit, Faculty of Medicine, Hat Yai, Thailand, [3]Guiyang Public Health Clinical Center, Department of Tuberculosis, Guiyang, China, [4]Affiliated Hospital of Zunyi Medical University, Department of Respiratory Medicine, Zunyi, China, [5]Guizhou Center for Disease Prevention and Control, Department of Tuberculosis Prevention and Control, Guiyang, China.
e-mail: fafafa3936@126.com

Background and challenges to implementation: China, where the Global Fund has terminated its support for the tuberculosis program, has the second highest multidrug-resistant tuberculosis (MDR-TB) burden. Guizhou is a low-income province in southwest China having a high MDR-TB burden. Nearly all households are under various public health insurance schemes in Guizhou, none of which fully covers MDR-TB.
Intervention or response: We aimed to quantify the household financial burden due to MDR-TB and household's coping strategies in Guizhou and to identify predictors of catastrophic total costs. A cross-sectional study combining hospital-based patient interviews and household visits was conducted from November 2017 to August 2018.
Results and lessons learnt: A total of 161 eligible households with MDR-TB patients were investigated. The median (interquartile range) of total healthcare costs due to MDR-TB for the first 12 months was US$7,787 (5,122-10,090), which included 50% direct out-of-pocket payments, 23% productivity loss and 27% insurance payments. The median annual household income predisease was US$10,430. Overall, 53% of households

were shared by direct out-of-pocket payment and productivity loss. While various health insurance schemes covered 97% of the affected families, 87% households faced catastrophic total costs and 22% were pushed into poverty. In order to cope with the financial burden, 37% of households tried to save money, 39% reduced daily expenses and 63% were forced to borrow money. Predictors of catastrophic total costs were households in which the patient was the primary income earner, patients with a long inpatient stay, and those who lost their job after getting MDR-TB.
Conclusions and key recommendations: During this post-Global Fund period, the current Chinese health insurance could not serve as a safety net for households affected by MDR-TB. This may accelerate the spread of MDR-TB in the near future. Hence, more investment is needed to maintain a uniform insurance support system for MDR-TB in China.

OA-10-374-31 Business unusual: patient-centred and costed national strategic plan for Kenya

N Omale,[1] E Omesa,[1] M Kamene,[1] E Masini,[2] [1]Ministry of Health, National Tuberculosis, Leprosy and Lung Disease Program, Nairobi, Kenya, [2]Stop TB Partnership/UNOPs, Regional Advisor, Geneva, Switzerland.
e-mail: nomale@nltp.co.ke

Background and challenges to implementation: Tuberculosis is the leading cause of morbidity in Kenya with historical TB control strategies allocation of equal resources in an all size-fit-all approach based on programmatic experience and routine reporting. Recent evidence demonstrated that this approach may have gaps evidenced by the prevalence survey 2016 demonstrating that Kenya was missing > 40% of people with TB (PWTB) with 67% failing to seek care, mostly men, whereas 80% of those who did, were missed; and inadequate alignment of TB services where patients sough initial care. In addition, 84% of TB patients incurred catastrophic costs while seeking care.
Intervention or response: This informed the need to develop a differentiated patient-centered strategy of finding missing PWTB in the first ever costed and comprehensive National Strategic Plan (NSP) 2019-23 regionally to achieve the END TB targets. This process incorporated review of existing evidence, prioritization of differentiated interventions and impact evaluations and modelling to optimize effectiveness to close gaps along the patient pathway.
Results and lessons learnt: The process resulted in an NSP that laid out the strategic and technical direction for the elimination of TB in Kenya that represents the vision as well as to achieve targets that align with END TB strategy goal. The immediate implementation of the framework, prior to its launch, led to an increase in TB detection of over 10%, with an outcome target of 542,000 adults and 55,000 children with TB, 4,500 MDR TB patients and 900,000 people initiated on LTBI by 2023. Mathematical modelling for the most impactful, yet minimal-cost interventions to achieve targets with a reduction of: incidence by 80%, death by 90%, chronic lung diseases by 90% compared to 2015 and 0% patients incurring catastrophic costs by 2030.
Conclusions and key recommendations: Evidence-based, patient-centered strategy in a high burden resource-limited setting is paramount to achieve global END TB strategy targets and should be adopted by NTPs.

OA-10-375-31 The social and financial costs of seeking child tuberculosis care in Kampala, Uganda

D Jaganath,[1,2,3] E Wobudeya,[4] P Wambi,[4] R Crowder,[2,3] P Shete,[2,3] C Adithya,[2,3] [1]University of California (UCSF), Pediatric Infectious Diseases, San Francisco, CA, United States of America, [2]University of California (UCSF), Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [3]University of California (UCSF), Center for Tuberculosis, San Francisco, CA, United States of America, [4]Mulago National Referral Hospital, Directorate of Paediatrics and Child Health, Kampala, Uganda.
e-mail: devan.jaganath@ucsf.edu

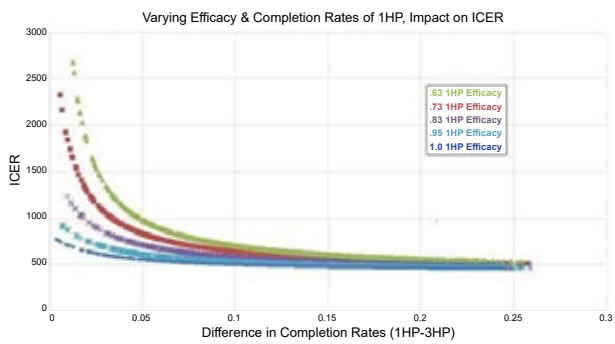
Background: Eliminating catastrophic costs from tuberculosis (TB) is a key goal of the End TB Strategy. Research on patient costs has focused on adults. We determined the pre-treatment costs to households of children with presumptive TB in Kampala, Uganda.
Methods: We enrolled consecutive children who were referred to a pediatric TB clinic and met clinical criteria for presumptive TB. We administered surveys to adult caregivers on the child's clinical status and household socio-demographics. They also completed an adapted WHO TB patient cost survey to capture loss of income, dissavings practices, and coping strategies.
Results: Of 61 children with presumptive TB from 53 caregivers, the median age was 3.4 years (IQR 1.1-5.9), 44% were female (95% CI 32-57), 18% (95% CI 10-30) were HIV-infected, and 11% (95% CI 4-27) had severe acute malnutrition. Children had a median of 3 (IQR 2-5) medical visits before their current TB evaluation. The median annual household income was $730 USD (IQR $324-$1,375), and most (49/53, 93%) caregivers reported that household finances were negatively affected by their child's illness. The majority of households reported lost income (45/52, 87%), and eight (20%) incurred costs that were catastrophic. The majority missed work (42/51, 83%), and about half (23/48, 48%) had to pay more for child care during the illness. Dissavings strategies, including selling livestock, taking out a loan, or selling other assets, were reported by 23/50 (46%) caregivers. Almost two-thirds of school-age children missed school (19/31, 61%), and over half (31/56, 55%) were perceived to be lagging in learning or development because of the illness.

Conclusions: Prior to treatment, families of children with presumptive TB already face a large financial and social burden. Our results suggest childhood TB has unique costs that should be integrated into the discourse on social protection for TB-affected households.

OA-10-376-31 Cost-effectiveness of preventive therapy for tuberculosis: one-month daily isoniazid and rifapentine vs. three-month weekly isoniazid and rifapentine

O Ferguson,[1] D Dowdy,[1] K Johnson,[1] A Tucker,[1] Y Jo,[1] [1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America.
e-mail: ofergus1@jhu.edu

Background: Investing in preventive therapy is key to reducing the burden of tuberculosis (TB). Implementation of isoniazid preventive therapy (IPT) for six months or more is challenging in high-burden settings. Alternatives to IPT include a three-month regimen of weekly isoniazid and rifapentine (3HP) and, most recently, a one-month regimen of daily isoniazid and rifapentine (1HP). The conditions under which 1HP might be cost-effective relative to 3HP remain uncertain.
Methods: We combined a decision analysis of preventive therapy outcomes with a Markov state-transition model of costs and outcomes to estimate the incremental costs and effectiveness (ICER) of 1HP versus 3HP in a simulated cohort of 1000 patients attending an HIV clinic in a low income, high burden setting. ICER was expressed as 2017 US dollars per disability-adjusted life year (DALY) averted over a 20-year time horizon from a system perspective. For the base case, 1HP was assumed to be noninferior in terms of efficacy and completion rates. We estimated cost-effectiveness under varying assumptions regarding the difference between 3HP and 1HP in terms of completion and efficacy, as well as latent TB prevalence and rifapentine price.
Results: For 1HP to achieve the same level of effectiveness as 3HP on an identical population, 1HP resulted in an additional $13,888 in total costs. A multivariate sensitivity analysis, showed significant impact of completion rates and drug efficacy on the incremental cost effectiveness (ICER) of 1HP relative to 3HP.



[Multivariate Analysis]

Conclusions: The cost-effectiveness of the 1HP regimen is likely to depend on the cost of rifapentine, drug completion rates and efficacy, and the local willingness to pay (WTP). A reduction in the price of rifapentine would decrease the cost of the 1HP and 3HP regimens, thus increasing the probability a country would be willing to pay.

OA-10-377-31 It's not all about new drugs: impact of economic migration and social factors on loss to follow-up among patients receiving bedaquiline and delamanid in Armenia

N Khachatryan,[1] A Madoyan,[2] O Kirakosyan,[2] L Yegiazaryan,[3] L Kocharyan,[4] H Atchemyan,[2] L Hovhannisyan,[2] A Serobyan,[2] A Melikyan,[2] C Hewison,[5] [1]Médecins Sans Frontières, Armenia, Paris, France, [2]Médecins Sans Frontières, Armenia, Yerevan, Armenia, [3]National Tuberculosis Control Centre of the Ministry of Health of the Republic of Armenia, National Tuberculosis Control Centre MDRTB Unit, Yerevan, Armenia, [4]National Tuberculosis Control Centre of the Ministry of Health of the Republic of Armenia, National Tuberculosis Control Centre, Yerevan, Armenia, [5]Médecins Sans Frontières, Medical Department, Paris, France.
e-mail: cathy.hewison@paris.msf.org

Background: Emigration for socio-economic reasons is common in Armenia, with approximately 25% of the population living outside the country. Migration impacts TB diagnosis and treatment outcomes. We examine reasons for lost to follow-up amongst MDR-TB patients starting new TB drugs in Armenia.
Methods: This is a mixed method study that included patients started on MDR-TB treatment containing bedaquiline or delamanid between April 2015 and March 2018. Patients' data were entered prospectively into an electronic medical record and medical staff and a subset of patients were interviewed.
Results: Amongst 155 patients who started delamanid or bedaquiline in the reporting period, 27.1% (42/155) were lost to follow-up. Amongst those lost to follow-up: the majority were men (83.3%, 35/42), previously treated for TB (36/42, 85.7%) with a median age of 43.1. The majority of patients (33/42, 78.6%) were lost to follow-up before 12 months: 23.8% (10/42) at 1-3 months, 26.2% (11/42) at 4-6 months and 21.4% (9/42) at 7-9 months. Reasons for lost to follow-up: 54.8% (23/42) economic migration (Russian Federation 42%, Europe 12%), 14.3% (6/42) stigma, denial of diagnosis or patient refusal, 11.9% (5/42) social problems, 19% (8/42) other reasons including treatment delivery model incompatible with childcare or working hours, inaccessibility due to remote location and transport issues.
Patient interviews commonly reported the necessity to provide financially for the family as a reason for migration. As a consequence TB treatment was interrupted despite awareness of the negative impact on TB disease.

Conclusions: In Armenia, despite social support provided by the National Tuberculosis Program and Médecins Sans Frontières, a high proportion of the patients were lost to follow-up, most of them due to economic reasons or social problems. In addition, the treatment delivery model may not be adapted to the patients' needs. Alternative patient centred treatment models allowing travel or additional social support may encourage treatment completion.

OA-10-378-31 Addressing social determinants of health to reduce TB burden - nutritional support for all TB patients in India!

D Balasubramanian,[1] B Vadera,[1] R Rao,[1] R Ramachandran,[2] KS Sachdeva,[1] [1]Ministry of Health & Family Welfare, Central TB Division, New Delhi, India, [2]World Health Organisation, TB Control Programme, New Delhi, India. e-mail: deep19882000@gmail.com

Background and challenges to implementation: Undernutrition and tuberculosis (TB) have a bidirectional relationship, which at the population level contributes to an estimated 55% of annual TB incidence in India. Government of India launched a scheme for nutritional support - "Nikshay Poshan Yojana" for all TB patients registered in the online portal "Nikshay" of National TB program.

This scheme entails transfer of 500 INR every month throughout the course of treatment directly into the bank account of the beneficiary. Nutritional support can provide for reduced out-of-pocket expenditure, improved treatment success rates and thereby decreasing transmission. This article documents the learning′s of implementing this scheme nation-wide.

Intervention or response: The article presents an analysis of secondary data collected though Nikshay portal under the National TB programme from April 2018 to July 2018. Beneficiaries considered include those diagnosed with TB and registered from 01st April 2018 to 30th June 2018 and have completed at least 1 month of treatment.

Results and lessons learnt: As on 31st July 2018, nearly 4,88,213 eligible beneficiaries were identified across all States/Union territories (UTs) in the country. Among whom only 15% (71132) of the beneficiaries had received the benefits, ranging from 2% to 31% across States/UTs. Moreover, nearly 46% (2,26,955) beneficiaries did not have their bank account details seeded in Nikshay portal, with the gap ranging from 87% to 17% across States/UTs.

Conclusions and key recommendations: Wider dissemination of information on provision of monthly support for nutrition to enhance demand generation, further emphasis on seeding of bank account details and processing of payment through a simplified approach needs to be carried out.

Sno	State	Total TB beneficiaries eligible for Nikshay Poshan Yojana (N)	Total TB beneficiaries with valid Bank account among eligible (N)	(N/%)	Total TB beneficiaries payment processed among those initiated in Nikshay (N)	(N/%)
1	Andhra Pradesh	20533	16980	83%	5669	28%
2	Arunachal Pradesh	1036	457	44%	189	18%
3	Assam	10648	4392	41%	1662	16%
4	Bihar	15907	7514	47%	1557	10%
5	Chandigarh	2095	658	31%	152	7%
6	Chhattisgarh	7130	3801	53%	526	7%
7	D & N Haveli	214	123	57%	64	30%
8	Daman and Diu	149	48	32%	19	13%
9	Delhi	22406	5461	24%	1567	7%
10	Goa	579	274	47%	92	16%
11	Gujarat	33803	12870	38%	4635	14%
12	Haryana	16128	8351	52%	3268	20%
13	Himachal Pradesh	5184	2605	50%	221	4%
14	Jammu & Kashmir	3823	1641	43%	497	13%
15	Jharkhand	11085	6604	60%	2848	26%
16	Karnataka	23329	11121	48%	2975	13%
17	Kerala	4035	2382	59%	990	25%
18	Lakshadweep	4	2	50%	0	0%
19	Madhya Pradesh	36654	20240	55%	3200	9%
20	Maharashtra	34123	16066	47%	5028	15%
21	Manipur	443	204	46%	83	19%
22	Meghalaya	848	209	25%	29	3%
23	Mizoram	815	397	49%	108	13%
24	Nagaland	802	107	13%	19	2%
25	Odisha	13812	8609	62%	2819	20%
26	Puducherry	1085	585	54%	42	4%
27	Punjab	14683	6342	43%	1726	12%
28	Rajasthan	39570	19014	48%	2848	7%
29	Sikkim	437	262	60%	18	4%
30	Tamil Nadu	26248	15928	61%	7786	30%
31	Telangana	12380	5926	48%	1850	15%
32	Tripura	734	561	76%	231	31%
33	Uttar Pradesh	93403	60987	65%	12031	13%
34	Uttarakhand	5178	3409	66%	1372	26%
35	West bengal	28910	17128	59%	5011	17%
36	INDIA	488213	261258	54%	71132	15%

[State wise status of bank account seeding in Nikshay and coverage of Nikshay Poshan Yojana scheme]

OA-10-379-31 Public investments in the clinical development of bedaquiline

D Gotham,[1] L McKenna,[2] M Frick,[2] E Lessem,[3] [1]Independent, London, United Kingdom, [2]Treatment Action Group, TB Project, New York, NY, United States of America, [3]Treatment Action Group, Programs, New York, NY, United States of America. e-mail: lindsay.mckenna@treatmentactiongroup.org

Background: In 2012, bedaquiline became the first new treatment for multidrug-resistant TB (MDR-TB) to be approved in nearly five decades. In 2018, the WHO published new treatment guidelines establishing a new bedaquiline-based standard of care for MDR-TB. A range of public (governmental and non-profit) entities have contributed to the development of bedaquiline. Estimating the total public investments in the development of a key new treatment can inform access approaches and future planning of drug development.

Methods: We identified various avenues of public monetary contributions to the development of bedaquiline: direct funding of clinical studies, tax credits and deductions to the proprietor pharmaceutical company, and the revenues resulting from the priority review voucher (PRV) awarded to the proprietor upon bedaquiline's approval (a PRV can be applied by the owner to any future regulatory submission to secure faster regulatory

review, allowing earlier market entry). Data on clinical trial funding were gathered through direct contact with study leads and/or funders; for non-responses, published phase-specific average costs were substituted. Tax credits were calculated based on assumed proprietor trial costs (using aforementioned published averages); deductions estimates were based on assumed claimed manufacturing costs, according to methods provided in US statutes. The value of the PRV was estimated through application of a published model.

Results: Total public expenditures on clinical trials were estimated at US$237 million (Table). Tax credits available to the proprietor were estimated at US$18-31 million. Tax deductions for donated bedaquiline were estimated at US$5 million. The value of the PRV to the proprietor was estimated at US$300-400 million.

Trial	Phase	Organisation(s)	Cost (US$)
TB Alliance trials	Various	TB Alliance	119,000,000*
endTB observational	3	MSF, PIH, others	31,000,000
STREAM stage 2	3	The Union	21,000,000*
endTB interventional	3	MSF, PIH, others	18,000,000
endTB-Q	3	MSF, PIH, others	13,000,000
InDEX	4	CAPRISA	8,000,000
TB-PRACTECAL	2/3	MSF, TB Alliance, DNDi, others	8,000,000
TRUNCATE-TB	2/3	UCL, NUHS, SCRI	7,000,000
NEXT	2/3	UCT, UoL, WSU, UoS, UCTLI	4,000,000

*[Overview of key publicly funded clinical trials on bedaquiline (not exhaustive, figures with * are based on reported phase-specific averages)]*

Conclusions: Overall public investments in the clinical development of bedaquiline were estimated at US$560-673 million. Total public investments in the clinical development of bedaquiline have thus likely exceeded those of the proprietor pharmaceutical company, which has cited total bedaquiline-related investments at US$500 million.

OA-11-C11 TB training and education initiatives to build capacity and improve outcomes

OA-11-380-31 Improving "FAST" indicators and health workers' knowledge through targeted training; findings from facility-based studies in Abia State, Nigeria

E Iwuoha,[1] O Okorie,[2] [1]Abia State University Teaching Hospital, Community Medicine, Aba, Nigeria, [2]Ministry of Health, Abia State TB Program, Umuahia, Nigeria.
e-mail: iwuohacarol@gmail.com

Background: Nigeria is a high burden country for TB."FAST" strategy a focused approach to stopping TB spread in congregate settings was developed by TB Care1. It stands for **F**inding TB cases **A**ctively, **S**eparating safely, and **T**reating effectively. We assessed the effect of health workers training and implementation of the strategy on knowledge of health workers and the "FAST" indicators (FI) at Abia State University Teaching Hospital (ABSUTH); a tertiary referral facility with crowded waiting areas.

Methods: This was a facility based interventional study using equivalent control group design methods with ABSUTH as the intervention facility while Federal Medical Centre Umuahia(FMCU) was the control. Health workers (74 across cadres) selected through stratified random sampling were trained to ensure daily cough surveillance and screening for TB among patients at the General outpatient, medical wards and HIV clinic of ABSUTH under supervision of a "FAST" focal person. Baseline knowledge of health workers(using pre-tested questionnaires) before and after the intervention and FI in the facility TB records of newly diagnosed TB patients 3 months before and 3 months after the intervention were obtained. Having a knowledge score of 8 and above out of a possible maximum of 16 was graded as good knowledge while below 8 was poor.

Results: Mean knowledge scores at baseline were 6.99 ± 2.59 for the study group and 8.12 ± 2.84 for the control. The intervention increased mean knowledge score of study group to 12.39± 2.55 while no significant change was observed in the control. Statistically significant difference in FI was observed in the intervention facility (see table 1) unlike the control facility where no significant difference was observed.

Conclusions: The intervention significantly improved health workers knowledge, reduced diagnostic delays and increased number of TB patients commenced on treatment. It can be scaled up to other facilities in similar settings.

"FAST Indicators	Pre-intervention Values	Post-intervention Value	% change in value	Independent-t value	P value
Average time to diagnosis (days)	7.3	3.5	52	8.69	0.013*
presumptive TB cases/ number of persons seen	93/2670	203/2683	>100	7.78	0.016*
Diagnosed TB patients/number of persons seen	23/2670	46/2683	100	6.12	0.03*
Total TB patients started on treatment/no of persons seen	22/2670	42/2683	94	5.44	0.032* *statistically significant

[Table 1: "FAST" Indicators in study facility before and after the intervention]

OA-11-381-31 The association of three interventions with TB knowledge, attitudes and practices of male inmates in South African correctional centres

A Best,[1,2] D Cooper,[2] M Mabena,[3] A Scheibe,[4] H Hausler,[5] [1]TB HIV Care, Communications, Cape Town, South Africa, [2]University of the Western Cape, School of Public Health, Cape Town, South Africa, [3]Department of Correctional Services, Health Services, Cape Town, South Africa, [4]TB HIV Care, Strategic Information, Cape Town, South Africa, [5]TB HIV Care, Executive, Cape Town, South Africa. e-mail: alison@tbhivcare.org

Background: Tuberculosis (TB) prevalence within South African correctional centres (prisons) is higher than in the general population, a trend seen throughout the world (Baussano et al. 2010). A patient-centred approach to responding to TB, pillar one of the World Health Organization's End TB Strategy, includes providing health education to TB-affected people. Interventions that seek to improve the TB knowledge, attitudes and practices of inmates in correctional centres, a TB key population, include a peer education programme, an edutainment programme called 'Kick TB/HIV', and routine HIV counselling and testing (HCT). This research assessed the association of these three interventions with TB-related knowledge, attitudes and practices of male inmates.

Methods: A quantitative cross-sectional survey was conducted with 336 sentenced, male inmates over 18 years old in six correctional centres in the Western and Eastern Cape, South Africa. Inmates who met eligibility criteria were randomly selected for inclusion, were interviewed, and then completed a self-administered questionnaire. Ethics approval was obtained from the University of the Western Cape and the Department of Correctional Services.

Data was analysed by performing a Chi-squared test on each outcome (measures of TB knowledge, TB attitudes, TB practices) in relation to each exposure (HCT, peer education, 'Kick TB/HIV'), as well as socio-demographic factors. A multivariate logistic regression was then run for each outcome and all the exposure variables that had shown statistical significance (at a level of $p \leq 0{,}05$) for that outcome in bivariate analysis.

Results:

	HCT		Peer education		Kick TB/HIV	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Knowledge of three of four TB symptoms	1,08 (0,47-2,52)	0,85	0,89 (0,58-1,39)	0,62	1,64 (1,04-2,58)*	0,03
Able to identify correct method of curing TB	1,06 (0,43-2,66)	0,89	1,56 (0,96-2,54)	0,07	2,55 (1,50-4,36)*	0,0005
Willing to care for family member with TB	7,68 (2,32-25,39)*	0,0008	0,56 (0,19-1,60)	0,27	3,87 (1,05-14,28)*	0,04
Willing to tell cellmate about TB diagnosis	3,47 (1,38-8,73)*	0,008	1,20 (0,67-2,26)	0,57	1,26 (0,68-2,37)	0,46
High likelihood of adherence to TB medication post-release	1,45 (0,52-4,06)	0,48	1,50 (0,82-2,75)	0,19	1,18 (0,65-2,14)	0,60
High likelihood of seeking care as soon as suspects TB	0,80 (0,18-3,50)	0,76	1,43 (0,69-2,97)	0,33	1,00 (0,49-2,05)	1

*[*After multivariate analysis]*

Conclusions: Exposure to Kick TB/HIV is associated with greater knowledge of TB, some positive attitudes to TB but no difference in TB practices. Exposure to HCT is associated with positive attitudes towards TB, while peer education showed no associations. Further research on the impact of Kick TB/HIV would be of value. It should be considered as an intervention to increase TB knowledge among male inmates.

OA-11-382-31 A pilot tuberculosis treatment literacy intervention to improve retention-in-care in South Africa

S Law,[1] A Daftary,[2,3] B Seepamore,[4] N Sikhakhane,[3] S Chetty,[5] H Dawood,[3,6] O Oxlade,[2] N Padayatchi,[3] D Menzies,[2,7] [1]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [2]McGill University, McGill International TB Centre, Montreal, QC, Canada, [3]University of KwaZulu-Natal, Centre for the AIDS Programme of Research in South Africa (CAPRISA), Durban, South Africa, [4]University of KwaZulu-Natal, Department of Social Work, Durban, South Africa, [5]KwaZulu-Natal Department of Health, East Boom Community Health Centre, Pietermaritzburg, South Africa, [6]Greys Hospital, Infectious Diseases Unit, Pietermaritzburg, South Africa, [7]McGill University, WHO Collaborating Centre for TB Research, Montreal, QC, Canada. e-mail: lawsteph@gmail.com

Background: Sub-optimal tuberculosis (TB) treatment outcomes in South Africa may be attributed to patient attrition across the care cascade. We used a pragmatic mixed-methods approach to develop and pilot test a TB treatment literacy intervention at an urban primary healthcare clinic in KwaZulu-Natal to reduce initial and treatment losses-to-follow-up.

Methods: The intervention included: 1) group health talks to all clinic patients in queue (highlighting the merits of TB testing, learning one's test results and treatment initiation); and 2) one-on-one counselling with diagnosed TB patients at weeks one and six of treatment (including practical and individualized adherence strategies). Messaging was developed through a participatory workshop with clinic staff and delivered by trained social work students assigned to the clinic for academic practicums. We compared TB testing and treatment outcomes during the study period (May-Sep 2018) against a historical control period (May-Sep 2017) using descriptive, univariate and multivariate logistic regression analyses. We assessed acceptability via focus groups with students and patient exit surveys.

Results: During the study period, absolute number of TB tests increased by 37.0% and TB treatment initiation amongst diagnosed patients increased by 8.2% (95%CI -1.3% to 17.7%), compared to the control period. Student focus groups suggested the health talks increased patient interest, TB knowledge and uptake of TB testing and treatment. Of 170 patients diagnosed during the study period, 87 (51.1%) received at least one counselling session. Patients who received any counselling were more likely to complete the intensive phase [aOR 1.88 (95%CI 1.11-3.16)] and entire treatment [aOR 1.68 (95%CI 1.02-2.75)]. Patients found the counselling sessions helpful, convenient and increased their self-confidence.

Conclusions: Providing TB treatment literacy at the time of testing and early treatment can improve retention throughout the care cascade. Acceptability and uptake may be promoted through a participatory clinic-centered approach that utilizes existing human resources.

OA-11-383-31 Unlocking the value of diagnostic data to strengthen TB programmes: the TB Data Fellowship programme

N Gous,[1] N Myrick,[2] B Cunningham,[3] C Macek,[4] AU Nyaruhirira,[5] [1]SystemOne, Sales, Johannesburg, South Africa, [2]Tableau Foundation, Global, Seattle, WA, United States of America, [3]SystemOne, Implementation, Johannesburg, South Africa, [4]SystemOne, SystemOne, Northampton, MA, United States of America, [5]Management Sciences for Health (MSH), Laboratory Services, Pretoria, South Africa.
e-mail: cmacek@systemone.id

Background and challenges to implementation: The collection, aggregation, analysis and actioning of diagnostic data is crucial to successful TB programs to enable timely reporting, monitoring effectiveness, identifying gaps, planning interventions and data-driven decision-making. Diagnostic technologies (E.g.GeneXpert), produce vast amounts of rich, electronic data, that can be passively collected through connectivity platforms. This data represents an untapped wealth of information but is not being used as tools and cadre of staff required to analyse, understand and translate this data into improved program and patient outcomes, do not exist.

Intervention or response: We developed and piloted a novel training and mentorship program to build in-country capacity for analysis and understanding of TB data. The program, designed as a 'package', included curriculum, training (5-days centralized/6-months remote), webinars, recorded sessions, software tools (Tableau Desktop, Tableau Online), reporting templates, best practices, recommendations, ongoing mentorship and technical support. We piloted the program in countries utilizing GxAlert connectivity platform to leverage existing infrastructure and gain access to GeneXpert MTB/Rif data.

Results and lessons learnt: Representatives from NTP, NTRL and MoH from 6 countries (Bangladesh,Ethiopia,Ghana,Malawi,Mozambique,Nigeria) enrolled in the pilot (n=18 participants). Participant feedback was positive but indicative that centralized training was intensive and requires longer duration to ensure appropriate skills transfer. n=15/18 participants completed the program and served as a real-time remote supportive mechanism which has impacted in decreased expenses in supervision at country-level, improved quality of data reporting, program management and procurement.

The mentorship has led to 2 symposia presentations, 7 conference abstracts, 1 invited speaking engagement and a published technical brief. These massive data dissemination at country-level and international forums has attracted interest of donors such USAID, Global Fund, WHO.

Conclusions and key recommendations: The program empowers local MoH /NTP/NRL staff to lead the ongoing analysis of TB-related data, discover and fix criti-

cal inefficiencies, provide high-level technical and operational support to the TB program. Stakeholder engagement is required to ensure sustainability.

OA-11-384-31 Translating knowledge to action: impact of TB Union training in finding the missing people with tuberculosis in Tharaka Nithi County, Kenya

F Mukami,[1] L Mugambi,[2] M Mutegi,[1] M Micheni,[1] A Njeru,[1] J Ng'ang'a,[3] [1]County Government of Tharaka Nithi, Health, Tharaka Nithi, Kenya, [2]Centre for Health solutions, USAID - TB ARC, Nairobi, Kenya, [3]Amref Health Africa in Kenya, Global Fund Tuberculosis Project, Nairobi, Kenya. e-mail: mukamifk@gmail.com

Background and challenges to implementation: Tharaka Nithi County is located in the eastern Kenya and has a population of 441, 405. The county TB notification rate was 278/100,000 in 2017. The estimated number of missing people with TB was 850 in 2017. Lack of Knowledge on TB data among the health care workers was identified as one of the contributing factor to the missing people with TB.
Intervention or response: TB coordinators in the county were trained by the TB Union on Principles of Tuberculosis Care and Prevention in February 2018 covering the following areas; Interpreting TB data, supportive supervision and TB diagnosis. Feedback meetings to the county health management team and representatives of health facilities were carried out. The county undertook to implement the lessons learnt to find the missing people with TB. Using the estimated facility catchment population and TB prevalence, expected number of TB cases per facility was calculated. This was compared with the actual numbers notified and targets were set per facility. Various strategies were implemented/ strengthened including; Active Case Finding (ACF), Contact tracing, targeted screening among others. Monthly progress monitoring chart were developed and distributed to track performance on a monthly basis. Support supervision was carried out on a regular basis.
Results and lessons learnt: Three sensitization meetings were carried out and 67 facilities were sensitized. 100% of the facilities sensitized embraced the use of monthly performance tracking tool. 22% increase in TB cases was recorded in 2018 (1248 cases in 2017, 1505 cases in 2018). 8 health facilities that had not recorded any case in 2017 reported TB cases in 2018.
Conclusions and key recommendations: Case finding increased by 22% in 2018. Use of TB data is key in advising on the areas that need focus. Routine tracking of progress and support supervision plays a key role in achieving targets.

OA-11-385-31 The design and implementation of in-service trainings on TB prevention and management among PLHIV in India: a PERT application

RR Allam,[1] R Pant,[2] C Utthappa,[2] R Aggarwal,[3] G Oruganti,[1] VV Yeldandi,[2] KS Sachdeva,[4] RS Gupta,[5] [1]SHARE INDIA, Research, Hyderabad, India, [2]SHARE INDIA, Research, New Delhi, India, [3]Center for Disease Control/ CGH/DGHT, HIV-TB, New Delhi, India, [4]Central TB Division, Govt of India, Central TB Division, New Delhi, India, [5]National AIDS Control Organization, HIV, New Delhi, India. e-mail: rameshallam@sharefoundations.org

Background and challenges to implementation: A major strategic initiative by the government is to strengthen the collaboration between the National AIDS Control Programme (NACP) and the Revised National TB Control Programme (RNTCP). A key challenge is training human resources on updated guidelines before they become redundant. This paper documents the rapid design, implementation and evaluation of a pan India training programme on intensive case finding (ICF), daily anti-TB treatment (ATT) and airborne infection control (AIC).
Intervention or response: Project Evaluation and Review Technique (PERT) and Critical Path Method (CPM) was used to develop three-day training for staff of Antiretroviral Therapy Centres (ARTC). The curriculum was designed using a mix of didactic, participatory, and experiential methods of instructional design for adult learners. Short-term evaluation was done using pre and post-test assessment. Long-term curriculum retention and detection of HIV-TB co-infection rates was followed-up through short surveys periodically.
Results and lessons learnt: 956 ART staff (429 Medical Officers and 527 Nurses) from 510 ARTC were trained over a short span of three months. The assessment of knowledge gained was significant (Mean diff.,=3.27, p-value< 0.001). Follow-up indicated that ARTC from 17 states have established CBNAAT linkages, 18 have started intensive case finding and revised treatment protocols. Some staff required periodic reinforcement and mentoring for four symptoms (4S) screening and reporting and recording formats.
Conclusions and key recommendations: A scientifically designed, fast paced training programme implemented using PERT was successfully rolled out to build capacity of ARTC staff for sustained interlinking of the HIV and TB programmes in India. Public health programmes in other low and middle income countries can benefit from evidence generated by India's endeavours.

OA-11-386-31 The allies approach: tuberculosis stigma reduction for healthcare institutions - a pilot project in Almaty, Kazakhstan

G Umutbayeva,[1] L Yeraliyeva,[1] Z Sapiyeva,[2] T Pushkina,[3] M Idrissova,[3] S Pak,[3] EMH Mitchell,[4] S van de Berg,[5] I Leimane,[6] V Mirtskhulava,[5] [1]National Scientific Center of Phthisiopulmonology, Scientific, Almaty, Kazakhstan, [2]Center of Phthisiopulmonology, Phthisiopulmonology, Almaty, Kazakhstan, [3]KNCV Tuberculosis Foundation, Representative Office in Central Asia, Almaty, Kazakhstan, [4]Erasmus University, Institute for Social Studies, The Hague, Netherlands, [5]KNCV Tuberculosis Foundation, Team Evidence, The Hague, Netherlands, [6]KNCV Tuberculosis Foundation, Team Access, The Hague, Netherlands.
e-mail: veriko.mirtskhulava@kncvtbc.org

Background: Stigmatization in health care facilities (HCFs) is impedes care seeking, adherence, and quality of care. Fear of contracting TB, and an association of TB with disvalued characteristics and behaviors contribute to stigmatization by healthcare workers (HCWs). KNCV Tuberculosis Foundation developed and tested a blended-learning training and policy change intervention to improve the knowledge, attitudes, and working conditions of HCWs to foster provision of empathic, patient-centered TB care.
Methods: A quasi-experimental study was conducted in Five randomly selected intervention HCFs and five control HCFs in Almaty, Kazakhstan between September 2018 and January 2019. Drivers and confounders of TB Stigma were measured using self-administered anonymous questionnaires before and after intervention. Fear of TB transmission was measured by a six-item 4-point Likert scale, Corrigan's stigma scale was used to measure the association of TB with disvalued characteristics, and HCWs' attitudes toward patient's rights to seek second opinion and to refuse TB treatment was assessed by 7-point Likert scale. Measured confounders included Maslach Burnout Inventory (MBI) and other stigmatized identities and co-morbidities.
Results: We included 129 HCWs, 96% were female, and the median age was 42 years (IQR: 18 years) which matches age and gender distributions of TB HCWs in Kazakhstan. After intervention with "the Allies Approach", fear of TB transmission decreased (Mean Difference (MD): 0.29, p-value = 0.048), and HCWs were more respectful to patient rights (MD: 0.62, p-value: 0.036). There was no significant change in associating TB with disvalued characteristics (MD: 0.16, p-value: 0.606). The MBI personal accomplishment score increased (MD: 0.38, p-value < 0.05). No significant changes in HCWs' attitudes were observed in control HCFs.
Conclusions: This pilot suggests that "The Allies Approach" has potential for reducing TB stigma among HCWs by addressing drivers.

OA-11-387-31 A pilot model of patient education and counselling for drug-resistant tuberculosis in Daru, Papua New Guinea

T Keam,[1] A Kuma,[1] T Haihuie,[2] M Hapolo,[2] S Islam,[1] B Akumu,[1] K Chani,[1] L Morris,[3] M Taune,[2] T Adepoyibi,[1] [1]Burnet Institute, Tuberculosis Elimination and Implementation Science, Melbourne, VIC, Australia, [2]Daru General Hospital, Tuberculosis Program, Daru, Papua New Guinea, [3]Western Province Health Department, Rural Health Services, Daru, Papua New Guinea.
e-mail: tess.keam@burnet.edu.au

Background and challenges to implementation: Daru, a small island in PNG's Western Province, is the site of an outbreak of drug-resistant TB (DR-TB). It is characterized by poor socio-economic conditions and overcrowding, which in turn contribute to food, water and accommodation insecurity for patients already facing an arduous treatment journey.
Intervention or response: In 2016, a patient education and counselling (PEC) model was piloted in Daru. The model is centered on the empowerment of peer counsellors, termed 'TB-PALS' (People Affected by, Living with, or having Survived TB). PEC was fully integrated into the community & facility-based model of care. Six standard counselling sessions are provided to all DR-TB patients, utilising visual aides and games as educational tools for children and adolescents. Counselling is also provided in the context of preventative therapy with a focus on education guardians of children 0-5 years, who receive 3 standard sessions. Additional special sessions are conducted on an ad hoc basis for any number of reasons including treatment interruption, palliative care, initiation of new drugs and HIV co-infection. A patient charter is provided to each patient, outlining their rights and responsibilities.
Results and lessons learnt: The pilot project has so far successfully trained 3 lead counsellors and 10 PALS, who have provided PEC services to a cumulative total of 331 DR-TB patients registered from 2015-2017. PEC contributed to the reduction in patients who were lost to follow up from 18% (2014 cohort) to 4% (2015 cohort).
Conclusions and key recommendations: The PEC pilot successfully trained people affected by or living with TB as peer counsellors, empowering them to deliver much needed services. PEC has been an integral component of the successful model of TB care in Daru, highlighting the importance of increased investment in comprehensive psycho-emotional and social support in DR-TB within PNG. Scalable models should be explored.

SHORT ORAL ABSTRACT SESSIONS (SOA)

SOA-01-B1 Thinking beyond current diagnostics

SOA-01-1000-31 Pooling sputum: an effective strategy to reduce costs in high TB burden settings

M Chry,[1] M Smelyanskaya,[2] D Cazabon,[3] J Creswell,[2] K Mom,[4] [1]Cambodia Anti-Tuberculosis Association, Program, Phnom Penh, Cambodia, [2]Stop TB Partnership/TB REACH, Innovation & Grants Team, Geneva, Switzerland, [3]McGill International TB Centre, Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [4]Cambodia Anti-Tuberculosis Association, Management Team, Phnom Penh, Cambodia.
e-mail: rath@thecata.org.kh

Background: The broad use of rapid molecular diagnostics, such as Xpert MTB/RIF, to test large numbers of people for TB is still limited by the relatively high cost of the cartridge, especially in high TB burden settings. Pooled testing is a cost-saving strategy used to test large numbers of individuals for infectious disease by combining several specimens (e.g. blood or urine) into a common pool. Negative pools are eliminated and samples from a positive pool are re-tested individually to confirm the diagnosis. This strategy has not been frequently utilized for sputum specimens testing in TB, but has potential to significantly reduce costs and allow for higher throughput.
Methods: 2.5 of 8 Operational districts TB REACH active case finding interventionin rural Cambodia, we utilized a pooling system using Xpert MTB/RIF Ultra. We screened individuals using chest x-ray (CXR) and symptoms to identify presumptive TB. Sputum was collected and samples were classified based on CXR results: 1) active for TB 2) suspect for TB 3) healed TB/other lung abnormality 4) CXR normal and cough > 2 weeks and 5) any CXR (from 1-4). Each pool included four samples from each CXR category (1 through 5 above). All positive pools were retested and a sample of negative pools was retested for quality assurance.
Results: We tested 671 pools from 2638 samples. 74 (11%) pools were positive and all samples were retested. We identified 315 B+ individuals including 7 who were rifampicin resistant. No discrepancies were found in 10% of quality assurance pools. In total, 967 cartridges were used, saving 1,671 cartridges (USD16,710) and 3,342 hours of lab staff time by pooling samples.
Conclusions: Pooling sputum samples is feasible in rural Cambodia and should be further explored for other areas, especially during case finding campaigns where overall yield is expected to be low.

SOA-01-1001-31 The utility of pooling sputum samples for mass screening for tuberculosis in prisons using Xpert MTB/RIF Ultra

P Santos,[1] A Santos,[1] R Verma,[2] R Oliveira,[3] C Camioli,[4] E Lemos,[3] E Cunha,[5] C Gonçalves,[3] J Andrews,[2] J Croda,[3] [1]Federal University of Grande Dourados, Postgraduate Program in Health Sciences, Dourados, MS, Brazil, [2]Stanford School of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford, CA, United States of America, [3]Federal University of Mato Grosso do Sul, Postgraduate Program in Infectious and Parasitic Diseases, Campo Grande, MS, Brazil, [4]Universidade Federal da Grande Dourados, Health Science Research Laboratory, Dourados, MS, Brazil, [5]Health Secretariat of Mato Grosso do Sul, Central Laboratory, Campo Grande, MS, Brazil.
e-mail: vrenu@stanford.edu

Background: Systematic screening for tuberculosis (TB) in high-risk groups and community settings is recommended by the WHO to reduce disease transmission; however, it is not widely implemented in prisons and other vulnerable populations due to cost constraints. The improved sensitivity of the new Xpert Ultra cartridge makes it an attractive tool for mass screening. Despite the concessionary pricing, use of Xpert Ultra for mass screening of TB in resource-constrained settings is still limited by costs. The aim of this study was to evaluate the sensitivity of testing pooled sputum on Xpert Ultra as a screening strategy in prisons.
Methods: We collected 1,120 sputum samples from inmates at three prisons in Mato Grosso do Sul, Brazil, tested them all individuals using Xpert and culture, and then selected samples for mixing in pools of 4, 8, 12 and 16, which were then tested using Xpert Ultra. In each sputum pool, a single positive sample of different semiquantitative MTB level load (high, medium, low and very low) was used. Additionally, 10 negative sputum pools of 16 samples each were also analyzed on Xpert Ultra.

Pool size	Xpert semiquantitative MTB load of the positive sample				
	High (%)	Medium (%)	Low (%)	Very low (%)	Total (%)
4	5/5 (100)	5/5 (100)	5/5 (100)	4/5 (80)	19/20 (95)
8	5/5 (100)	5/5 (100)	5/5 (100)	5/5 (100)	20/20 (100)
12	5/5 (100)	4/5 (80)	3/5 (60)	4/5 (80)	16/20 (80)
16	10/10 (100)	10/10 (100)	10/10 (100)	9/10 (90)	39/40 (97)
Total (%)	25/25 (100)	24/25 (96)	23/25 (92)	22/25 (88)	94/100 (94)

[Sensitivity of sputum pooling by pool size (each with a single positive sample pooled with negatives) using Xpert Ultra, stratified by different level]

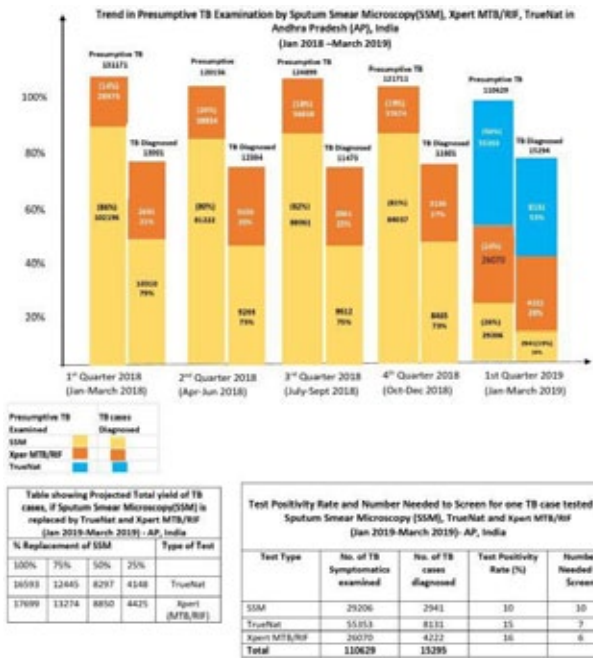
Results: One-hundred pools were evaluated using Xpert Ultra (Table 1). The overall sensitivity of sputum pooling was 94% (n=94/100; 95% CI: 87-98%). The specificity was 100% (n=10/10). The sensitivity of pools in which the single positive sample had a high mycobacterial load was 100% (n=25/25), even in pools up to 16.

For the pooled samples containing only one positive sample with very low mycobacterial load, the sensitivity dropped to 88% (n=22/25; 95% CI: 68-97%).
Conclusions: Xpert Ultra was able to detect MTB across all dilutions with high sensitivity. These findings suggest that screening pooled sputum samples on Xpert Ultra, followed by individual testing of samples in positive pools, can be a sensitive and cost-effective strategy for TB screening in resource limited settings.

SOA-01-1002-31 "TrueNat" for diagnosis of tuberculosis, replacing sputum smear microscopy at peripheral health facilities in Andhra Pradesh, India: early lessons from the field

S Achanta,[1] M Gorla,[1] S Anand,[1] R Tekumalla,[2] J Peravali Carel,[1] M Parmar,[1] K Janardhana Naga Sai,[2] S Mase,[1] KS Sachdeva,[3] R Ramachandran,[1] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]Government of Andhra Pradesh, State TB Cell, Department of Health & Family Welfare, Vijayawada, India, [3]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: achantas@rntcp.org

Background: Posing a serious threat to End TB Strategy, India misses 1.1 million tuberculosis(TB) cases every year. Sputum Smear Microscopy (SSM), with sensitivity of < 50%, continues to be the basis-of-diagnosis of microbiologically confirmed TB, in most States. In 2018, Indian Council of Medical Research recommended that TrueNat (indigenous NAAT by Molbio, India Ltd), a rapid molecular test for TB should replace SSM. Following this, Andhra Pradesh (AP) deployed **TrueNat** machines at high-burden (≥5 symptomatic patients tested /day) TB Microscopy-Centers (MC), in addition to existing Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, United States). We share an interim-analysis of the results of this intervention.
Methods: Approximately 125,000 presumptive TB patients are tested every quarter across AP and ~70% of TB diagnostic tests happen in high-burden MCs. AP has 610 MCs and 225 of these high-burden centers, were given TrueNat machines and 45 centers had Xpert MTB/RIF. Mechanisms have been devised to strengthen specimen transportation from all other MCs to these molecular diagnostic (MD) sites . Data was collected from January-March 2019 and analyzed using Microsoft Excel.
Results: Of 110628 patient specimens, 55353(50%) were tested using TrueNat,26070(24%) using Xpert MTB/RIF and 29206 (26%) using SSM. Of the 81423 (73%) specimens receiving MD testing 12,353 TB cases (15%) were diagnosed. SSM detected 2941 TB cases out of 29206 specimens tested. Test Positivity Rate of TrueNat, Xpert MTB/RIF and SSM was 15%,16% and 10% respectively. To detect a new case of TB the Number Needed to Screen (NNS) was 7 for TrueNat,6 for Xpert MTB/RIF and 10 for SSM. Testing 100% samples with MD incrementally increases detection by ~7400 cases/annum (additional 139 cases/million/annum).
Conclusions: MD services must replace SSM completely to detect microbiologically confirmed TB cases early, with incremental yield for the same effort. Efficient sample transportation and testing more presumptive TB is key for maximizing diagnostic yield.



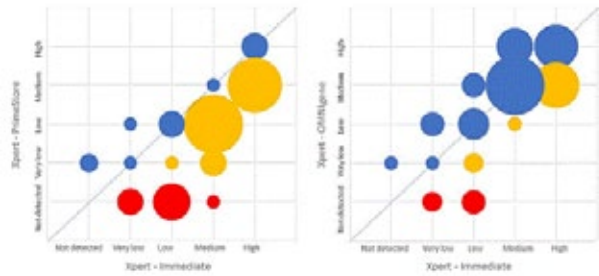
[Figure showing presumptive TB examination trend, projected yield of TB cases and NNS -TrueNat]

SOA-01-1003-31 OMNIgene and PrimeStore transport media for sputum samples. Can we skip the cold chain?

K Kontogianni,[1] T Edwards,[2] EE Bassey,[3] J Bimba,[3] L Lawson,[3] J Dominguez,[4] LE Cuevas,[1] [1]Liverpool School of Tropical Medicine, Clinical Sciences, Liverpool, United Kingdom, [2]Liverpool School of Tropical Medicine, Parasitology, Liverpool, United Kingdom, [3]Bingham University, Zankli Research Laboratory, Karu, Nasarawa, Nigeria, [4]Hospital Universitari Germans TriasiPujol, Institut d'Investigació Germans TriasiPujol, Universitat Autònoma de Barcelona, Servei de Microbiologia, Badalona, Spain. e-mail: luis.cuevas@lstmed.ac.uk

Background: Sputum transportation is needed to facilitate access to current diagnostics such as Xpert and culture. Transportation is time sensitive, as the specimens need to be tested in < 7 days, and requires a cold chain to avoid contamination and degradation of Mycobacterium tuberculosis DNA (MTB DNA) due to the action of normal flora and enzymes of saliva and white cells. It is proposed that solutions to preserve DNA maintain the DNA integrity without a cold chain, but there are few independent evaluations.

Methods: We evaluated two MTB DNA preservation solutions, OMNIgene-SPUTUM and PrimeStore-MTM. Sputum samples were obtained from 268 consecutive patients in Nigeria and split into three aliquots. One sample was tested immediately (t0) with Xpert MTB/RIF. One sample was stored with OMNIgene-SPUTUM and one with PrimeStore-MTM for 14 days, without air conditioning and then tested with Xpert (t14).
Results: 248 patients had valid culture results. 62 were culture-positive and had been tested with OMNIgene-SPUTUMand PrimeStore-MTM.56 of the 62 culture positive direct(t0) samples were Xpert-positive. At t14, 56of the samples stored inOMNIgene-SPUTUM were positive (sensitivity 90.3, 95% CI: 80.1-66.8%), while-49of the samples stored withPrimeStore-MTM were Xpert-positive (sensitivity 79%, 95% CI: 66.8%). The specificity of Xpert MTB/RIF in samples stored in OMNIgene-SPUTUMand PrimeStore-MTMwas 99.5% and 98.4% respectively. Specimens preserved in OMNIgene-SPUTUMand PrimeStore-MTM had lower DNA loads than samples tested directly at t0 (fig 1).
Conclusions: Fluids for the preservation of MTB DNA maintain the DNA in samples transported to the laboratory without a cold chain. OMNIgene-SPUTUM had a better agreement with specimens tested directly at the time of collection than PrimeStore-MTM. Both fluids resulted in lower Xpert DNA concentrations and studies with larger sample size are needed.



[Figure 1]

SOA-01-1004-31 Magnetic bead assay: sensitive, rapid and cost-effective test for diagnosis of tuberculous meningitis

K Sharma,[1] M Modi,[2] M Sharma,[1] A Sharma,[3] [1]PGIMER, Medical Microbiology, Chandigarh, India, [2]PGIMER, Neurology, Chandigarh, India, [3]PGIMER, Internal Medicine, Chandigarh, India. e-mail: sharmakusum9@yahoo.co.in

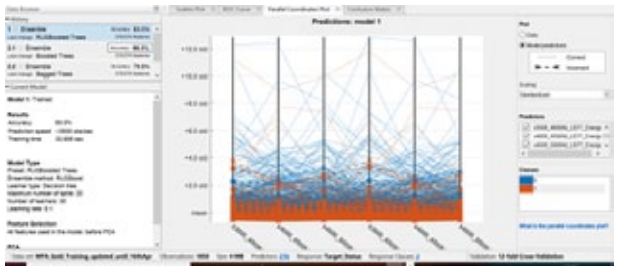
Background: Rapid and specific diagnosis of tubercular meningitis (TBM) is crucial . We designed a test based on detecting amplified DNA via magnetic beads bridging flocculation technique (MBF). The assay is inexpensive and rapid (60 minutes), with a sensitivity approaching a single cell of Mycobacterium tuberculosis. Therefore, the present study was undertaken to compare Gene Xpert MTB/RIF (GX) assay and Magnetic beads bridging flocculation (MBF) technique using two targets IS6110 and MPB64 LAMP (loop mediated isothermal primers) primers.
Methods: MBF technique and GX assay were carried out on CSF samples of 125culture confirmed &100 clinically suspected patients of TBM. Composite reference standard (CRS) was taken as reference in clinically suspected patients of TBM .CSF samples from 50 non-TB infectious meningitis were included as control group. Phenotypic drug susceptibility testing(PDST) of 125 cultures was carried out by 1% proportion method for rifampicin (RIF)and isoniazid (INH). Sequencing of rpoB &KatG was also carried out in all positive cases.
Results: In total number of 225TBM patients, GX was positive in **105/225** (**46.66%**) and MBF was positive in **201 /225**(**89.93%**) cases. Both tests were negative in all controls (50 control group). RIF resistance was detected in 11 of 105 GX positive, and in 10 out of 201MBF technique positive cases with rpoB gene sequencing. Out of the 125 culture isolates subjected to PDST, 115 were sensitive to both Rif & INH. However, 10 were found to be resistant to both Rif and INH. Thus, there was one case of false Rif resistance detected by GX, which was Rif sensitive on rpoB gene sequencing and PDST. Cost of doing MBF technique is less than 1 dollar where as GX is 10$.
Conclusions: MBF is robust and cost effective method for diagnosis of TBM in low resource and high endemic country.

SOA-01-1005-31 TimBre: acoustic-based non-invasive point of care screening of tuberculosis

R Pathri,[1] [1]Docturnal Pvt. Ltd., R&D, Hyderabad, India. e-mail: rahul@docturnal.com

Background: As per WHO report Death due to TB was estimated to be around 1.3 million among HIV negative and an additional 3 lakhs death from HIV positive individuals in year 2017 . The ambitious goal of the End TB strategy aiming to achieve 95% reduction in mortality by 2035 will not be possible without new tools to fight TB, hence proper and rapid diagnosis is the key to controlling TB. To solve this problem, the diagnostic test also needs to be highly sensitive and specific whilst being low cost, rapid and easily deploy-able specially in remote settings with minimum training requirements for the health workers.
Methods: Cough for known Pulmonary Tuberculosis patients was recorded alongside obtaining clinical & demographic variables to create a Machine Learning & Deep Learning Models. Large number of spectral features were extracted from cough sound in their frequency domain for their predictive abilities. After the feature extraction ensemble RUSBoost classifier was used as a classification model combining different machine learning models hence creating an ensemble model.

Results: Our Ensemble model predicted that within the data set of 1831 suspects, the accuracy of the model was observed to be 84.4% with sensitivity at 75% with the specificity at 87%.



[TimBre - Parallel Coordinate Graph - XAI]

Conclusions: Multisite clinical trial is ongoing with different high-risk groups such as Diabetic and HIV patients along with other immunocompromised & healthy candidates. In a mass surveillance scenario, we want to score a higher specificity. We have also introduced an IVR approach for immunocompromised patients to collect cough which is need of the hour for subjects that are unable to access a PHC but conduct the screening from comfort of their home but do not have the resources to install the App (TimBre) from Playstore.

SOA-01-1006-31 Is the current cutoff value of adenosine deaminase (ADA) for diagnosis of TB pleurisy appropriate in an intermediate burden country?

HW Kim,[1] JH Ha,[1] KH Kim,[1] JS Kim,[1] [1]Catholic University of Korea, Department of Internal Medicine, Division of Pulmonology, Incheon, Korea, Republic of.
e-mail: jiongyou@naver.com

Background: As the burden of tuberculosis in South Korea decreases slowly but that of malignancy increases rapidly with aging society, the etiologies of pleural effusion are changing. The aim of this study is to investigate the diagnostic value of adenosine deaminase (ADA) for diagnosis of TB pleurisy in this circumstance.
Methods: The medical records of patient who underwent medical thoracoscopy or VATS pleural biopsy for diagnosis of lymphocyte-dominant pleural effusion from December 2013 to December 2018 in Incheon St. Mary hospital were retrospectively reviewed. TB pleurisy was defined as 1) granuloma in pleural tissue, or 2) positive TB PCR or culture in pleural fluid or tissue with no other specific pathologic diagnosis (e.g. malignancy) in pleural tissue.
Results: Total 136 cases - 66 cases of malignant effusion, 41 cases of non-specific pleural inflammation and 29 cases of TB pleurisy were included. The area under receiver characteristic curve (AUROC) of ADA for diagnosis of TB pleurisy was 0.976, with the best cutoff value of 84 IU/L. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ADA=84 IU/L were 0.93, 0.96, 0.87 and 0.98, respectively. However, those of ADA=40 IU/L were 1.00, 0.61, 0.41 and 1.00, respectively. Among the 34 patients whose ADA levels in pleural fluid were within range of 40-84 IU/L, 18 patients (52.9%) were diagnosed as malignant effusion, 14 patients (41.2%) as non-specific inflammation and only the other 2 patients (5.9%) as TB pleurisy.
Conclusions: As the prevalence of TB decreases in South Korea, the false positive cases may increase with the current ADA cutoff value of 40 IU/L. To reduce such cases, raising the cutoff value of ADA to improve the specificity of ADA is required in the intermediate burden countries with decreasing TB burden.

SOA-01-1007-31 The performance of pleural fluid T-SPOT.TB assay for diagnosing pleural tuberculosis in China: a two-centre prospective cohort study

F Wang,[1] [1]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Department of Laboratory Medicine, Wuhan, China.
e-mail: fengwang@tjh.tjmu.edu.cn

Background: The performance of T-SPOT.TB (T-SPOT) assay in diagnosing plTB is inconsistent.
Methods: We compared the performance of peripheral blood (PB) and pleural fluid (PF) T-SPOT assay in diagnosing plTB. Between July 2017 and March 2018, 218 and 210 suspected plTB patients were prospectively enrolled from Wuhan (training) and Guangzhou (validation) cohort, respectively. PB T-SPOT, PF T-SPOT, and other conventional tests were simultaneously performed.
Results: We demonstrated that 1×10^5 is the optimal number of pleural fluid mononuclear cells for performing PF T-SPOT, which is the biggest difference between PF T-SPOT and PB T-SPOT. Our data showed the performance of PB T-SPOT in diagnosing plTB was limited, especially with low sensitivity.
However, the results of early secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10) in PF T-SPOT were significantly increased compared with those in PB T-SPOT in plTB patients. If using 76 as the cutoff value of MAX (the larger of ESAT-6 and CFP-10) in Wuhan cohort, the sensitivity and specificity of PF T-SPOT to diagnose plTB were 89.76% and 96.70%, respectively.
The diagnostic accuracy of PF T-SPOT was better than other routine tests such as pathogen detection methods (acid fast stain, PCR, culture) and biochemical markers. The diagnostic accuracy of PF T-SPOT in Guangzhou cohort was similar to that in Wuhan cohort, with a sensitivity and specificity of 91.07% and 94.90%, respectively. Furthermore, $CD4^+$ T cells were more activated in PF compared with PB, and the frequency of mycobacterium tuberculosis-specific $CD4^+$ T cells in PF was significantly higher than that in PB in plTB patients.

Conclusions: The performance of PF T-SPOT is obviously better than PB T-SPOT or other laboratory tests, which suggests that PF T-SPOT assay has been of great value in the diagnosis of pleural tuberculosis.

SOA-01-1008-31 Evaluation of HBHA-IGRA in combination with QuantiFERON-TB Gold Plus for tuberculosis diagnosis and monitoring treatment efficacy: preliminary data from Bangladesh in the multi-country HINTT study

MKM Uddin,[1] S Biswas,[1] J-L Berland,[2] C Chedid,[2] G Delogu,[3] H Endtz,[2] D Goletti,[4] JE Bryant,[2] S Banu,[1] J Hoffmann,[2] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh, [2]Fondation Mérieux, Laboratoire des Pathogènes Emergents, Centre International de Recherche en Infectiologie, Lyon, France, [3]Università Cattolica del Sacro Cuore, Microbiology, Rome, Italy, [4]Istituto Nazionale Malattie Infettive 'Lazzaro Spallanzani' di Roma' (INMI), Dipartimento di Epidemiologia e di Ricerca Preclinica, Rome, Italy. e-mail: kmuddin@icddrb.org

Background: Improved diagnostics for tuberculosis screening, triage and monitoring treatment efficacy are urgently needed to improve patient management and care, particularly regarding treatment duration and resistance testing, and to facilitate adherence counselling. Currently there is no widely accepted test of cure, and the one used (smear microscopy) is limited in sensitivity and ability to differentiate live from dead Mycobacteria. To address these fundamental challenges in tuberculosis diagnostics, the Fondation Mérieux is coordinating a multi-country study (Bangladesh, Georgia, Lebanon, Paraguay, and Madagascar) to evaluate the potential of immunodiagnostic approaches as a supportive tool for staging tuberculosis disease progression and monitoring treatment efficacy.
Methods: The study investigated the utility of Heparin-Binding Hemagglutinin Antigen (HBHA) that is known to be strongly associated with latency and effective containment of Mtb replication. In Bangladesh, a cohort of 42 individuals with either drug-susceptible TB (DS-TB, N=23) or drug resistant TB (DR, N= 19) were followed throughout their anti-TB treatment. Regimens were prescribed per last WHO recommendations. Host-related immune markers were evaluated at 4 time points using QuantiFERON-TB Gold Plus (QFT-P), and HBHA-Interferon gamma release assay (IGRA) for each individual during the specific time-courses of anti-TB treatment.
Results: Preliminary results show a significant increase in IFN-y production following HBHA stimulation between baseline (0.84 [0.28 - 1.54] IU/ml) and after 6-months of treatment (9.95 [5.19 - 10] IU/ml) for 21 individuals (Figure 1) who converted smear microscopy and culture at month-2 (P< 0.001). Significant differences (P=0.025) were found considering TB2 values from QFT-P during treatment follow-up.

Conclusions: The preliminary results of the HINTT study in Bangladesh has demonstrated key principle that HBHA monitoring highly correlates with the successful anti-tuberculosis treatment, and can allow in-depth investigation of additional novel biomarkers as supportive toolkits for TB diagnosis and treatment monitoring.

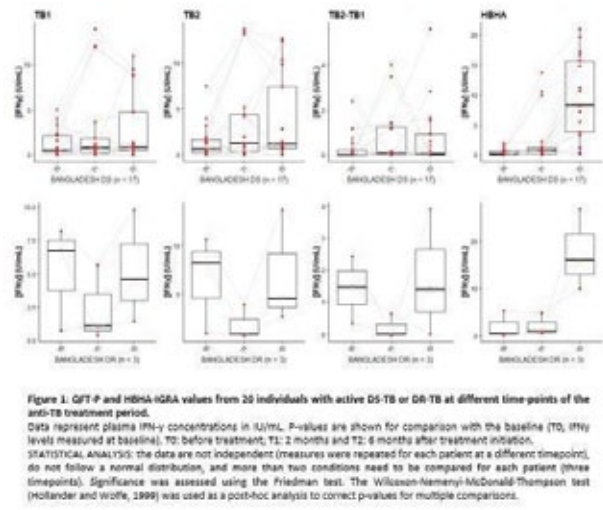


Figure 1: QFT-P and HBHA-IGRA values from 20 individuals with active DS-TB or DR-TB at different time-points of the anti-TB treatment period.
Data represent plasma IFN-γ concentrations in IU/mL. P-values are shown for comparison with the baseline (T0, IFNγ levels measured at baseline). T0: before treatment; T1: 2 months and T2: 6 months after treatment initiation.
STATISTICAL ANALYSIS: the data are not independent (measures were repeated for each patient at a different timepoint), do not follow a normal distribution, and more than two conditions need to be compared for each patient (three timepoints). Significance was assessed using the Friedman test. The Wilcoxon-Nemenyi-McDonald-Thompson test (Hollander and Wolfe, 1999) was used as a post-hoc analysis to correct p-values for multiple comparisons.

[QFT-P and HBHA-IGRA values from DS or DR-TB patients at different points of anti-TB treatment period]

SOA-01-1009-31 Diagnostic accuracy and predictive value of Ultra and Xpert for TB diagnosis in an HIV-endemic setting in patients with a recent history of previous tuberculosis

H Mishra,[1] BWP Reeve,[1] Z Palmer,[1] J Caldwell,[2] P Nabeta,[3] SG Schumacher,[3] C Denkinger,[3] F Marx,[4] R Warren,[1] G Theron,[1] Clinical Mycobacteriology & Epidemiology (CLIME) Group DST/NRF Centre of Excellence for Biomedical Tuberculosis Research SU/ SA-MRC Centre for Tuberculosis Research Division of Molecular Biology and Human Genetics Stellenbosch University [1]Stellenbosch University, Molecular Biology and Human Genetics, Cape Town, South Africa, [2]City of Cape Town Department of Health, Department of Health, Cape Town, South Africa, [3]Foundation for Innovative New Diagnostics (FIND), FIND, Geneva, Switzerland, [4]Stellenbosch University, Desmond Tutu TB Centre, Cape Town, South Africa. e-mail: hridesh@sun.ac.za

Background: After tuberculosis (TB) treatment completion, Mycobacterium tuberculosis (Mtb) genomic DNA can persist in patients and cause positive PCR results in the absence of active disease. Simultaneously, recently-treated patients are at high risk for recurrence. There are limited data on Xpert MTB/RIF Ultra (Ultra) in these patients, who form a significant part of the TB burden in many settings and represent a diagnostic dilemma.
Methods: Decontaminated sputum sediments (n=352) from patients with presumptive pulmonary TB who also finished treatment for a prior episode within two years

(101 culture-positive, 251 culture-negative; culture reference standard) were included. Sediments were randomly allocated to Ultra or its Xpert MTB/RIF (Xpert).
Results: The sensitivity and specificity of Xpert was 92% (47/51) and 84% (107/127), and 86% (38/44; p=0.359) and 69% (86/124; p=0.005), respectively for Ultra. After reclassifying the lowest Ultra semi-quantitative category ("trace") to negative, specificity increased by 16% (95% CI: 6, 19) and sensitivity decreased by -5% (-13, -4). In a situation where 20% of presumptive TB patients with recent TB are culture-positive, the PPV of Ultra, Ultra (trace reclassified), and Xpert will be approximately 39% (38, 41), 55% (53, 56) and 61% (60, 63), respectively. Under a four culture reference standard best case Ultra specificity scenario, specificity in smear-negatives would be 71% (62, 79).
Conclusions: Ultra has lower specificity than Xpert in patients with recent previous TB. With Ultra, 4/10 positive results in recently treated patients will be true-positive, compared to 6/10 with Xpert. These data have implications for diagnostic algorithms, the implementation of new TB diagnostic tests, and underscore the need for culture, adjunct tests, and clinical decision making in recently previously-treated patients.

SOA-01-1010-31 Accuracy of Xpert Ultra and Xpert MTB/RIF in people living with HIV initiating antiretroviral treatment who have minimal TB symptoms

BWP Reeve,[1] Z Palmer,[1] J Jackson,[1] T Dolby,[2] P van Helden,[1] R Warren,[1] G Theron,[1] [1]Stellenbosch University, Biomedical Sciences, Cape Town, South Africa, [2]National Health Laboratory Services, Green Point, Tuberculosis, Cape Town, South Africa.
e-mail: byronreeve@sun.ac.za

Background: Tuberculosis (TB) is the biggest cause of death in people living with HIV (PLHIV). Xpert MTB/RIF Ultra (Ultra) is replacing Xpert MTB/RIF (Xpert) as the frontline TB test. However, comparative data in PLHIV remains limited, especially in patients with early-stage disease where Ultra's incremental yield may be highest.
Methods: We did a head-to-head evaluation of Xpert vs. Ultra accuracy in PLHIV initiating antiretroviral treatment (ART) in Cape Town, South Africa. Participants were recruited irrespective of TB symptoms and underwent sputum induction. Ultra and two liquid cultures were separately done on three sputa. Decontaminated remnants after culture were used for Xpert. A head-to-head comparison was only done on patients with matching specimens and actionable results (n=437).
Results: The overall TB prevalence was 12%. The sensitivity of Ultra increased vs. Xpert [69% (95% confidence interval (CI) 55, 81) vs 47% (33, 61); p=0.012), however, Ultra had decreased specificity [99% (97, 100) vs. 100% (99, 100); p=0.033]. After stratification by World Health Organization TB symptom criteria, 48% participants were symptomatic and 52% were asymptomatic for TB; 18% and 7% of which were culture-positive, respectively. In symptomatic participants, Ultra sensitivity increased [82% (65, 93) vs. 57% (40, 73) for Xpert; p=0.024] and negative predictive value (NPV) was similar [96% (92, 99) vs. 92% (87, 96); p=0.078]. For asymptomatic participants, Ultra sensitivity increased [42% (19, 68) vs. 24% (7, 50) for Xpert; p=0.003] and NPV was similar [96% (92, 98) vs. 95% (91, 97); p=0.557].
Conclusions: Ultra has improved sensitivity compared to Xpert in PLHIV, however, Ultra should be used in conjunction with culture in PLHIV with minimal TB symptoms (1/20 symptomatic and asymptomatic Ultra-negative PLHIV will be culture-positive).

SOA-02-D1 The prevention cascade: prevent, treat, retain

SOA-02-1011-31 Prophylaxis in diabetic patients to prevent tuberculosis progression: a multi-cohort study

L Martinez,[1] O Cords,[1] J Andrews,[1] Tuberculosis Observational Studies Consortium [1]Stanford University, Department of Infectious Disease and Geographic Medicine, Stanford, United States of America.
e-mail: leomarti@stanford.edu

Background: Globally, tens of millions of diabetic patients are at high-risk to develop tuberculosis. Despite this, critical questions regarding this relationship are unexplored. Drawing upon a multi-cohort collaboration of research groups, we aimed to explore two questions: (i) what is the contribution of tuberculosis infection and disease activation to the increased risk among diabetics? and (ii) does preventive therapy protect infected diabetics against tuberculosis disease progression?
Methods: We pooled participant-level data from seven case-contact cohort studies including diabetic and non-diabetic patients and data on tuberculosis infection. Participants healthy at baseline were followed for tuberculosis progression, loss to follow-up, death, or study completion. We used mixed-effects parametric survival-time models including a random intercept for each study to calculate adjusted hazard ratios (AHR) and confidence intervals (CI). We conducted a mediation analysis to assess how tuberculosis infection altered the hazard between diabetes and tuberculosis progression. We also estimated the effectiveness of preventive therapy by assessing tuberculosis-infected diabetics using propensity score matching.
Results: 285,388 participants were included, of which 18,342 (6.4%) were diabetic. Over 1.41 million years of follow-up, 1584 incident tuberculosis cases were diag-

nosed. Incident tuberculosis was more common in diabetics with baseline tuberculosis infection (AHR, 2.20, 95% CI, 1.55-2.18). In a multivariable model not including tuberculosis infection, diabetics had 85% greater hazard of tuberculosis progression (AHR, 1.85, 95% CI, 1.56-2.18). When adjusting for tuberculosis infection, the hazard of tuberculosis progression decreased 9% (AHR, 1.73, 95% CI, 1.46-2.05). Among 986 diabetics with baseline tuberculosis infection, 381 (39%) were given preventive therapy. Over 1652 years of follow-up, the effectiveness of prophylaxis was 82% (AHR, 0.18, 95% CI, 0.06-0.52).
Conclusions: The increased risk of tuberculosis among diabetics is driven predominantly due to progression from infection to disease. Preventive therapy was highly effective in preventing disease progression in infected diabetics.

SOA-02-1012-31 Latent tuberculosis infection treatment registry of cases is important for follow-up

S Ozkara,[1] S Ozkan,[2] A Yildirim,[3] T Keskin,[4] D Oztomurcuk,[5] S Simsir,[6] E Yegin,[7] M Aydin,[8] Z Kazgan Arica,[9] E Kabasakal,[3] [1]Atatürk Chest Diseases and Chest Surgery Hospital, Tuberculosis Unit, Ankara, Turkey, [2]Yenimahalle Camlica Family Health Center, AH, Ankara, Turkey, [3]General Directorate of Public Health, Tuberculosis Department, Ankara, Turkey, [4]Provincial Health Directorate, Provincial Tuberculosis Coordinator, Bursa, Turkey, [5]Provincial Health Directorate, Provincial Tuberculosis Coordinator, Samsun, Turkey, [6]Provincial Health Directorate, Ali Halim Bayer Tuberculosis Unit, Izmir, Turkey, [7]Provincial Health Directorate, Provincial TB coordinator, Antalya, Turkey, [8]Provincial Health Directorate, Provincial TB Coordinator, Izmir, Turkey, [9]Provincial Health Directorate, Tuberculosis Unit, Malatya, Turkey.
e-mail: ozkaraseref@yahoo.com

Background: Latent tuberculosis infection (LTBI) treatment is a part of tuberculosis control programs. With World Health Organization's Guidelines this intervention is expanding. Registry of cases receiving LTBI treatment is important programmatically. With the 2016 national LTBI treatment registry results of Turkey, we want to show that this recording system is a useful tool.
Methods: All TB units in Turkey have a registry system of LTBI treatment. Demographic data, tuberculin skin test (TST) results, indications and outcomes of LTBI are registered. The registers of 2016 cases were collected. These individualized data were entered to an Excel file by 9 experienced physicians. Data corrections and clearing double registries were done. Cases that progressed to TB disease and deaths were checked.
Results: Among 27,848 registries 27,546 were left after clearing the duplicates. Indications for LTBI treatment are shown in Table 1. LTBI treatment outcomes were as follows: completion 61.6%, discontinuation 31.1%, transferred out 1.3%, TB diagnosis 0.3%, deaths 0.2%, and others 5.4%. Treatment adherence was found to be higher in immune suppression group (67.4%) and TST positivity (69.8%) than in contacts of TB cases (56.5%). Lowest completion rates were found in age groups between 15 to 29 years old. Sex and nationality did not influence treatment outcomes. Isoniazide (99.1%) and rifampin were used for LTBI treatment.
Conclusions: LTBI treatment registry is important for monitoring the intervention. With other years' data, these registries reveal that the immune suppressed group among LTBI treatment cases is increasing year by year. Treatment outcomes show us discontinuation is high. Factors that affect treatment completion can be analyzed using this data which can be addressed in program improvement studies.

	Number	Percentage
Contacts of TB cases	15,068	54.7
Immune suppression	10,587	38.4
TST positive children <15 years old	1,809	6.6
TST conversion	43	0.2
Fibrotic sequel on chest X-ray	17	0.1
Others	22	0.1
Total	27,546	100.0

[Table 1. Indications for latent tuberculosis infection treatment.]

SOA-02-1013-31 Low rate of completion of isoniazid preventive therapy and associated risk factors in Beira, Mozambique: retrospective cohort study

D Rodrigues,[1] M Lisboa,[2] [1]Instituto Superior de Ciências e Tecnologia Alberto Chipande, Health, Beira, Mozambique, [2]Beira Operations Research Center, National Institute of Health, Health Systems Research, Beira, Mozambique.
e-mail: miguelhetelisboa@gmail.com

Background: Iimplementation of isoniazid preventive therapy (IPT) for the prevention of Mycobacterium tuberculosis infection among people living with HIV in resource constrained settings remains limited. This study was designed to assess completion of IPT and associated factors among HIV+ patients enrolled in the HIV/AIDS care and treatment (HACT) in Beira city, Mozambique.
Methods: retrospective cohort study of all HIV+ patients enrolled in the HACT in six health facilities and screened for TB over a 2-year period (January 2016 to December 2017) in Beira city was conducted. Data were extracted from the HIV/AIDS care and treatment registers. To analyze the associations between unsuccessful results IPT and clinic-demographic characteristics, logistic regression model was used.
Results: a total of 12.163 patients under HACT and screened for TB, 24% (2.919) had active TB, 76% (9.244) were eligible for IPT. Among 9.244 eligible, only

51% (4.737) started taking IPT, from which, 75% were female, 96% were adult, 61% were in the WHO clinical 1st stage of HIV and 65% on highly active antiretroviral therapy (HAART). For a 6-month course of IPT, only 2% (36/1.803) of assessed patients completed the course. Male sex (aOR=3,4; 95% CI: 1,5-8,0), WHO clinical 1st stages of HIV (aOR=4,2; 95% CI: 2,7- 6,7) and not being on HAART (aOR=3,6; 95% CI: 2,8-5,1) were associated with unsuccessful IPT, adjusting for other clinic-demographic factors.

Conclusions: The proportion of HIV+ starting and completing IPT a 6-month course of IPT in Beira is low. Broader and integrated HIV/TB services efforts prioritizing men and new HIV+ patients entering in the HACT services are needed. Implementation science research should be helpful to assess locally sustainable strategies to improve IPT uptake among HIV patients.

SOA-02-1014-31 Improved INH preventive Therapy (IPT) coverage for PLHIV through implementing tailored interventions in Tigray Regional State, Ethiopia

M Abraha,[1] E Michael,[1] A Werede,[1] H Sebagadis,[1] T Gebrehiwot,[1] A Gebremedhin,[2] N Hiruy,[3] A Ayalew,[1] D Gemechu,[3] P Suarez,[4] [1]Management Sciences for Health (MSH), Health Programs Group (HPG), Mekelle, Ethiopia, [2]Tigray Regional Health Bureau, Health Promotion, Disease Prevention and Control Cor-Process, Mekelle, Ethiopia, [3]Management Sciences for Health (MSH), Health Programs Group (HPG), Addis Ababa, Ethiopia, [4]Management Sciences for Health (MSH), Health Programs Group (HPG), Arlington, VA, United States of America. e-mail: mebrahtom2@yahoo.com

Background and challenges to implementation: Prevention of new infections of Mycobacterium tuberculosis and their progression to tuberculosis (TB) disease is critical to reduce the burden of disease and death caused by TB, and to achieve the End TB Strategy targets set for 2030 and 2035. Provision of INH preventive treatment (IPT) for eligible people living with HIV (PLHIV) is an available option to treat latent TB infection. However, the IPT coverage for PLHIV in Tigray region has persistently been below 30%.

Intervention or response: IPT sensitization was provided for 210 health professionals and 52 woreda health office TB experts. A monthly patient level telephone monitoring and support system was instituted. In addition to strengthening quarterly joint supportive supervision (SS) to ART health facilities through the use of customized checklists by USAID funded Challenge TB project. Quarterly collected routine health management information system (HMIS) TB data and verified SS findings were analyzed for the period July 2017 - June 2018. The SS TB data included all health facilities reached through monthly telephone patient level monitoring and quarterly SS. The HMIS data was collected from all ART sites in the region.

Results and lessons learnt: The IPT coverage for PLHIV improved from the baseline 30.9% (310/1,012) in July-Sep 2017 to 58.4% (513/878) in April-June 2018, based on the HMIS data. The IPT coverage also increased from 39.7% (264/794) in July-Sep 2017 to 72.6% (439/703) in April-June 2018 based on standard of care data. Nearly a double increase in IPT coverage was observed in April-June 2018 as compared to the baseline data (table 1).

Conclusions and key recommendations: IPT sensitization and patient level telephone monitoring, contributed to the improvement of IPT coverage. Such strengthened patient level monitoring and enhanced technical supports are necessary to further improve IPT coverage among PLHIV.

	July-Sep 2017	July-Sep 2017	Oct-Dec 2017	Oct-Dec 2017	Jan-Mar 2018	Jan-Mar 2018	April-June 2018	April-June 2018
	HMIS*	SS	HMIS*	SS	HMIS*	SS	HMIS*	SS
# of ART sites	105	66	105	98	105	95	105	82
# of new PLHIV	1012	794	991	896	889	819	878	703
# of PLHIV put on IPT	310	264	443	376	488	445	513	439
IPT uptake (Coverage) for PLHIV	30.6%	39.7%	44.7%	45.1%	54.9%	60.1%	58.4%	72.6%

[IPT coverage among newly enrolled PLHIV, Routine report (HMIS) Vs Supportive supervision finding by quarter, Tigray, Ethiopia]

SOA-02-1015-31 IPT use by HIV-positive patients in Zimbabwe: analysis of the Zimbabwe Population-based HIV Impact Assessment (ZIMPHIA) survey

M Takamiya,[1] K Takarinda,[2] S Balachandra,[3] G Musuka,[4] E Radin,[5] A Hakim,[6] M Pearson,[6] R Choto,[2] C Sandy,[7] J Rogers,[3] [1]PHI/CDC Global Health Fellowship, Division of Global HIV and Tuberculosis, Harare, Zimbabwe, [2]Ministry of Health and Child Care, AIDS & TB Department, Harare, Zimbabwe, [3]U.S Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis, Harare, Zimbabwe, [4]ICAP, ICAP, Harare, Zimbabwe, [5]ICAP, ICAP New York, New York, NY, United States of America, [6]U.S Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis, Atlanta, GA, United States of America, [7]Minisrty of Health and Child Care, AIDS & TB Department, Harare, Zimbabwe. e-mail: ote6@cdc.gov

Background: AlthoughIsoniazid Preventive Therapy (IPT) has been recommended for people living with HIV (PLHIV) in Zimbabwe since 2012, IPT use in this population is unknown. We performed a cross-sectional study to estimate, and explore factors associated with, IPT use among PLHIV, using the ZIMPHIA 2015-2016 data.

Methods: The ZIMPHIA asked PLHIV aged 15 years old or older whether they have ever received IPT for TB prevention. To assess the association between IPT use

and relevant covariates, we used crude odds ratios (cOR) in bivariate analysis and adjusted odds ratios (aOR) in weighted logistic regression analysis. Covariates identified with p£0.20 in bivariate analyses were included in the final complete case regression analysis. Our analyses accounted for the multistage survey design and were restricted to PLHIV who were eligible for IPT per the national TB/HIV guidelines. Operable sample size (N) for regression analysis was restricted to PLHIV with complete data for all covariates included in the model.

Results: Of 3417 PLHIV who have ever received IPT, 42.9% were men and 48.4% lived in rural areas. The median age was 41.6 years old. One in ten (12.6%) of the PLHIV reported ever having received IPT. Bivariate analysis showed IPT use was associated with living in Harare and Bulawayo (cOR: 3.39, 95% confidence interval (CI):1.76-6.51 and cOR:4.16, 95%CI: 2.17-7.98), in urban areas (cOR:2.22, 95%CI:1.67-2.96) and being male (cOR:1.50, 95%CI:1.13-2.01). On multivariate analysis including sex, age, rural/urban residence, education level, antiretroviral therapy and alcohol intake, IPT use remained associated with living in urban areas (aOR:2.20, 95%CI:1.63-2.98) and being male (aOR:1.44, 95%CI:1.06-1.95).

Conclusions: We found low IPT use among PLHIV in Zimbabwe. IPT use was associated with living in urban areas and being male. Effective implementation and scale up of IPT is urgently needed to reduce TB and TB-related mortality among PLHIV, particularly in rural areas and among women.

	Covariates	Having ever received IPT	Having never received IPT	cOR (95% CI)	aOR (95% CI)
Total N=3417		424 (12.6)	2993 (87.4)		
Operable N=1835		329 (18.6)	1506 (81.4)		
Sex	Male	123 (42.9)	431 (33.3)	1.50 (1.13-2.01)	1.44 (1.06-1.95)
	Female	206 (57.1)	1075 (66.7)	(ref)	(ref)
Rural/ urban residence	Rural	178 (48.4)	1093 (67.5)	2.20 (1.63-2.93)	2.20 (1.63-2.98)
	Urban	151 (51.6)	413 (32.5)	(ref)	(ref)

[Crude ORs and adjusted Ors for associations between IPT use, sex and rural/urban residence, adjusted for education, ART and alcohol intake.]

SOA-02-1016-31 Uptake of tuberculosis preventive treatment among people living with HIV in Zambia, 2018

M Melgar,[1] R Shiraishi,[1] N Mwananyambe,[1] C Tende,[2] S Mwanza,[3] D Mwakazanga,[3] K Kapungu,[4] M Tembo,[3] P Lungu,[5] L Podewils,[1] [1]Centers for Disease Control and Prevention (CDC), Division of Global HIV and Tuberculosis, Atlanta, GA, United States of America, [2]Tropical Diseases Research Centre, Clinical Sciences Department, Ndola, Zambia, [3]Tropical Diseases Research Centre, Biomedical Sciences Department, Ndola, Zambia, [4]Tropical Diseases Research Centre, Social Sciences Department, Ndola, Zambia, [5]Zambia Ministry of Health, National Tuberculosis and Leprosy Control Programme, Lusaka, Zambia.
e-mail: okv5@cdc.gov

Background: The Zambia Ministry of Health recommends tuberculosis preventive treatment (TPT) with 6 months daily isoniazid for all people living with HIV (PLHIV) after ruling out active tuberculosis disease. We sought to estimate the percentage of eligible PLHIV who receive TPT and to identify challenges with TPT implementation in two provinces, Lusaka and Copperbelt, with the highest tuberculosis burden in Zambia.

Methods: In this cross-sectional survey, we used a two-stage cluster sampling method. First, we sampled 12 healthcare facilities with probability-proportional-to-size. Patient volume determined facility cluster size. From each facility, we systematically sampled medical records of approximately 30 adult PLHIV (age ≥15 years) and up to 30 children living with HIV (CLHIV, age < 15 years) to estimate TPT initiation and completion rates among eligible individuals. Estimates were weighted and controlled for complex survey design. Additionally, we interviewed one healthcare worker at each facility regarding TPT knowledge and challenges.

Results: We sampled 482 PLHIV (including 128 CLHIV). Four-hundred-twenty-two were TPT-eligible, of whom 24% (95% confidence interval [CI]: 9-49%) initiated TPT. TPT initiation was significantly lower for CLHIV compared with adults (8% vs 24%, Rao-Scott-adjusted chi-square p=0.04). PLHIV with a positive initial tuberculosis symptom screen, but who ultimately were not diagnosed with active tuberculosis disease after additional work up, had a significantly lower TPT initiation rate than those with a negative initial symptom screen (11% vs 28%, Rao-Scott-adjusted chi-square p=0.03). Among PLHIV who initiated TPT, 79% (95% CI: 93-99%) completed 6 months of treatment. Among interviewed healthcare workers, only 41% (unweighted) correctly relayed recommended target populations for TPT. Seventy-five percent (unweighted) reported insufficient stockpile of isoniazid for completion at the time of TPT initiation.

Conclusions: TPT initiation for eligible PLHIV is low overall, with initiation among CLHIV even lower. The Ministry of Health should prioritize provider education and isoniazid procurement.

SOA-02-1017-31 Delivery of isoniazid preventive therapy to incarcerated individuals in Southern Africa correctional facilities

L Chimoyi,[1] H Smith,[2] J Olivier,[3] H Hausler,[4] K Fielding,[5] C Hoffmann,[1,6] S Reid,[2,7] M Herce,[2,8] S Charalambous,[1,9] [1]The Aurum Institute, Implementation Research, Johannesburg, South Africa, [2]Center for Infectious Disease Research In Zambia, Implementation Research, Lusaka, Zambia, [3]Centers for Disease Control and Prevention, Key Population, Pretoria, South Africa, [4]TB HIV Care, Executive, Cape Town, South Africa, [5]London School of Hygiene and Tropical Medicine, Center for Biostatistics, London, United Kingdom, [6]Johns Hopkins Bloomberg School of Medicine, Epidemiology, Baltimore, MD, United States of America, [7]University of Alabama, School of Medicine, Division of Infectious Diseases, Department of Medicine, Birmingham, AL, United States of America, [8]University of North Carolina School of Medicine, Chapel Hill, Institute for Global Health & Infectious Diseases, Chapel Hill, NC, United States of America, [9]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa.
e-mail: lchimoyi@auruminstitute.org

Background: Isoniazid preventive therapy (IPT) is globally recommended for tuberculosis control. In correctional facilities where tuberculosis risk is magnified and transmission high, preventive therapy may be more important. This study describes IPT delivery in these settings.

Methods: We conducted an exploratory analysis on delivery of IPT to HIV-positive inmates aged ≥18 years in four correctional facilities in Southern Africa (one Zambia, three South Africa) from 06/2016-03/2018 nested in a larger cohort study investigating feasibility of implementing universal test and treat for HIV. Medical records were abstracted for tuberculosis screening performed by GeneXpert (Zambia) and symptoms (South Africa), diagnosis and treatment, ART uptake, demographics, laboratory results, including alanine aminotransferase (ALT), and IPT prescribing. Median (interquartile range [IQR]) and proportions summarized the study population and differences of IPT delivery at country-level.

Results: IPT information was available on 809/977(83%) participants: median age 32(IQR:27-37) years. 409/809(51%) received IPT; of those not on IPT, 51/400(13%) were discharged from facilities within a month of enrolment. ART was initiated in 752/809(93%) and among those, IPT was prescribed in 396/752(53%); 67/396(17%) before,139/396(35%) within and 190/396(48%) after 2 weeks of ART initiation. Zambia had a higher IPT delivery than South Africa [265/419(63%) vs.144/390(48%); p< 0.0001]. ALT information was collected on 440 participants, mostly from Zambia (95%). Elevated ALT was reported in 54/440(13%) where 19/52(37%) participants with elevated ALT were not prescribed IPT. Tuberculosis was screened and diagnosed for 762/809(94%) and 467/762(61%) respectively. Overall, 36/467(8%) cases were diagnosed with more from GeneXpert screening 33/36(92%) and 23/33 (70%) from Zambia. Tuberculosis treatment was initiated in 26/36(72%). Two tuberculosis cases were reported in participants on IPT.

Conclusions: These findings demonstrate the feasibility of IPT delivery in correctional settings. Screening with GeneXpert, as is policy in Zambia, may have increased tuberculosis yield. Further implementation of strategies and country-specific policy change may be needed to achieve target levels.

Indicator	Overall (N=809)	South Africa (n=390)	Zambia (n=419)
Initiated on IPT	409 (51%)	144 (35%)	265 (65%)
Initiated on ART	752 (93%)	333 (44%)	419 (56%)
Initiated on ART and IPT	396 (53%)	131 (33%)	265 (67%)
Screened for TB	762 (94%)	346 (65%)	416 (55%)
Diagnosed for TB	467 (61%)	121 (26%)	346(74%)
Total diagnosed with TB	36 (8%)	13 (36%)	23 (64%)
Started TB treatment	26 (72%)	4 (15%)	22 (85%)
IPT delivered within 2 weeks of ART initiation	139 (35%)	44 (29%)	108 (71%)
IPT delivered >2 weeks after ART initiation	190 (48%)	35 (18%)	155 (82%)

[Delivery of IPT among HIV positive inmates on ART in correctional facilities in Southern Africa (2016-2018)]

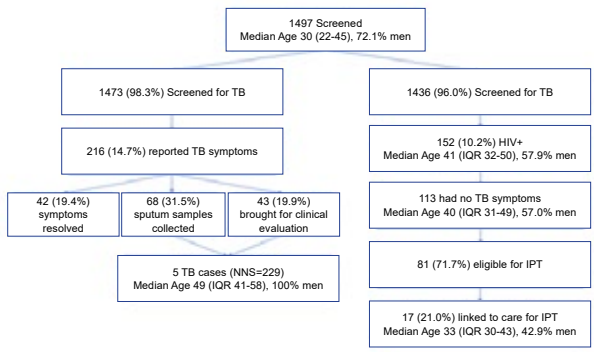
SOA-02-1018-31 Community-based TB case finding and IPT referrals from alcohol venues in rural South Africa

A Moll,[1] K Choi,[2] G Friedland,[3] S Shenoi,[4] [1]Philanjalo NGO, Philanjalo NGO, Tugela Ferry, South Africa, [2]Stony Brook School of Medicine, Medicine, Stony Brook, NY, United States of America, [3]Yale School of Medicine, Medicine, New Haven, CT, United States of America, [4]Yale University School of Medicine, Medicine, New Haven, CT, United States of America. e-mail: sheela.shenoi@yale.edu

Background: Alcohol use is increasingly recognized as a risk factor for TB disease. Community-based intensive case finding is an effective strategy to reach those who do not engage in health care. We report on efforts to screen community members who frequent alcohol venues (shebeens) for TB in rural South Africa, using an integrated communicable and noncommunicable disease screening platform.

Methods: In rural KwaZulu-Natal, South Africa, community health workers stationed outside shebeens engaged patrons for health education and voluntary confidential screening inside a mobile clinic. Prior to alcohol consumption, a WHO endorsed TB symptom screen (with sputum collection for GeneXpert if ≥1 symptom), HIV rapid test, random glucose (elevated >7mmol/L), and blood pressure (elevated >140 or >90mmHg) were offered. Community members with positive results were referred to their primary care clinic.

Results: Among 1497 screened, median age was 30 (IQR22-45), 72.1% men, 24.3% received government grants, went to shebeens mean 4 visits/week, and 42.3% reported harmful drinking as defined by elevated AUDIT scores. Among participants, 1473 (98.3%) consented to TB symptom screening and 216 (14.7%) reported TB symptoms, of whom 53.7% had cough>2 weeks. Five TB cases were detected and referred for treatment, with number needed to screen=299. All TB cases had elevated AUDIT scores; the number needed to screen among those with elevated AUDIT score was 125. Among those identified as HIV positive and not on ART, all were referred for ART. Among those HIV positive without TB symptoms (n=113), 71.7% of were eligible and referred for IPT; 50.6% linked to care and were provided counselling on IPT and 21% initiated IPT.
Conclusions: Community-based efforts to expand TB case finding and referral for isoniazid preventive therapy is feasible at alcohol venues in rural South Africa. Targeting those with harmful levels of alcohol consumption may provide higher yield for active TB case detection.



[Community-based screening for TB, HIV, and IPT at alcohol venues]

SOA-02-1019-31 Clients' perceptions about weekly, rifapentine-based tuberculosis preventive therapy in an urban HIV/AIDS clinic in Uganda

FC Semitala,[1,2,3] A Musinguzi,[3] J Kadota,[4] F Welishe,[3] J Nabunje,[3] A Katamba,[5] MR Kamya,[1,3] DD Dowdy,[6] A Katahoire,[7] A Cattamanchi,[8] [1]Makerere University College of Health Sciences, Internal Medicine, Kampala, Uganda, [2]Makerere University Joint AIDS Program (MJAP), Care and Treatment/ Research, Kampala, Uganda, [3]Infectious Diseases Research Collaboration, Research, Kampala, Uganda, [4]UCSF School of Medicine, Internal Medicine, San Francisco, CA, United States of America, [5]Makerere University College of Health Sciences, Clinical Epidemiology and Biostatistics, Kampala, Uganda, [6]Johns Hopkins Bloomberg School of Public Health, Public Health, Maryland, MD, United States of America, [7]Makerere University College of Health Sciences, Child Health and Development Centre, Kampala, Uganda, [8]UCSF School of Medicine, Pulmonary Medicine and Critical Care, San Francisco, CA, United States of America.
e-mail: semitala@gmail.com

Background: A new 12-dose, once-weekly regimen of isoniazid and rifapentine (3HP) is effective in preventing tuberculosis (TB), but the best approach to its delivery in high-burden settings remains uncertain. We sought to understand potential barriers to scale-up of 3HP from a client perspective in a routine HIV care setting in Kampala, Uganda.
Methods: We conducted semi-structured interviews with PLHIV attending the Mulago AIDS clinic. Interviews were guided by the Capability, Opportunity and Motivation for changing Behavior (COM-B) model and assessed clients' understanding of TB, social and contextual factors, and beliefs/emotions that might influence their decisions to accept and complete 3HP.
Results: Of 25 PLHIV interviewed, 17 were female. Nearly all (n=24) were aware that TB is a dangerous airborne disease. They were generally unaware (n=19) that TB can be prevented using medicines. While nearly all (n=24) expressed willingness to initiate therapy, concerns were expressed regarding pill burden, potential side effects, potential negative interaction with ARVs, and potential stigma associated with taking TB medicines. Nearly all (n=20) preferred self-administered therapy, which was perceived as convenient and less costly, but many (n=13) were concerned about forgetting to take the weekly dose at home. The few (n=5) who preferred directly-observed therapy valued face-to-face interaction with health care providers, especially for quick identification of drug-related side effects, but were concerned about transport costs for additional clinic visits. Nearly all (n=24) had access to a mobile phone and were open to receiving and responding to phone reminders/ check-ins.
Conclusions: PLHIV were aware that TB is dangerous and were willing to take 3HP. Effective counseling, reimbursement of transport costs for additional clinic visits

and use of digital adherence technologies to monitor adherence and provide reminders and support/motivation via SMS or interactive voice response should be further evaluated as part of 3HP scale-up.

SOA-02-1020-31 Providers' perceptions on delivery of weekly, rifapentine-based tuberculosis preventive therapy in an urban HIV/AIDS clinic in Uganda

A Musinguzi,[1] FC Semitala,[1,2,3] A Katamba,[4] J Nabunje,[1] F Welishe,[1] JL Ssemata,[1] MR Kamya,[2,5] DW Dowdy,[6] A Cattamanchi,[7] AR Katahoire,[8]
[1]Infectious Diseases Research Collaboration, Implementation Research, Kampala, Uganda, [2]Makerere University College of Health Sciences, Internal Medicine, Kampala, Uganda, [3]Makerere University Joint AIDS Program (MJAP), Mulago AIDS Clinic, Kampala, Uganda, [4]Makerere University, College of Health Sciences, Clinical Epidemiology and Biostatistics, Kampala, Uganda, [5]Infectious Diseases Research Collaboration, Research, Kampala, Uganda, [6]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America, [7]University of California, Division of Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [8]Makerere University, College of Health Sciences, Child Health and Development Centre, Kampala, Uganda. e-mail: amusinguzi@idrc-uganda.org

Background: A new 12-dose, once-weekly regimen of isoniazid and rifapentine (3HP) is effective in preventing tuberculosis (TB) disease, but there is uncertainty regarding how best to deliver it in high-burden settings. We sought to understand how best to scale-up 3HP from a provider perspective in a routine HIV care setting in Uganda.
Methods: We conducted semi-structured interviews with different cadres of healthcare providers at the Mulago AIDS clinic in Kampala: 3 doctors, 3 nurses, 2 clinical officers and 2 pharmacists. The interview guide was developed using the Capability, Opportunity and Motivation for changing Behavior (COM-B) model to explore and analyze providers' knowledge of, resource and contextual factors related to, and beliefs/emotions about delivery of 3HP to HIV patients.
Results: The 10 providers interviewed all prioritized counseling patients about TB preventive therapy. All were aware of and believed 3HP would be better accepted by patients compared to isoniazid alone (the current standard) despite the potential challenges of pill burden, drug side effects, potential interactions with ARVs, and stigma. Most providers (n=06) preferred directly observed therapy (DOT) to ensure drug adherence and for easier management of side effects, even though it would increase their daily workload and weekly clinic visits would be expensive for patients. They also acknowledged that most patients would prefer self-administered therapy (SAT; with digital adherence monitoring) for convenience. However, SAT would pose a challenge of low fidelity adherence data. Less than half of providers (n=04) preferred digital adherence monitoring due to convenience with their biggest concerns being reliability of the technology and lack of experience using digital adherence tools.
Conclusions: Providers believed that 3HP would be better accepted by patients compared to daily isoniazid for six months. However, streamlining patients' clinic visits, and training providers on digital adherence tools are important for the scale up of 3HP.

SOA-02-1021-31 Integrating isoniazid preventive therapy (IPT) with ART differentiated service delivery (DSD) improves IPT completion rates in resource limited settings: lessons from East-Central Uganda

R Nyinoburyo,[1] N Ruhinda,[2] AK Muwonge,[2] A Muhwezi,[2] N Tumwesigye,[2] [1]University Research Co., LLC, USAID RHITES EC Project, TB/HIV, Jinja, Uganda, [2]University Research Co., LLC, USAID RHITES EC Project, Health Systems Strengthening, Jinja, Uganda.
e-mail: rnyinoburyo@urc-chs.com

Background and challenges to implementation: Uganda is one of the 30 high TB/HIV burden countries in the World. The country adopted the implementation of IPT among eligible PLHIV in 2014 to reduce the burden of TB in HIV However, IPT implementation was hampered by poor completion rates;only 27% of clients that started IPT completed the 6-month course of Isoniazid (INH) by September 2017. Patients who do not complete the 6-month course of INH do not get the optimal TB preventive benefit and are at risk of developing drug resistance. One of the factors responsible for sub-optimal completion rates is the requirement for patients started on IPT to make monthly health facility visits for drug refills.
Intervention or response: The national guidelines on management of HIV, adopted Differentiated Service Delivery (DSD), a patient centered approach that tailors HIV care to patient needs especially for PLHIV that are stable in care. One of such DSD models is the community client ART delivery model (CCLAD) where PLHIV form community groups in which they receive care without necessarily coming to the health facility.
The USAID Regional Health Integration to enhance Services in East-central Uganda (RHITES-EC), recognizing that the disharmony between the HIV care policy on DSD and IPT guideline affects adherence on IPT leading to poor IPT completion rates, supported 5 high volume health facilities to integrate IPT and ART DSD (specifically CCLAD) where by INH was also delivered with ART in the community groups.
Results and lessons learnt: In the implementation sites, IPT completion rates improved from 43% during the quarter Oct-Dec 2018 to 85% in the quarter Jan-Mar

2019. This was also higher than the regional average IPT completion rate of 69% during the same period.
Conclusions and key recommendations: Integrating IPT into HIV DSD models improves IPT completion rates and should be adopted and standardized in resource limited settings.

SOA-03-C7 Person-centred care: a spectrum of activities

SOA-03-1022-31 Accompanying patients through the care chain: a dispatch from rural India

M Bhardwaj,[1] T Garg,[2] D Sen,[1] M Varyani,[1] S Kumar,[1] M Kumar,[1] R Sharma,[1] R Shankar,[1] R Mahto,[1]
[1]Innovators in Health, Operations, Patna, India, [2]Innovators in Health, Research, Patna, India.
e-mail: tgarg@innovatorsinhealth.org

Background and challenges to implementation: Despite free NTP services, access is a challenge in rural India. Diagnosis requires multiple visits, and accessing the private system to fill public gaps. Treatment requires periodic travel to obtain drugs. Adherence support is limited to DOT. These barriers are reflected in the low public notification rate of 47/100,000 pop. in the rural state of Bihar, compared with 109/100,000 nationally.
Intervention or response: An intervention was piloted in 3 blocks of (pop. 1.02M) of the Samastipur district in rural Bihar. The role of rural community health workers (CHWs, known locally as "ASHA") was expanded from DOT supervision to assisting the patient throughout diagnosis and treatment. CHWs transported sputum to reduce patient travel. All patients received a transport allowance (USD 1.5). CHWs accompanied patients to help them navigate public services, and directed them to accredited private facilities, if needed. The program negotiated reduced prices with labs and pharmacies. Transactions were cashless - the program covered private costs (about USD 8/pt). CHWs recorded patient histories and organized lab results, facilitating the patient-physician interaction in overburdened OPDs. They administered DOT at patient homes, preventing loss of workdays due to travel to DOT centers. CHWs also helped manage side-effects, and ensured follow-up labs. They received case-finding and treatment supervision incentives, now made standard by the NTP.
Results and lessons learnt: From Q2'17-Q1'18, 4595 presumptive cases resulted in 1012 confirmed cases, a rate of 97/100,000 pop. (pre-intervention rate: 52/100,000). The pre-treatment loss to follow-up (PTLFU) was 2.2%, compared with the district's 25% (NTP data, 2017 cohort). The success rate was 92%. The state's success rate was 67-74% with 16-20% outcomes unknown (NTP data).
Conclusions and key recommendations: It is practical and cost-effective to assist patients across the care chain. Such patient-centric programs feed a virtuous cycle that builds confidence in the NTP. CHWs in rural areas offer a pathway to such comprehensive care.

SOA-03-1023-31 Understanding men's preferences for improved tuberculosis care and treatment services, Buffalo City Metro Health District, Eastern Cape Province, South Africa

A Medina-Marino,[1] K Glockner,[1] E Grew,[2] D Olivier,[1] C Bezuidenhout,[1] N Ngcelwane,[3] AM Kipp,[4] J Daniels,[5]
[1]Foundation for Professional Development, Research Unit, East London, South Africa, [2]Northeastern University, College of Sciences, Boston, MA, United States of America, [3]Buffalo City Metro Health District, TB Program, East London, South Africa, [4]Vanderbilt University Medical Center, Institute for Global Health, Nashville, TN, United States of America, [5]Charles R. Drew University of Medicine and Science, Psychiatry, Los Angeles, CA, United States of America. e-mail: josephdaniels@cdrewu.edu

Background: Men with tuberculosis (TB) in South Africa struggle with treatment adherence compared to women. Limited research exists exploring men's preferences for treatment support. Guided by the Network-Individual-Resource (NIR) model, we explored men's experiences while in TB care and preferences for a male-centered care intervention.
Methods: In-depth interviews were conducted with men at different points along the TB care cascade in Buffalo City Metro Health District, South Africa. Interview protocol domains included: TB testing; treatment support; clinical care experiences; disclosure to and support from family/friends; stigma; and preferences for a future treatment support intervention. Interviews were conducted in Xhosa, and translated into English. Guided by the NIR model, transcripts were analyzed using a constant comparison approach. Frequency analysis of intervention preferences were calculated.
Results: Thirty-one men aged 18-60 years living in urban and peri-urban townships were interviewed. Men cited denial and fears of appearing weak, "not real men," as reasons for delayed seeking of treatment or hiding of their TB status. During treatment, challenges of hunger and job insecurity prevented men from performing their typical family roles, compounding concerns around fulfilling masculine expectations.
The most frequently preferred interventions were peer-to-peer support (58.1%), community meetings (51.6%), and awareness-raising campaigns (51.6%). Preferences are explained by men's perceptions of masculinity as a barrier to TB treatment access and adherence.
Participants stated that they would have appreciated peer-to-peer support from other men who had completed TB treatment, and volunteered themselves as mentors.

Conclusions: TB illness and care experience may contrast with perceived ideals of masculinity. Peer-to-peer support programs may improve men's TB care by challenging masculine stereotypes, decreasing stigma, promoting male camaraderie, and ultimately changing the conversation around male health and illness. Such programs should be implemented along with other community-based interventions.

SOA-03-1024-31 Video-observed therapy (VOT) application to promote treatment adherence in tuberculosis patients in Georgia

I Gabisonia,[1] M Danelia,[1] G Kuchukhidze,[2] I Khonelidze,[1] L Chapurishvili,[3] Z Avaliani,[4] M Davitashvili,[5] E Oniani,[3] [1]National Center for Disease Control and Public Health, Global Fund Programs Implementation Unit, Tbilisi, Georgia, [2]World Health Organisation, Regional Office for Europe, Copenhagen, Denmark, [3]National Center for Tuberculosis and Lung Disease, DOT/VOT Service, Tbilisi, Georgia, [4]National Center for Tuberculosis and Lung Disease, Tuberculosis and Lung Diseases, Tbilisi, Georgia, [5]National Center for Tuberculosis and Lung Disease, Management and Coordination Service, Tbilisi, Georgia.
e-mail: i.gabisonia@ncdc.ge

Background and challenges to implementation: High loss-to-follow up among multidrug and extensively drug-resistant (M/XDR) patients was identified as one of the main challenges of the national tuberculosis (TB) response in Georgia. Survey pointed at Directly Observed Therapy (DOT) as an inconvenient option for working patients and those in need to travel a long distance to DOT point. Easy to use VOT application was suggested as an option providing the same level of trust for healthcare provider as DOT.
Intervention or response: The mobile application (app) for Android system called "Adhere-TB" was built. It allows user to take medicines at any convenient time, even without access to internet, record the intake of drugs, report adverse events (if any) and send it to supervisor nurse daily whenever internet is accessible. Nurses have the administrative panel, where they see videos, and can confirm/reject the process of the drug intake. In addition smart-phones were procured for the project.
Results and lessons learnt: Since 2018, 190 (76 M/XDR and 114 Sensitive) patients were recruited in "Adhere-TB" app across the country, 63 have finished and 127 (50 M/XDR and 77 Sensitive) are on ongoing treatment. From 104 M/XDR patients currently registered in capital Tbilisi 48 (46%) are using VOT and one nurse now can supervise about 40 patients on "Adhere-TB" app.
With "Adhere-TB", patients can take medication at any time. The absolute majority take drugs at bedtime to be able to continue usual daily activities. Platform made work of nurses more flexible. App also helps to save about 5 GEL (2 USD) of transportation expenses per M/XDR patient per day. All information is collected electronically, statistical charts of treatment compliance and side effect data are automatically visualized, making it easier to analyze.
Conclusions and key recommendations: Introduction of "Adhere-TB" considered to improve treatment adherence as no loss-to-follow up case was reported. Smartphone App is more accepted by younger and middle age generations.

SOA-03-1025-31 Factors influencing patients' willingness to return to private providers for TB diagnostic care: insight from a standardised patient study in South Africa

J Boffa,[1,2] S Moyo,[3] J Chikovore,[4] A Salomon,[1] T Mkhombo,[3] A Kwan,[5] B Daniels,[6] S Wu,[1] M Pai,[1,7] A Daftary,[1,8] [1]McGill University, McGill International TB Centre, Montreal, QC, Canada, [2]University of KwaZulu-Natal, Centre for Rural Health, Durban, South Africa, [3]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Cape Town, South Africa, [4]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Durban, South Africa, [5]University of California, Health Policy, Berkeley, CA, United States of America, [6]World Bank, Development Research Group, Washington, DC, United States of America, [7]Manipal McGill Centre for Infectious Diseases, Manipal Academy of Higher Education, Manipal, India, [8]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa.
e-mail: smoyo@hsrc.ac.za

Background: Quality of TB care involves prompt and accurate testing, diagnosis, and treatment; however, patient satisfaction also plays a key role. We undertook a quality of care study utilising standardised patient actors (SPs) to evaluate TB management in South Africa's private sector. In addition to medical practices, SPs were asked about their willingness to return to their consulting provider. We hypothesised that correct management would be one of many influential factors.
Methods: Eight SPs undertook 220 interactions with 96 providers over four months in 2018. We ran logistic regression in Stata 15 using forward selection with a 10% cut off, testing various factors against self-reported willingness to return to the provider. We considered number of medications prescribed, length of interaction, patient-provider gender concordance, language of interaction, consultation fee, community, SP case description, first versus last 10 interactions for each SP, and correct TB management (defined as referral for TB test or to clinic) as independent variables.
Results: SPs were willing to return to the provider in 112/220 interactions (51%). SPs indicated that they would return to the provider in 43 interactions (20%) in which TB was incorrectly managed and would not return to the provider in 46 interactions (21%) in which TB was correctly managed. Factors that significantly increased SPs' willingness to return included interactions lasting longer than five minutes (OR_a=11.30,

95%CI=5.72-22.33), correctly managed TB (OR_a=2.34, 95%CI=1.23-4.46), and interactions occurring in the SPs' home language (OR_a=2.08, 95%CI=1.03-4.21).
Conclusions: In addition to correct medical management, SPs in our study displayed a preference to return to private providers who spent more time with them and spoke their home language. Findings suggest that even when correctly managed, diagnostic delays and disease progression may occur when a provider has not spent adequate time or effort to ensure patient comfort.

SOA-03-1026-31 Treatment outcomes of patients with tuberculosis who received controlled treatment and social support compared to patients who did not receive such services

I Varchenko,[1] I Terleieva,[2] V Liashko,[3] [1]State Institute 'Public Health Center of the MOH of Ukraine', Coordination of TB Programs, Kyiv, Ukraine, [2]Public Health Center of the MOH of Ukraine, Coordination of TB Programs, Kyiv, Ukraine, [3]Public Health Center of the MOH of Ukraine, Directorate, Kyiv, Uganda.
e-mail: y.varchenko@phc.org.ua

Background and challenges to implementation: The low treatment outcomes of the tuberculosis (TB) in Ukraine are due to the high number of patients lost for follow up, an inadequate level of treatment control.
Intervention or response: Outpatient tuberculosis treatment with the involvement of non-governmental organizations (NGO). Data of treatment outcomes of drug sensitive TB (DSTB) cohort of 2017, multidrug-resistance (MDR) and extensively drug resistance (XDR) TB cohort of 2016 were taken from the TB Register. Compared patients on the medical-social support (MSS) and without MSS. NGO´s services included daily delivery of drugs and controled treatment, product packeges for patients, psychological, legal, social support as needed.
Results and lessons learnt: Successful treatment of DSTB in patients on MSS (4954 (93.7%) was significantly higher (P< 0.0001, OR 6.82, 95% CI: 6.08-7.65) compared to DSTB group without MSS (12597 (68.5%)) due to the decrease of the unsuccessful treatments (172 (3.3%) and (1783 (9.7%)), mortality (94 (1.8%) and 2357 (12.8%)), lost for follow-up (68 (1.3%) and 1 654 (9%)). Successful treatment of MDR patients on MSS was in 2760 (73.7%) persons and was significantly higher (P< 0.0001, OR 6.75, 95% CI: 6.08-7.50) compared to MDR patients without MSS (968 (29.3%) due to the reduction in unsuccessful treatment (470 (12.5%) compared to 634 (19.3%)), mortality (286 (7.6%) and 890 (26.9%)), cases of lost for follow up (230 (6.1%) and 708 (24.5%)). Successful treatment of XDR patients on MSS was in 252 (62.1%) persons and was significantly higher (P< 0.0001, OR 6.75, 95% CI: 6.08-7.50) compared to XDR patients without MSS (132 (24.3%) due to the reduction in unsuccessful treatments (104 (25.6%) and 184 (33.9%)), mortality (29 (7.1%) and 135 (24.9%)), cases of lost for follow up (21 (5.2)% and 92 (16.9%)).
Conclusions and key recommendations: It is recommended that NGO be involved to the provision of the controlled treatment and psychosocial supportfor of TB patients for for improvement treatment outcomes.

SOA-03-1027-31 Video-observed treatment to monitor compliance of tuberculosis patients: five years of Ankara experience

S Ozkan,[1] AC Simsek,[2] K Altunay,[2] D Erisen,[2] DD Duman,[2] [1]MoH, Ankara Provincial Health Directorate, Yenimahalle Camlica Family Health Center, Ankara, Turkey, [2]MoH, Ankara Provincial Health Directorate, Presidency of Public Health Services, Ankara, Turkey.
e-mail: suozkan@gmail.com

Background: Directly observed treatment(DOT) is the standard of medication delivery for tuberculosis(TB) patients, in Ankara, since 2008. In order to prevent DOT disruptions caused by some difficulties like transportation, stigmatisation, or still working; using internet has come to mind. In 2012, video observed treatment(VOT) was initiated in order to ensure compliance of the patients to supervised drug intake.
Methods: The data of the VOT of TB patients, treated in Ankara between 2012 and 2016 were analyzed retrospectively. Health staff of dispensary had been assigned to follow VOT applications and system service (placecam 4.6.2 by Daviko GmbH) had been purchased. During planning of treatment, the patient was informed about VOT and accepters were included in the study. The program was downloaded to the patient´s computer, and the use of camera and microphone was controlled. TB patients were connected to the computer in the dispensary at the time determined, on each working day and had video interviews with the health worker and drink their medications. The supervisor was disconnected after making sure that the drug was drunk. On weekends, patients drank their medications themselves.
Results: VOT was applied to 108 patients in 5 years. 55 of them are pulmonary TB. In the 5-year period, 106 of 108 TB patients (98%) completed the treatment successfully, one patient was lost to follow-up and one patient had treatment failure.(Table-1) In the same years, the average treatment success was 86% except for the VOT.
Conclusions: VOT is an easy-to-use, cost-effective, patient-centered and time-saving method. It has been found to be highly successful in increasing compliance with treatment and completion of successful treatment. Since there were no smartphones in those years, the video conferencing program was used through desktops or laptops. Nowadays, with the widespread use of smartphones, it eliminates the difficulty of place and time in the implementation of VOT.

Years	2012	2013	2014	2015	2016	Total
Total number of TB cases undergoing VOT	30	14	27	21	16	108
Pulmonary TB	13	7	16	12	7	55
Extra-pulmonary TB	17	7	11	9	9	53
TB cases with treatment success	29	14	26	21	16	106
TB case who lost to follow-up	1	0	0	0	0	1
TB case with treatment failure	0	0	1	0	0	1

[Table-1. The number, site of disease and treatment results of TB patients, with video observerved treatment in the year 2012 to 2016]

SOA-03-1028-31 Patient and stakeholder perspectives on the social isolation of TB patients in Zambia and South Africa

M Gondwe,[1] V Bond,[1,2] D Wademan,[3] T Mainga,[1] G Hoddinott,[3] L Mureithi,[4] K Shanaube,[5] H Ayles,[5,6]
[1]Zambart, Social Science, Lusaka, Zambia, [2]London School of Hygiene & Tropical Medicine, Global Health and Development, London, United Kingdom, [3]Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Cape Town, South Africa, [4]Health Systems Trust, Health Systems Research Unit, Cape Town, South Africa, [5]Zambart, Research Directorate, Lusaka, Zambia, [6]London School of Hygiene & Tropical Medicine, Clinical Research, London, United Kingdom. e-mail: gbond@zambart.org.zm

Background: Social isolation includes self-isolation, social distancing and forced isolation and impacts healthcare seeking behaviour, diagnostic and treatment journeys. Qualitative research on social isolation is a critical part of TB stigma research to improve inclusion in care.
Methods: Enquiry on TB stigma was carried out within a qualitative component of a cluster-randomized trial of the effects of community wide TB and HIV interventions (TREATS) study implemented in 8 Zambian and 6 South African study communities (2018-2021). In-depth interviews were held with TB patients (n=81), health workers (n=9), alternative health providers (n=14) and TB stakeholders (n=3), and focus-group discussions with TB stakeholders (participants=179). Data were analysed thematically around key forms, drivers and consequences of TB stigma.
Results: Participants said that overall TB stigma "had reduced". However, experiences of social isolation were common. In the household, the most common forms were using different cups, plates, soap and bedding, eating alone, friends and relatives not visiting and moving the patient. In the community, not attending church and ceasing work were common. At the health facility, demarcated TB services led to TB patients being isolated from other clients. Health-worker messaging to patients and families was contradictory, both advocating for and against social isolation. TB patients perceived social isolation as protecting their families whilst acknowledging it made them "think too much", led to loneliness and undermined their income. Both patients and other participants advocated not isolating TB patients to reduce TB stigma. Some differences in forms of isolation were observed between Zambia and South Africa.
Conclusions: Social isolation persists as a form of TB-related stigma in families, communities and health facilities. Health provider messaging is contradictory and confusing. TB service delivery needs to reflect and revise social isolation advice and recognize the value of social protection (e.g. disability grant) in reducing exclusion.

SOA-03-1030-31 BRAC shasthya shebikas (SS): changing the TB scenario in Bangladesh

IA Rifat,[1] MA Islam,[1] S Islam,[1] S Reja,[1] F Khatun,[1] SMI Mohsin,[1] [1]BRAC, Communicable Diseases Programme (TB), Dhaka, Bangladesh. e-mail: azmary.rifat@brac.net

Background and challenges to implementation: BRAC, the largest international NGO has been implementing community based TB control programme in Bangladesh since 1984 under the guidance of National TB Control Programme (NTP). Currently, BRAC is providing TB control services in 45 districts covering 322 upazillas and 11 city corporations with population coverage of 101 million. This has been possible due to the valuable contribution from Shasthya Shebikas (SS) who are working relentlessly to achieve TB free Bangladesh.
Intervention or response: Shasthya Shebika plays a key role in diagnosis and treatment of patients and is appointed from within the local communities with the objective to play a dual role in TB management at the grass roots level. Following selection, the SS undergo basic and refresher training. Their task involves visiting households to disseminate TB messages individually, identifying presumptive, and referring them to the nearest laboratory. After treatment is initiated by a graduate physician, the SS ensures DOT and sputum follow-up test to make sure treatment adherence is there. To motivate the SS, incentive of BDT 600 for every patient that successfully completes treatment is provided.
Results and lessons learnt: In BRAC supported areas, 193,424 TB patients were identified in 2018; nearly half of whom were referred by SS. The treatment success rate was 94% in 2017. More than 67,000 community health workers are working across Bangladesh in an effort to eradicate TB from Bangladesh.
Conclusions and key recommendations: SS are an integral part of the programme. They are widely accepted by the community because they are recruited from the same community, accountable to the communities for their activities, and supported by the health care system through BRAC and the Government of Bangladesh. The success of the TB control programme largely depends on their dedication, performance and willingness to serve the society as the first point of care.

SOA-03-1031-31 Acceptability of video-observed TB treatment among private providers in Ho Chi Minh City, Viet Nam

PTM Nguyen,[1] RJ Forse,[2] T Dam,[2] AJ Codlin,[1] HB Huynh,[2] LNQ Vo,[3,4] TN Vu,[5] GT Le,[5] HB Nguyen,[6] NV Nguyen,[6] [1]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [3]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [4]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [5]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam, [6]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam. e-mail: phuong.tran@tbhelp.org

Background: The World Health Organization recently recommended the use of video observed treatment (VOT) as one option for monitoring TB treatment adherence. However, acceptability of VOT in the private sector, where observation of dosing implementation is rare, has not yet been evaluated.

Methods: For this TB REACH-funded study, we designed a survey to measure private provider perceptions of VOT across seven constructs of healthcare intervention acceptability.

The survey was administered using the open-source Ona platform and ODK Collect app on Android tablets. We approached clinicians working in Ho Chi Minh City, who were known to be treating TB in their private clinics.

We calculated the median and rank sum from Likert-scale responses, stratified by provider willingness to use VOT, and tested for significant differences in responses between these groups using the Mann-Whitney U test.

Results: 40 private providers completed the survey. 28 (70%) agreed that using VOT would help them identify patients at risk of stopping treatment more quickly (intervention coherence) and 25 (63%) felt VOT would improve TB treatment adherence and outcomes (perceived effectiveness).

However, just 22 (55%) of the survey providers stated they would use VOT in their practice if given the opportunity. Between providers who would and would not use VOT, there are statistically significant differences in their confidence providing differentiated care (self-efficacy), belief that VOT would save them time (opportunity cost), and in their affective attitude: perception of whether VOT addresses a problem which patients face, whether it would be beneficial for patients, and whether VOT is relevant for all their TB patients.

Conclusions: Private providers in Ho Chi Minh City have an overall positive view towards using VOT. Future VOT implementation in the private sector should focus the clinician affective attitude, by emphasizing the benefit and relevance of VOT during recruitment, and should provide support for implementing differentiated care.

Constructs of healthcare intervention acceptability and their components	Would use VOT (n= 22)		Would not use VOT (n=18)		P-Value
	Median (IQR)	Rank sum	Median (IQR)	Rank sum	
Ethicality					
Belief that observation is best strategy for adherence	4 (4-5)	491	4 (4-4)	329	0.19
Willingness to test new approaches	4 (4-4)	481	4 (3-4)	339	0.32
Intervention Coherence					
Identify side effects faster	4 (2-4)	506	2.5 (2-4)	314	0.10
Identify people at risk of stopping treatment faster	4 (3-4)	443	4 (4-4)	377	0.77
Burden					
Time requirement from doctor	2 (1-3)	423.5	2 (2-3)	396.5	0.43
Time requirement from patient	2 (2-3)	441.5	2 (2-4)	378.5	0.78
Opportunity Cost					
Save time for doctor	4 (3-4)	529	2 (2-4)	291	**0.02**
Save money for doctor	2 (2-4)	506	2 (2-2)	314	0.08
Perceived Effectiveness					
Help in providing differentiated care	4 (3-4)	478	4 (2-4)	342	0.38
Help patients adhere to treatment	4 (3-4)	496	4 (2-4)	324	0.17
Self-Efficacy					
Confidence monitoring treatment through VOT	4 (3-4)	508	2 (2-4)	312	0.09
Confidence providing differentiated care through VOT	4 (4-4)	529	4 (2-4)	291	**0.01**
Affective Attitude					
Addresses problems which patients face	4 (3-4)	545	2.5 (2-4)	275	**0.01**
Be beneficial for doctor's practice and patients	4 (4-4)	561	2 (2-3)	259	**0.001**
Be relevant for all of doctor's TB patients	2 (2-2)	504.5	2 (2-2)	315.5	**0.02**

[VOT acceptability constructs by physician cohort]

SOA-03-1032-31 Optimising novel tuberculosis medication adherence technologies utilising human-centred design

C Berger,[1] D Patel,[2] K Neville,[3] J Ggita,[4] A Kityamuwesi,[4] P Turimumahoro,[4] K Farr,[5] A Katamba,[4] A Cattamanchi,[1] A Sammann,[2] [1]University of California, Pulmonary / Critical Care, San Francisco, CA, United States of America, [2]University of California, Surgery, San Francisco, CA, United States of America, [3]Stanford University School of Medicine, Engineering, Palo Alto, CA, United States of America, [4]Uganda Tuberculosis Implementation Research Consortium, U-TIRC, Kampala, Uganda, [5]University of California, Division of General Internal Medicine Zuckerberg San Francisco General Hospital, Pulmonary / Critical Care, San Francisco, CA, United States of America.
e-mail: christopher.berger@ucsf.edu

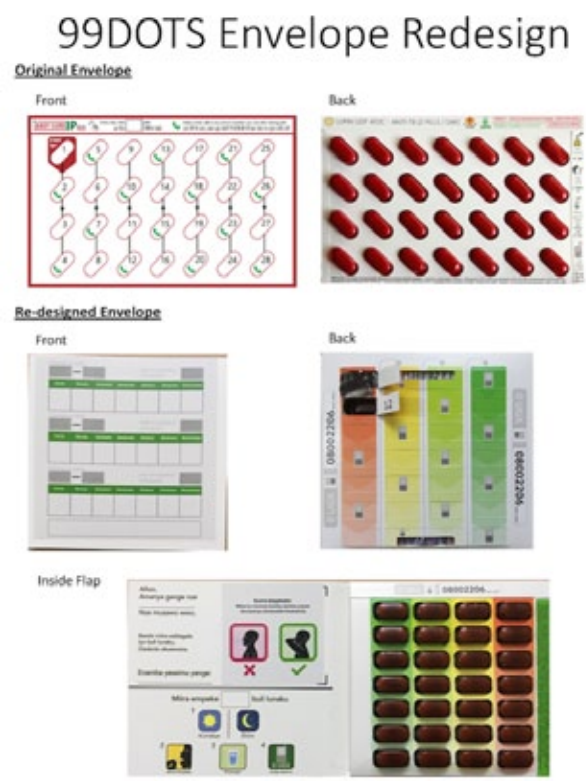
Background and challenges to implementation: Tuberculosis (TB) treatment success rates remain far below the World Health Organization's 90% target. 99DOTS (Everwell Health Solutions, India) is a low-cost digital adherence technology that involves patients calling toll-free phone numbers hidden underneath pills in blister packs to self-report medication dosing. As part its first deployment in sub-Saharan Africa, we used human-centered design (HCD) methodology to improve fit to the local context.

Intervention or response: We performed 46 unstructured interviews at eight TB treatment units in Uganda. Interviewees included TB patients, family members, clinicians/nurses, community health workers, and local community leaders. Key quotes and themes were elicited from transcribed interviews and translated into actionable insights that guided 99DOTS customization.

Results and lessons learnt: We discovered seven main insights:

(1) education about TB is an essential and strongly desired component;

(2) gamification, entertainment, celebrities and politicians are not motivators,
(3) health workers are trusted members of patients' TB journeys,
(4) food was a major adherence barrier,
(5) pill packs had the potential to serve as adherence tools,
(6) stigma surrounding TB is deeply pervasive, and
(7) patients want to feel gratitude and celebration.
Based on these insights, the pill pack envelope was re-designed to convert it into a booklet that conceals the pills, and adds space to record health worker's contact information and educational/motivational stickers to customize the pill pack. In addition, audio messages associated with patients' daily calls were recorded by health workers to convey educational/motivational messages that celebrated patient adherence.
Conclusions and key recommendations: HCD allows researchers to better design person-centered interventions that directly address users' needs. The insights uncovered provided a foundation upon which to re-design key aspects of 99DOTS to reflect the wants and needs of its key users, thus avoiding the pit-falls of a "one size fits all" approach.



[99DOTS Envelope Redesign]

SOA-04-C1 TPT: old and new regimens

SOA-04-1033-31 High treatment completion rates using a three-month isoniazid-rifampicin regimen during a community-wide latent TB screening and treatment campaign on Cu Lao Cham Island, Viet Nam

TTT Dong,[1] RJ Forse,[2] LP Nguyen,[1] LNQ Vo,[3,4] AJ Codlin,[5] PN Tran,[6] HB Nguyen,[7] HV Le,[7] NV Nguyen,[7] [1]Friends for International TB Relief, Operations, Hanoi, Viet Nam, [2]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [3]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [4]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [5]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [6]Pham Ngoc Thach Hospital Quang Nam, Provincial TB Program, Tam Ky, Viet Nam, [7]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam. e-mail: thuy.dong@tbhelp.org

Background and challenges to implementation: Viet Nam's UNGA HLM commitment includes a target for treating 291,500 people for latent TB infection (LTBI) between 2018-2022. The current LTBI treatment regimen in Viet Nam is nine months of isoniazid for adults (≥15 years), posing a major challenge for LTBI treatment adherence and completion.
Intervention or response: As part of the TB REACH-funded SWEEP-TB project, a population-level TB screening campaign was conducted on the island of Cu Lao Cham in January 2019. Over 90% of the island's 2,026 residents were screened for LTBI (tuberculin skin test ≥10mm). After ruling out TB disease by chest X-ray screening and Xpert testing, 435 adults had normal liver enzymes and were considered eligible for treatment with daily rifampicin and isoniazid for 3 months (3HR). 377 (86.7%) of these people were started on the shorter regimen. Four local commune health officers and two community health workers supported the provision of LTBI treatment, which included weekly adverse event monitoring.
Results and lessons learnt: Among the 377 adults started on 3HR, 337 (89.4%) have successfully completed treatment or are in the final month of treatment and are expected to complete the full regimen. 13 individuals (3.7%) experienced adverse events (AEs); no episodes of hepatotoxicity were recorded. The most common side effects were itching (61.5%), fatigue (38.4%), numbness (23.1%) and muscle pain (15.4%). Of the people who discontinued 3HR treatment early, 29 (7.7%) were elective discontinuations, 10 (2.7%) were due to side effects, and 1 (0.2%) person moved away from Cu Lao Cham island.
Conclusions and key recommendations: People with LTBI who were treated with 3HR had high treatment completion rates and low rates of AEs. These data sug-

gest that 3HR can be safely administered at the population-level and that follow-up care can be managed by the existing health system.

Outcome	Number	(%)
Initiating treatment with 3HR	377	
Treatment Completed	337	(89.4%)
Stopped early: adverse effect	10	(2.7%)
Stopped early: patient decision	29	(7.7%)
Stopped early: moved	1	(0.2%)

[3HR Treatment Outcomes]

SOA-04-1034-31 Weekly rifapentine and isoniazid for tuberculosis prevention in China: a randomised controlled study

Q Ruan,[1] X Huang,[2] Q Yang,[1] L Shao,[1] X Liu,[2] J Wu,[1] M Lin,[2] W Zhang,[1] Ke-chuan Pan Yao-jie Shen Li-min Cai Qiao Ling Tian Jiang Jin-jing Hong Xiao-dan Wang Chun-lian Ma Guan-qing Peng Xiu-zhen Wang Jin-chao Mao Tian-zhou Wu [1]Huashan Hospital Affiliated to Fudan University, Department of Infectious Diseases, Shanghai, China, [2]The First People's Hospital of Wengling, Department of Infectious Diseases, Taizhou, China. e-mail: ruan_qiao_ling@yahoo.com

Background: Preventive treatment for individuals at the highest risk of tuberculosis progressing to an active disease is vital in the successful control of TB. For preventive TB treatment, it is a challenge to balance the potential long-term benefit and immediate risk of therapy-related adverse events. Three-month, once-weekly rifapentine and isoniazid may be a promising regimen to shorten preventive tuberculosis treatment in the high-risk population of China.
Methods: In this open-label, randomized clinical trial, eligible silicotic participants were assigned to the rifapentine/isoniazid group and observation group with a sample size ratio of 1:1, according to stratified randomization by silicosis categories. All were followed up for 37 months after enrollment. The efficacy, safety, and completion rate of the regimen were evaluation in this silicotic population in China.
Results: We screened 1,227 adults with silica exposure or silicosis; 513 were finally enrolled and assigned to the rifapentine/isoniazid (n=254) or observation group (n=259). Median age was 57 years-old, median body mass index was 23.5 kg/m^2, all subjects were males, and none had human immunodeficiency virus. Twenty-eight participants were diagnosed with tuberculosis, 9 and 19 in the rifapentine/isoniazid and observation groups, respectively. Cumulative tuberculosis rates in the observation group were higher than that in the rifapentine/isoniazid group; a statistical significance was found using the per-protocol analysis (P=0.035), but not the modified intention-to-treat analysis (P=0.055). Due to an unexpected high frequency of any adverse event (70.4%) and Grade 3 or 4 adverse events (7.9%), the completion of rifapentine/isoniazid was 54.7%. Of the 26 (10.8%) cases with flu-like systemic drug reactions, nine led to hospitalization. Five subjects (2.1%) experienced hepatotoxicity.
Conclusions: Weekly rifapentine/isoniazid regimen was effective in preventing tuberculosis in the silicotic population in China; however, it was not well tolerated based on the unsatisfactory completion rate and decreased protection against tuberculosis.
Trial registration: www.clinicaltrials.gov (NCT02430259)

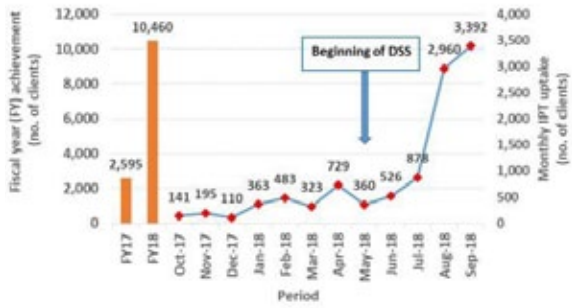
SOA-04-1035-31 Direct supportive supervision results in improved isoniazid preventive therapy implementation in the Nigerian Military HIV programme

S Meribe,[1] Y Adamu,[1] I Lawal,[1] I Amazue-Ezeuko,[1] N Okeji,[2] E Abikoye,[1] I Okoye,[1] P Coakley,[3] R Nelson,[1] L Chittenden,[1] [1]U.S. Army Medical Research Directorate-Africa/Nigeria, Walter Reed Army Institute of Research, Abuja, Nigeria, [2]Nigerian Ministry of Defense, Health Implementation Program, Abuja, Nigeria, [3]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Springs, MD, United States of America.
e-mail: smeribe@wrp-n.org

Background and challenges to implementation: Isoniazid preventive therapy (IPT) is recommended for tuberculosis (TB) prevention amongst people living with HIV (PLHIV) and other persons at high risk of TB. The Nigerian military HIV program had been facing numerous challenges since 2015, in increasing IPT uptake among its HIV clients, with a coverage rate of only 5% in fiscal year (FY) 2016. These challenges include; unstructured distribution and requisition system, healthcare providers' oversight to initiate clients on IPT, myths about the intervention, poor recording and reporting of IPT.
Intervention or response: Between October 2016 and September 2017 (FY2017), the program worked in conjunction with other U.S. government agencies to address supply chain bottlenecks, which increased coverage to approximately 9% of eligible PLHIV in FY2017. Seeking additional improvements, in May 2018, the program embarked on IPT specific "direct supportive supervision" (DSS). With this, most of the 27 comprehensive sites under the Nigerian military program sites were visited to conduct root cause analysis, and mentorship to address barriers to IPT initiation.
In addition, there was introduction of IPT monitoring tool, sticker-reminders on clients' folders, and bi-weekly IPT uptake data collection and collation.
Results and lessons learnt: DSS implementation led to increased IPT uptake, (Fig. 1) from monthly uptake of 360 clients in May 2018 to a monthly uptake of 3,392 clients in September, 2018.
The total achievement, from the beginning of DSS in May 2018 to September 2018 (8,116 clients), represented 78% of the total number of patients on IPT for the year,

while the total FY2018 achievement (10,460) represented 35% IPT coverage of all PLHIV in care, against 9% achieved in FY2017.

Conclusions and key recommendations: With a tailored supportive supervisory strategy and site specific context, programmatic barriers to IPT uptake can be easily identified and quickly addressed, resulting in better patient care.



[Fig. 1: IPT uptake trend]

SOA-04-1036-31 Risk factors for adverse events in contacts prescribed preventive treatment for drug-resistant TB exposure

A Malik,[1,2,3] N Gandhi,[1] T Lash,[1] L Cranmer,[4] S Omer,[1] J Fuad,[2] S Siddiqui,[2] H Hussain,[3] M Becerra,[5,6] [1]Emory University Rollins School of Public Health, Epidemiology, Atlanta, GA, United States of America, [2]Global Health Directorate, Indus Hospital, TB Program, Karachi, Pakistan, [3]Interactive Research and Development, TB Program, Karachi, Pakistan, [4]Emory University School of Medicine, Pediatrics Infectious Diseases, Atlanta, GA, United States of America, [5]Harvard Medical School, Global Health and Social Medicine, Boston, MA, United States of America, [6]Brigham and Women's Hospital, Global Health Equity, Boston, MA, United States of America.
e-mail: amyn.malik@emory.edu

Background: Completion of TB preventive treatment is important to optimize efficacy; treatment-related adverse events sometimes result in discontinuation. This study aims to describe the occurrence of adverse events and their associated risk factors during a 6-month 2-drug fluoroquinolone-based preventive treatment intervention for household contacts of drug-resistant TB patients in Karachi, Pakistan.

Methods: The primary outcome was development of any clinical adverse event during preventive treatment. Adverse events were categorized using the National Institute of Allergy and Infectious Diseases' Division of AIDS and National Institute of Health's Common Terminology Criteria for Adverse Events adverse events grading tables.

Time to event analysis with Kaplan-Meier curves and Cox proportional hazard models accounting for recurrence were used to analyze associated risk factors for adverse events.

Results: Of the 172 household contacts started on preventive treatment, 36 (21%) developed 64 adverse events during 812.9 months of treatment. The incidence of adverse events over 6 months of treatment was 7,873 per 100,000 person-months (p-m); 16,067 per 100,000 p-m with ethionamide and 4,384 per 100,000 p-m with ethambutol. Of the 64 clinical adverse events recorded, 53 (83%) were grade 1 and 11 were grade 2. There were no grade 3 or 4 adverse events. In multivariable analysis, the risk of adverse events was higher in contacts prescribed ethionamide as compared to ethambutol as the companion drug adjusting for age, sex and BMI (aHR: 2.05 [95% CI: 1.18-3.57]). Overall, there was no notable difference in treatment completion amongst the contacts who experienced an adverse event and those who did not (cOR: 1.13 [95% CI: 0.52-2.47]).

Conclusions: Fluoroquinolone-based regimen for infection treatment in DR-TB contacts is well tolerated with no grade 3 or 4 adverse events observed. Regimens with ethionamide are more likely to result in grade 1 or 2 adverse events, which may merit clinical counseling, but patients completion was not affected.

	UNADJUSTED			ADJUSTED		
	HR	95% CI	P-value	HR	95% CI	P-value
Ethionamide	2.16	1.22 - 3.81	0.008	2.06	1.09 - 3.88	0.026
Age <5 years		***Ref***			***Ref***	
Age 5-9 years	2.69	1.12 - 6.48	0.027	2.90	1.17 - 7.14	0.021
Age 10-19 years	3.93	1.80 - 8.56	0.001	3.22	1.47 - 7.05	0.003
Age >19 years	4.08	1.71 - 9.71	0.002	4.38	1.66 - 11.51	0.003
Sex (male)	0.91	0.56 - 1.48	0.709	0.72	0.44 - 1.18	0.194
BMI	1.00	0.98 - 1.03	0.700	0.99	0.94 - 1.04	0.689

[Risk of adverse events with preventive treatment for DR-TB exposure (accounting for recurrence)]

SOA-04-1037-31 Effectiveness of an IGRA-based latent tuberculosis screening programme in people initiating dialysis

K Romanowski,[1] C Rose,[2] V Cook,[1] A Levin,[3] O Djurdjev,[4] I Sekirov,[5] M Morshed,[6] J Johnston,[1]
[1]BC Centre for Disease Control, Provincial TB Services, Vancouver, BC, Canada, [2]BC Centre for Disease Control, Epidemiology and Biostatistics, Vancouver, BC, Canada, [3]BC Provincial Renal Agency, BC Provincial Renal Agency, Vancouver, BC, Canada, [4]Provincial Health Service Authority, PHSA Decision Support Services, Vancouver, BC, Canada, [5]BC Centre for Disease Control Public Health Microbiology and Reference Laboratory, Mycobacteriology, Vancouver, BC, Canada, [6]BC Centre for Disease Control Public Health Microbiology and Reference Laboratory, Zoonotic Diseases and Emerging Pathogens, Vancouver, BC, Canada. e-mail: kamila.romanowski@bccdc.ca

Background: In 2012, the Canadian province of British Columbia (BC) began rolling out a province-wide interferon-gamma release assay (IGRA)-based latent tuberculosis (LTBI) screening program, aimed at screening all people initiating chronic dialysis in BC, and treating for LTBI when appropriate. The objective of this study was to compare active tuberculosis (TB) risk in people screened using an IGRA-based protocol to those not screened during the same time period.
Methods: A retrospective cohort was created of all British Columbians who initiated at least 90 days of dialysis between January 2012 and May 2017. Individuals were stratified into a screened (defined as receiving an IGRA within 365 days of initiating dialysis) and non-screened group. Both groups were followed until they developed active TB, died, or until cohort-end. Multivariable Cox regression was used to determine the association of LTBI screening and risk of developing active TB.
Results: Of the 3190 individuals assessed, 1790 (56.1%) were screened. The incidence of active TB was 1.2 per 1000 person-years (PYs) (95% CI 0.5 - 2.3) in those screened and 2.6 per 1000 PYs (95% CI 1.4 - 4.5) in those not screened. After adjusting for baseline demographic and clinical variables, screened individuals had a 70% lower likelihood of developing active TB compared to those not screened (HR 0.3, 95% CI 0.1 - 0.8; P< 0.01). Of the 152 (8.5%) individuals who initiated LTBI treatment post-screening, none developed active TB.
Conclusions: Our results suggest that systematic screening of individuals initiating dialysis using an IGRA-based protocol can significantly decrease the risk of active TB in this high-risk population. Given the importance of screening high-risk groups in low-incidence countries, the results from this analysis could inform scale-up of TB screening in dialysis programs in other low incidence regions.

SOA-04-1038-31 Feasibility and effectiveness of a public health approach to increase latent tuberculosis infection treatment among contacts: a pilot study in Rio de Janeiro, Brazil

M Lisboa Bastos,[1,2] OO Oxlade,[2] A Benedetti,[2] F Fregonese,[2] C Valiquette,[2] E Faerstein,[1] JR Cavalcante,[1] P Hill,[3] D Menzies,[2] A Trajman,[2,4]
[1]Social Medicine Institute - State University of Rio de Janeiro, Epidemiology, Rio de Janeiro, RJ, Brazil, [2]Research Institute of the McGill University Health Centre, International TB Centre, Montreal, QC, Canada, [3]University of Otago Medical School, Preventive and Social Medicine, Otago, New Zealand, [4]Federal University of Rio de Janeiro, Internal Medicine Graduate Program, Rio de Janeiro, RJ, Brazil. e-mail: mayara_bastos@yahoo.com.br

Background: Losses in the cascade-of-care of contacts of tuberculosis index-patients limit the public health benefits of prevention of active disease through latent tuberculosis infection (LTBI) treatment. We conducted a pilot study to evaluate the feasibility and effectiveness of a public health approach to identifying and correcting problems in this cascade-of-care in two clinics in Rio de Janeiro.
Methods: Clinics underwent a six-month standardised assessment of barriers to management of contacts of newly-diagnosed index-patients. Short questionnaires regarding knowledge, perceptions and practices were administered to patients, their contacts and healthcare workers (HCW). Data on tuberculosis contact investigation at baseline were collected from pre-existing data sources at clinics. Subsequently, solutions targeted at specific LTBI cascade gaps were implemented during the following six months. The effectiveness of the approach was measured by the difference of contacts starting LTBI treatment per 100 index-patients pre- and post-implementation of solutions.
Results: Knowledge gaps among groups interviewed and losses in all steps of the cascade were identified. The solutions adopted included implementation of an index-patient-based contact registry book, a four-hour education session of HCW and the development of educational material consisting in booklets to HCW and flyers to index-patients and their contacts. In addition, a visual tool using excel graphs was developed to provide a feedback to HCW, and an experienced physician provided intensive in-service training using this tool. Contacts identified per index case increased from 1.90 to 2.49 after the intervention. LTBI treatment initiation also significantly increased from 5 to 49 contacts per 100 index case (**Table**).
Conclusions: Educational HCW activities with close in-service training by a credible HCW using a simple feedback tool resulted in an increase in contacts identified and initiating LTBI therapy. The approach considered in this pilot is currently under evaluation in a larger RCT (ACT4 Trial) in 5 countries.

	Pre-implementation (6 months)	Post-implementation (6 months)
Number of index cases identified	41	57
Number of contacts of index cases identified	78	142
Number of contacts identified per index case	1.90	2.49
Difference of contacts identified per index case (95% confidential interval)*	0.59 (0.21, 0.96)	
Number of contacts out of those identified who started LTBI treatment	2	28
Contacts initiating treatment per 100 Index-patients	5	49
Difference of contacts starting LTBI treatment per 100 index-patients (95% confidential interval)*	44 (23, 66)	

Using Poisson model.

[Table - Cascade of care of contacts of TB index-patients before and after implementation of solutions to enhance latent TB treatment initiation]

SOA-04-1039-31 Isoniazid preventive therapy (IPT) uptake in an urban TB treatment facility in Bangladesh

S Sultana,[1] KK Paul,[1] S Barua,[1] S Alam,[1] AS Sikder,[1] MJ Amin,[1] GI Chowdhury,[1] S Sarker,[1] RS Banu,[2] S Banu,[1] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh, [2]Directorate General of Health Services, National Tuberculosis Control Programme, Dhaka, Bangladesh. e-mail: sonia.sultana@icddrb.org

Background and challenges to implementation: According to World Health Organization (WHO) estimates, 1 million childhood tuberculosis (ChTB) incident cases occurred in 2016, including 210,000 TB related deaths in children. Administration of Isoniazid Preventive Therapy (IPT) for 6 months can reduce the risk of developing TB in children by nearly 60%.

However, national TB programs data showed that the rate of IPT uptake as well as adherence among those who starts IPT were between 21-58% and 13% respectively. In 2016, only 17% of an estimated 49,000 eligible children under five received IPT in Bangladesh. The main challenge to achieve high IPT coverage is in the implementation of the recommended strategies, especially counseling.

Intervention or response: There are six directly observed treatment short course (DOTS) facilities established by icddr,b within two metropolitan cities in Bangladesh. Physicians as well as health workers (HWs) working in these facilities were trained on screening and counseling for IPT. From January 2017 to December 2018, physicians as well as HWs counseled parents of eligible children for IPT in these centers. All the activities regarding IPT were closely supervised. Descriptive statistics were used to analyze routinely collected program data retrospectively.

Results and lessons learnt: Among 243 children eligible for IPT, 226 (93%) were invited for IPT, 200 (82%) were evaluated, TB was confirmed in one child (< 1%), and 198 (81%) started IPT. Among those who commenced IPT, 126 (64%) completed a full course of IPT, 42 (21%) dropped out and 30 (15%) are continuing the therapy.

Conclusions and key recommendations: This report is one of the first few to describe physician counseling to overcome the implementation challenges of IPT and achieve a higher IPT uptake as well as adherence rate than the reported data. Our result indicates that rigorous training on patient counseling, counseling provided by physician, and enhanced monitoring might help to achieve countrywide higher coverage of IPT in Bangladesh and elsewhere.

SOA-04-1040-31 Tuberculosis preventive treatment among child contacts of persons with pulmonary tuberculosis in two provinces in Zambia, 2018

M Melgar,[1] R Shiraishi,[1] M Tembo,[2] S Khondowe,[2] J Mulenga,[3] P Lungu,[4] K Malama,[5] A Silumesii,[6] L Podewils,[1] [1]Centers for Disease Control and Prevention (CDC), Division of Global HIV and Tuberculosis, Atlanta, GA, United States of America, [2]Tropical Diseases Research Centre, Biomedical Sciences Department, Ndola, Zambia, [3]Tropical Diseases Research Centre, Clinical Sciences Department, Ndola, Zambia, [4]Zambia Ministry of Health, National Tuberculosis and Leprosy Control Programme, Lusaka, Zambia, [5]Zambia Ministry of Health, Department of Technical Services, Lusaka, Zambia, [6]Zambia Ministry of Health, Department of Public Health, Lusaka, Zambia. e-mail: okv5@cdc.gov

Background: The Zambia Ministry of Health recommends household contact tracing (HHCT) for persons with pulmonary tuberculosis and tuberculosis preventive treatment (TPT) for identified household contacts aged < 5 years (child contacts) after ruling out tuberculosis disease. As a sub-study of a broader TPT assessment, we conducted a cross-sectional survey of child contacts in Lusaka and Copperbelt Provinces, which together represent >60% of the national adult tuberculosis prevalence, to estimate the percentage who proceed through each step in contact management.

Methods: Twelve facilities were selected across the two provinces for the overarching TPT assessment with probability-proportional-to-size sampling. Volume of patients on antiretroviral therapy determined facility cluster size. At each facility, we systematically sampled records of approximately 30 patients diagnosed with tuberculosis disease during January 1-June 30, 2018. We estimated rates of HHCT and TPT uptake among child contacts. Estimates were weighted for survey design. To identify barriers to TPT, we interviewed one healthcare worker at each facility.

Results: We sampled 337 patients with tuberculosis disease. Of 289 patients with pulmonary disease, 65 un-

derwent HHCT (25%, 95% confidence interval [CI]: 19-33%). HHCT implementation was higher among patients with positive sputum-smear microscopy compared with smear-negative patients (71% vs 9%, p< 0.01). HHCT identified 24 child contacts (0.3 per household, 95% CI: 0.1-0.5). Although all were screened and none were diagnosed with tuberculosis disease, only two initiated TPT. Both completed the course. Ten healthcare workers were available for interview. Two reported no HHCT at their facilities and eight reported HHCT only for smear-positive patients; none reported HHCT for all patients with pulmonary tuberculosis. Four of five respondents reported hesitancy to start TPT due to insufficient stockpile of pediatric-friendly isoniazid formulation.

Conclusions: Few child contacts are identified for tuberculosis screening and TPT in Zambia. More work is needed to disseminate current HHCT guidelines. Isoniazid forecasting should include pediatric-friendly formulations.

SOA-04-1041-31 Four months of rifampin vs. nine months of isoniazid: a comparison of health system costs for LTBI treatment in Canada from a randomised clinical trial

M Lisboa Bastos,[1,2] JR Campbell,[2] O Oxlade,[2] K Schwartzman,[2] NP Nsengiyumva,[2] A Uppal,[2] D Menzies,[2] The 4v9 RCT Team [1]Social Medicine Institute - State University of Rio de Janeiro, Epidemiology, Rio de Janeiro, RJ, Brazil, [2]Research Institute of the McGill University Health Centre, International TB Centre, Montreal, QC, Canada.
e-mail: mayara_bastos@yahoo.com.br

Background: Recently, a phase 3 (NCT00931736) randomized clinical trial (RCT) demonstrated that four months of rifampin (4R) had non-inferior effectiveness, superior safety, and superior completion compared to nine months isoniazid (9H) for latent tuberculosis infection (LTBI). However, before the new regimen can be adopted into routine practice, it is important to understand how much it will cost the health system. Using a subset of data from four Canadian sites from the RCT, we compared health system costs of 4R vs 9H.

Methods: Costs were estimated based on clinical activities recorded for patients who participated in the trial. Costs were divided into the following categories: drugs, treatment initiation, follow-up visits, and adverse events (AE). All activities and drugs were adjusted to 2018 Canadian dollars ($) using costs from Québec, Canada. Provincial fees were used for personnel- and service-related costs. Median costs (per patient) by cost category were compared between the regimens using the Mann-Whitney U test.

Results: In the Canadian sites, 1042 patients were randomized (518 to 4R and 524 to 9H). Median total cost per patient receiving 4R was $884 (interquartile range [IQR] $785, $1024) vs. $1027 (IQR $754, $1184) for 9H (p< 0.0001). Although the drug cost for 4R was higher, this was more than offset by savings related primarily to shorter follow-up as patients receiving 9H had 1.5 (95% confidence interval: 1.2-1.7) more visits during treatment (**Table**).

	4R (N=518)	9H (N=524)	p-value
Cost for LTBI drugs	$228 ($222, $228)	$181 ($51, $181)	<0.0001
Costs for treatment initiation	$252 ($252, $495)	$252 ($252, $484)	0.33
Costs during all follow-up visits	$391 ($283, $416)	$506 ($286, $632)	<0.0001
Costs per follow-up visit	***$100 ($95, $108)***	***$99 ($94, $103)***	***0.20***
Costs related to adverse events	$151 ($109, $234)	$181 ($116, $300)	0.29
Total costs	$884 ($785, $1024)	$1027 ($754, $1184)	<0.0001

[Table - Median costs (IQR) per patient by cost category for LTBI care, in 2018 Canadian dollars]

Conclusions: In the Canadian sites the 4R regimen was found to be cost-saving compared to 9H. This finding contributes to the growing body of evidence highlighting the advantages of 4R for treatment of LTBI compared to 9H. Cost analysis at other trial sites in low- and middle-income countries will provide insight into similarities and differences between treatment settings.

SOA-04-1042-31 Symptom syndromes associated with treatment discontinuation of 12-dose isoniazid-rifapentine (3HP)

R Webb,[1,2] S-H Wang,[3] B Stewart,[4] N Nwana,[5] R Moro,[6] T Chorba,[5] S Bamrah Morris,[5] C Ho,[7] the ,3HP Post-Marketing Assessment Group [1]University of Mississippi, Division of Infectious Disease, Jackson, MS, United States of America, [2]Mississippi State Department of Health, Communicable Disease, Jackson, MS, United States of America, [3]The Ohio State University, Division of Infectious Diseases, Columbus, OH, United States of America, [4]Centers for Disease Control and Prevention (CDC), Global Immunization Division, Atlanta, GA, United States of America, [5]Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination, Atlanta, GA, United States of America, [6]Centers for Disease Control and Prevention (CDC), Division of Healthcare Quality Promotion, Atlanta, GA, United States of America, [7]Centers for Disease Control and Prevention (CDC), Division of HIV/Tuberculosis/CDC India, Atlanta, GA, United States of America. e-mail: rmwebb@umc.edu

Background: Patients on 12-dose isoniazid-rifapentine (3HP) for latent tuberculosis infection (LTBI) treatment have reported systemic symptoms including fever, myalgia, or rarely, hypotension/syncope. U.S. Centers for Disease Control and Prevention (CDC) conducted post-marketing surveillance for adverse events (AE) and treatment outcomes. We analyzed AE profiles to identify and characterize possible syndromes and effects on treatment outcome.

Methods: Prospective observational cohort of LTBI patients initiated 3HP June 2011-December 2014 at 16 sites. All sites collected weekly reports of AE; a subset

of ten sites collected information on patient medications/co-morbidities. AE profiles excluded pre-existing AE; definitions of syndromes [flu-like, gastro-intestinal, respiratory, dermatologic, hematologic, hypersensitivity] were derived from published literature. We identified AE profile, frequencies, and relative risk (RR) of discontinuation by syndrome; for all patients and by presence or absence (healthy) of medications/co-morbidities. Treatment discontinuations included patients lost to follow-up.

Results: 1,174/3,288 (36%) patients on 3HP reported AE. For the 2,389 with medication/co-morbidity information collected, 417/1,056 (39%) with medications/co-morbidities reported AE, compared to 365/1,333 (27%) healthy patients reporting AE. The incidence of dermatologic or hematologic syndromes were rare (< 1%), while incidence of flu-like, gastro-intestinal, and hypersensitivity syndromes was 6.6%, 3.6% and 1.8%, respectively. Frequent AE for flu-like syndrome in descending order were fatigue, fever/chills myalgia, nausea, and headache. Nausea was most common for gastro-intestinal syndrome; diarrhea and abdominal pain were reported equally. Most patients meeting the definition of hypersensitivity syndrome had fever/chills, nausea, myalgia, and fatigue. Presence of any syndrome increased RR of treatment discontinuation. While AE were fewer among healthy patients for any syndrome, when AE were present, the likelihood of treatment discontinuation was greater, compared to patients with medications/co-morbidities.

Conclusions: Flu-like and gastro-intestinal syndromes, though rare, were associated with treatment discontinuation. Healthy patients reported fewer AE, but if existent, had greater RR of treatment discontinuation compared with those with medications/co-morbidities reporting AE.

Frequency of three AE syndromes and association with treatment discontinuation

Group (N)	Flu-like[1]			Gastro-intestinal[2]			Hypersensitivity[3]		
	No. (%)	No. 3HP stopped	3HP discontinued RR (95% CI)	No. (%)	No. 3HP stopped	3HP discontinued RR (95% CI)	No. (%)	No. 3HP stopped	3HP discontinued RR (95% CI)
All patients (3,288)	217(6.6)	98	4.29 (3.59, 5.14)	117 (3.6)	51	3.74 (2.98, 4.69)	59 (1.8)	41	5.91 (4.87,7.17)
Med/co-morbidities (1,056)*	95(9)	47	3.83 (2.95, 4.98)	51 (4.8)	30	2.61 (1.80, 3.79)	30 (2.8)	23	5.31 (4.15, 6.81)
No meds or co-morbidity* (1,333)	71(5.3)	34	4.80 (3.58, 6.43)	46 (3.5)	21	4.23 (2.97, 6.01)	21 (1.6)	14	5.99 (4.27,8.41)

*The sum of these two groups = 2,389 patients, those with medication/co-morbidity data
[1]Flu-like syndrome defined as reporting ≥2 of the following AE: fever/chills, myalgia/arthralgia, headache, fatigue
[2]Gastro-intestinal syndrome defined as ≥2 of the following AE: abdominal pain, nausea/vomiting, diarrhea
[3]Hypersensitivity defined as either hypotension, urticaria, angioedema, acute bronchospasm, conjunctivitis or ≥4 of the following AE: weakness, fatigue, nausea/vomiting, headache, fever/chills, aches, sweats, dizziness, shortness of breath, or flushing

[Frequency of three AE syndromes and association with treatment discontinuation]

SOA-04-1043-31 Shorter treatment does not improve adherence: an open-label cluster-randomised trial on preventive therapy for children exposed to tuberculosis in Guinea-Bissau

G Lemvik,[1,2] VF Gomes,[1,3] C Wejse,[4,5] [1]Bandim Health Project, TB Unit, Bissau, Guinea-Bissau, [2]Aarhus University Hospital, Pediatrics, Aarhus N, Denmark, [3]National TB Programme, Technical Dept, Bissau, Guinea-Bissau, [4]Aarhus University, Public Health, Aarhus C, Denmark, [5]Aarhus University Hospital, Infectious Diseases, Aarhus N, Denmark. e-mail: wejse@dadlnet.dk

Background: In a study of 9 months of isoniazid preventive therapy (IPT) in Guinea-Bissau, 76% of children exposed to tuberculosis (TB) at home completed 6 months of IPT. We aimed to test whether 4 months of rifampicin and isoniazid (RH) would improve adherence compared with 9 months of isoniazid (INH).

Methods: We conducted an open-label cluster-randomised study, including children< 15 years of age living with a TB case. The children were randomised by house to 4 months of RH or 9 months of INH. RH was given in a fixed-combination pill. The primary outcome was adherence; defined as ≥80% of prescribed dosages taken/month. Our aim was a total of 3 months RH or 6 months INH. Adherence was measured by pill count, the dates and reasons for not taking dosages were noted.

Results: 752 children from 223 houses were included, 354 in the INH-group and 398 in the RH group.

Overall, 77% of the prescribed pills were taken, and 57 % of the children took ≥80% of the pills. Adherence was higher in the INH group; 73% completed 6 months in total while 63% of the RH group completed 3 months in total, OR=1.52 (95% CI 1.02-2.27).

Reasons for non-adherence were similar in the two groups; moving or travelling constituted 50% of the missing dosages.

Conclusions: The shorter preventive therapy with 4 months RH did not show improved adherence. Travelling is the major obstacle for adherence in the mobile population of Guinea-Bissau.

SOA-05-E1 Patient detection and care innovations

SOA-05-1044-31 Preliminary outcomes from optimised TB case finding among contact persons from key populations in Ukraine

E Geliukh,[1] L Masiuk,[1] N Kamenska,[1] Z Islam,[1] [1]ICF 'Alliance for Public Health', Treatment, Procurement and Supply Management, Kyiv, Ukraine.
e-mail: geliukh@aph.org.ua

Background and challenges to implementation: In 2017, TB notification in Ukraine was 27.3 thousand cases (63.9 per 100 thousand populations). Ukrainian healthcare system provides passive and active TB case detection including routine contacts tracing. TB detection among contacts in Ukraine was 8.6 per 1000 contacts. However, according to WHO, about 26% of TB cases are still missing. It is obvious that the majority of non-detected TB cases focuse among key populations, who have limited access to healthcare.
Intervention or response: To reach key populations APH launched the project "Optimized TB case finding among risk groups" (OSF model) in six regions of Ukraine with the financial support of Global Fund. The project aimed at examination of TB for contacts with index-cases from the key populations. Every index-case patient is encouraged to bring up to eight contacts from his/her surroundings, which are examined for TB. If someone fro this group is diagnosed with an active TB he/she is enrolled on treatment and invited to bring his/her contacts also. Those contacts who aren´t diagnosed with an active TB are observed during the yera by providing regular TB screening, preventive treatment and psychosocial support. Result-based financing approach is applied for social workers´ stimulation.
Results and lessons learnt: Within the 8-months period (August 2018 - March 2019), 295 index-cases were enrolled in the project that brings 2207 of their contacts. 99 active TB cases were diagnosedand of which 98 were enrolled on treatment. 2108 contacts were observed throughout the period and 60 were provided with preventive treatment. TB detection among contacts within the project is 44.9 per 1000 contacts.

	Examined contacts	Active TB diagnosed	Enrolled on treatment	Number of contacts observed	Preventive treatment provided
PWID	763	24	23	739	12
Homeless people	436	28	28	408	6
Roma population	240	1	1	239	21
Ex-prisoners	30	3	3	27	0
Internally displaced persons	1	1	1	0	0
Others	737	42	42	695	21
Total	2207	99	98	2108	60

[OCF model preliminary results]

Conclusions and key recommendations: Despite the short duration of project implementation the intervention has shown promising results - TB detection rate among contacts from key populations have increased 5 times higher than in routine contacts tracing. Increased funding and advocacy actions are required to scale-up OSF model in all regions of Ukraine.

SOA-05-1045-31 High yield of tuberculosis from systematic screening among active intravenous drug users in Hai Phong, Viet Nam

LP Nguyen,[1] TTT Dong,[1] GT Hoang,[2] TTT Nham,[3] OTH Khuat,[4] HTT Duong,[2] N Nagot,[5] DC Des Jarlais,[6] HV Le,[7] D Laureillard,[8] [1]Friends for International TB Relief, Operations, Hanoi, Viet Nam, [2]Hai Phong University of Medicine and Phamarcy, Public Health Department, Hai Phong, Viet Nam, [3]Center for Supporting Community Development Initiatives, Community Development, Hai Phong, Viet Nam, [4]Center for Supporting Community Development Initiatives, Board of Directors, Hanoi, Viet Nam, [5]University of Montpellier, Public Health Department, Montpellier, France, [6]Don.DesJarlais@nyu.edu, Social and Behavioral Sciences, New York, NY, United States of America, [7]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [8]Agence Nationale de Recherche sur le Sida et les Hépatites Virales, Public Health Department, Hanoi, Viet Nam.
e-mail: lan.nguyen@tbhelp.org

Background and challenges to implementation: While there is evidence that previous diagnosis of tuberculosis (TB) is associated with increased mortality among injecting drug users in Viet Nam, the understanding of TB epidemiology in this population remains limited. Screening, testing and linkage to care for TB in drug users remain a challenge due to high costs and stigma.
Intervention or response: As part of the TB REACH-funded Zero TB Viet Nam project, participants of the DRIVE study (DRug Use and Infections in Hai Phong Viet Nam Among Persons Who Inject Drugs) were verbally screened for TB symptoms by community-based organization (CBO) staff between March-May 2018. CBO staff transported symptomatic participants to a public TB care facility for chest X-ray (CXR) screening. Persons with radiographic abnormalities were tested using the Xpert MTB/RIF assay. Persons diagnosed with TB linked to care. Two rounds of follow-up were conducted for persons lost throughout the TB care pathway. All tests and related costs were free of charge. Participants received modest payments for their time, effort and travel, and were accompanied and supported by CBO staff.
Results and lessons learnt: Among 888 participants who were screened, 430 (48.4%) presented with one or more TB symptoms. Among these, 90 (20.9%) had an abnormal CXR and 67 (74.4%) were tested using the Xpert MTB/RIF assay. 15 (22.4%) participants were diag-

nosed with bacteriologically-confirmed pulmonary TB (1,689/100,000) and two patients were found to be resistant to rifampicin. Among these patients, 14 (93.3%) were linked to treatment with the Hai Phong Provincial TB Programme.

Conclusions and key recommendations: The rate of TB in our study population was six times higher than Viet Nam's estimated TB prevalence rate (289/100,000 population). Social and economic support, provided in collaboration with CBO staff, was critical for ensuring high levels of testing and treatment enrollment. While administering services among drug users presents unique challenges for TB programs, this population should not be overlooked.

SOA-05-1046-31 Customised TB case finding among key affected populations: a case of farm workers in Sarah Baartman District, Eastern Cape Province, South Africa

L Lebona,[1] L Mayaphi,[1] B Dlamini,[1] M Khaebana,[1] G Jagwer,[1] R Matji,[2] C Ndlumbini,[3] [1]University Research Co., LLC - South Africa, USAID Tuberculosis South Africa Project, Pretoria, South Africa, [2]University Research Co., LLC (URC), Research Co., LLC, Pretoria, South Africa, [3]Eastern Cape Department of Health, Health, Humansdorp, South Africa. e-mail: lerato.lebona28@gmail.com

Background and challenges to implementation: Farm workers, especially seasonal workers, are at greater risk of tuberculosis (TB) infection and disease, with likely worse outcomes because of barriers in access to routine and continued healthcare services.

Contributing factors include poor living conditions as many migrant workers live in crowded, sub-standard and poorly ventilated houses where conditions favour the spread of respiratory infections; fear of loss of income due to long waiting periods at clinics; and lack of transportation.

These and other issues make it difficult for this vulnerable population to access services. USAID Tuberculosis South Africa Project developed and implemented a care model to improve farm workers' access to TB services.

Intervention or response: The objective of the intervention was to improve access to TB health services while ensuring patient-centered care. A customized model of care was developed to address barriers to accessing quality TB health services.

Enrolled nurses were contracted to provide daily health education, TB screening, sputum collection, and ensure treatment initiation of people living with TB on supported farms in Sarah Baartman district, Eastern Cape province. Buy-in from farm owners and managers enhanced the success of the model of care.

Results and lessons learnt: Since inception of the model of care in April 2017 until December 2018, 21,440 farm workers were reached, 92% (19,734) of whom were screened for TB. 94% (3,550) of people presumptive for TB were tested, 7% of whom (266) were diagnosed with TB. Of these, 91% (243) were initiated on appropriate treatment.

Conclusions and key recommendations: Targeted intervention models with active participation from all stakeholders enhance accessibility to adequate TB diagnosis and treatment among undeserved populations and communities. The model increased case identification and is a viable approach to find missing TB patients, to contribute to 90-90-90 targets, and to contribute towards the South Africa's efforts to end TB by 2035.

SOA-05-1047-31 Door-to-door TB screening to reach urban slum dwellers: lessons from field implementation

A Kazibwe,[1,2] D Lukanga,[1,2] H Ssentongo,[1,2] L Ruvwa,[3] S Turyahabwe,[3] A Nkolo,[1] [1]University Research Co., LLC (URC), USAID/Defeat TB, Kampala, Uganda, [2]The AIDS Support Organisation (U) Ltd, DPMCD, Kampala, Uganda, [3]Ministry of Health, National TB & Leprosy Division, Kampala, Uganda. e-mail: dlukanga@urc-chs.com

Background and challenges to implementation: In 2014, the World Bank estimated that slightly over 50% of Uganda's urban dwellers live in slums. Slum populations pose a significant challenge to TB control efforts due to poor housing conditions, congestion and limited access to formal health care services. Slum dwellers are also highly mobile constraining effective patient tracking. Slum populations are categorized as key populations in the Global Plan to End TB and failure to reach them with TB services is a missed opportunity.

Intervention or response: The USAID Defeat TB project supports direct service delivery in the largely urban areas of Kampala, Wakiso and Mukono. Between September-November 2018, Community Linkage Facilitators (CLFs) trained in TB screening engaged informal leadership structures within slum settlements; carried out door-to-door sensitization and screening for TB using the Intensive case finding guide. They documented phone contact and locator information for community members found with symptoms suggestive of TB, collected and transported sputum samples for testing to health facilities. They followed up and notified clients of investigation results and supported referral for treatment of those with confirmed TB.

Results and lessons learnt: Of 2,770 slum dwellers screened for TB, 318 were presumed to have active TB and seventy-three (2.6% yield) were diagnosed with TB (all forms). This yield was higher than that seen in community screening outreaches in male congregate settings and schools.All diagnosed patients were referred for and initiated on TB treatment. Informal community leadership structures were critical in community entry and facilitated patient linkage. Documentation of patient locator information and phone contacts at sputum sample collection was paramount.

Conclusions and key recommendations: The door-to-door approach addresses population level barriers to access of TB services by slum populations and leads to identification of additional TB patients. It can be scaled up for similar settings.

SOA-05-1048-31 Differences in tuberculosis detection yields by sex from mobile X-ray screening campaigns in Viet Nam

AJ Codlin,[1] TTT Dong,[2] RJ Forse,[3] LH Nguyen,[4] TH Mac,[5] PN Tran,[6] HB Nguyen,[7] HV Le,[7] NV Nguyen,[7] LNQ Vo,[8,9] [1]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Operations, Hanoi, Viet Nam, [3]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [4]Pham Ngoc Thach Lung Hospital, Provincial TB Program, Ho Chi Minh City, Viet Nam, [5]Hai Phong TB and Lung Hospital, Provincial TB Program, Hai Phong, Viet Nam, [6]Pham Ngoc Thach Hospital Quang Nam, Provincial TB Program, Tam Ky, Viet Nam, [7]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [8]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [9]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam. e-mail: andrew.codlin@tbhelp.org

Background and challenges to implementation: With a male:female ratio of 4.2-to-1 in tuberculosis (TB) burden, Viet Nam's sex disparity ranks among the highest in the world. While community outreach has been documented to be gender-sensitive, it is unclear whether community-based mass screening can promote health-seeking among women and girls.

Intervention or response: In 2018 we organized community-based, mobile chest x-ray (CXR) screening events at 180 locations in Ho Chi Minh City, Hai Phong and Hoi An as part of the TB REACH-funded Zero TB Viet Nam project. At the events, participants were screened for TB symptoms and by CXR. Persons with radiographic abnormalities were tested using the Xpert assay. We quantified the proportion of patients progressing through the TB care pathway and calculated odds ratios to measure sex differences.

Results and lessons learnt: In total, 32,804 people underwent a symptom screen. We screened 35.5% more women than men (18,875 vs 13,929), with the Hai Phong showing largest difference in mobilization (53.4% more women). Despite higher participation from women, significantly higher proportions of men had an abnormal CXR (19.3% vs 9.6%, OR=2.26 [21.-2.4]), were tested after an abnormal CXR (70.2% vs 52.7%, OR=2.12 [1.9-2.4]), and were diagnosed with Bac(+) TB (9.6% vs 4.7%, OR=2.13 [1.5-3.0]). A higher proportion of women were linked to treatment than men (84.4% vs 79.0%), but this difference was not significant.

Conclusions and key recommendations: While our CXR events were able to mobilize a greater proportion of women to seek health, the sex differences observed in CXR abnormality and Xpert positivity rates mirrored Viet Nam's prevalence survey results. Such differences are possibly due to the biological characteristics of TB, but this cannot explain the large sex difference in the sputum testing rate.

Future case finding initiatives should consider gender-responsive counselling on sputum production, the privacy of collection sites and expectoration aids to improve the proportion of females who are tested.

	Total	Females	Males	OR (95% CI)
All Three Cities				
Screened by CXR	32,804	18,875	13,929	N/A
CXR abnormal	4,491 (13.7%)	1,803 (9.6%)	2,688 (19.3%)	**2.26 (2.1-2.4)**
Tested by Xpert and/or AFB*	2,838 (63.2%)	950 (52.7%)	1,888 (70.2%)	**2.12 (1.9-2.4)**
Diagnosed with Bac(+) TB	226 (8.0%)	45 (4.7%)	181 (9.6%)	**2.13 (1.5-3.0)**
Bac(+) TB started on treatment	181 (80.1%)	38 (84.4%)	143 (79.0%)	0.69 (0.3-1.7)
Ho Chi Minh City				
Screened by CXR	18,140	10,054	8,086	N/A
CXR abnormal	2,904 (16.0%)	1,170 (11.6%)	1,734 (21.4%)	**2.07 (1.9-2.2)**
Tested by Xpert and/or AFB*	1,718 (59.2%)	551 (47.1%)	1,167 (67.3%)	**2.31 (2.0-2.7)**
Diagnosed with Bac(+) TB	149 (8.7%)	25 (4.5%)	124 (10.6%)	**2.5 (1.6-3.9)**
Bac(+) TB started on treatment	121 (81.2%)	21 (84%)	100 (80.6%)	0.79 (0.2-2.5)
Hai Phong				
Screened by CXR	13,747	8,322	5,425	N/A
CXR abnormal	1,453 (10.6%)	585 (7.0%)	868 (16.0%)	**2.52 (2.3-2.8)**
Tested by Xpert and/or AFB*	1,059 (72.9%)	380 (65.0%)	679 (78.2%)	**1.94 (1.5-2.4)**
Diagnosed with Bac(+) TB	71 (6.7%)	19 (5.0%)	52 (7.7%)	1.58 (0.9-2.7)
Bac(+) TB started on treatment	54 (76.1%)	16 (84.2%)	38 (73.1%)	0.51 (0.1-2.0)
Hoi An				
Screened by CXR	917	499	418	N/A
CXR abnormal	134 (14.6%)	48 (9.6%)	86 (20.6%)	**2.43 (1.7-3.6)**
Tested by Xpert and/or AFB*	61 (45.5%)	19 (39.6%)	42 (48.8%)	1.46 (0.7-3.0)
Diagnosed with Bac(+) TB	6 (9.8%)	1 (5.3%)	5 (11.9%)	2.43 (0.3-22.4)
Bac(+) TB started on treatment	6 (100%)	1 (100.0%)	5 (100.0%)	-

* AFB testing occasionally occurred when there were Xpert cartridge shortages and/or challenges with laboratory capacity.

[Breakdown of TB care pathway by city and sex]

SOA-05-1049-31 Characteristics and care pathways of private drug-resistant TB patients in South Africa: a descriptive cohort study

L Dickson-Hall,[1] H Cox,[1] A Grant,[2] J Black,[3] M Loveday,[4] M Moshabela,[5] M Nicol,[6] [1]University of Cape Town, Medical Microbiology, Cape Town, South Africa, [2]London School of Hygiene & Tropical Medicine, Public Health, London, United Kingdom, [3]Livingstone Hospital, Microbiology, Nelson Mandela Bay, South Africa, [4]Medical Research Council of South Africa, Public Health, Durban, South Africa, [5]University of Kwazulu Natal, Public Health & Nursing, Durban, South Africa, [6]University of Cape Town, Microbiology, Cape Town, South Africa. e-mail: moshabela@ukzn.ac.za

Background: In 2016, 24% of South Africans considered their 'normal place of health care' to be in the private sector. Private patients are 'key' as they are a large group and are at risk for non-linkage to care, inadequate DR-TB regimens, incomplete drug sensitivity testing and co-payment expenses. Many patients use both public and private sectors, depending on their needs. Private patients may belong to vulnerable sub-groups such as miners, health care workers, children and the elderly.

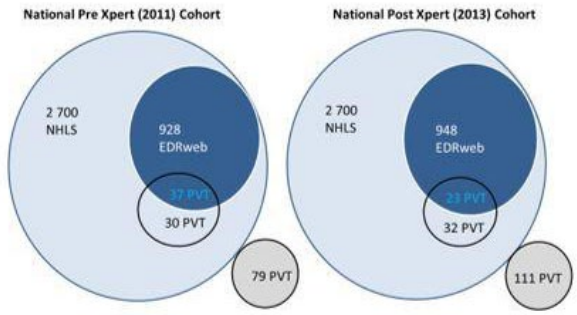
South Africa is number 9 of the 15 priority countries for engaging all providers urgently, in order to reduce 'missing' DR-TB patients.

Methods: A retrospective observational cohort study was conducted across South Africa. The National Health Laboratory Services (NHLS) data warehouse was inter-

rogated to find newly diagnosed RR-TB patients in 2011 and 2013. Patients were matched and linked to the Electronic DS-TB and DR-TB databases and private laboratory data sets. Data from private patients diagnosed during the same period were analysed separately. Patients were followed through time and space to describe linkage to care, time to treatment, pathways to care, distances traveled and patient outcomes. Laboratory and health data were analysed using SPSS Statistics, version 24.

Results: Around 6% of South Africa's new RR-TB patients in 2013 were diagnosed in the private sector. Of those patients diagnosed privately in 2011, 25% (n=37) were notified to the health department and 21% (n=30) received additional DR-TB management in the state sector. In 2013, despite an overall private DR-TB case increase of 19% over 2 years, 14% (n=23) were notified and 19% (n=32) were co-managed.

Conclusions: The contribution towards the fight against DR-TB by the private sector and by private public partnerships should receive focus and support, in order to harness all providers to combat the pandemic.



[The involvement of the private sector to the public DR-TB cohort & EDRWeb registry in 2011/13.]

SOA-05-1050-31 Armed conflict and tuberculosis mortality in Colombia, 1998-2015

S Valencia-Aguirre,[1] C Castañeda-Orjuela,[1] D Diaz-Jimenez,[1] J Gutierrez-Clavijo,[1] KP Cotes Cantillo,[1] [1]Instituto Nacional de Salud, Observatorio Nacional de Salud, Bogotá, Colombia.
e-mail: salomevalenciaaguirre@gmail.com

Background: Colombia has suffered an armed conflict that lasted more than 50 years. It caused several impacts on physical and mental health. Prevalence of TB increased among displaced populations of several countries with history of armed conflict. The objective of this study is to classify the small areas of Colombia according to the intensity of armed conflict and identify the differences in TB mortality between populations that resided in areas with greater intensity versus those less affected by this phenomenon, in Colombia between 1998-2015.

Methods: Retrospective ecological analysis. Through an expert consensus we defined a conceptual framework with two dimensions of analysis: types of violence and financial sources. We implemented the Pearson Correlation and the Kaiser-Meyer-Olkin test to select the variables. We generated the Index of Conflict Intensity (ICI) through the principal component analysis (Varimax). We calculated the Age-Standardized Mortality Rates (ASMR) by sex for three periods (1998-2003, 2004-2009 and 2010-2015), by quintile of ICI. To identify the differences between extreme quintiles we estimated the Rate Ratios (RR).

Results: The ICI included ten variables: homicides, kidnappings, forced disappearance, massacres, minor's recruitment, damage to noncombatant civilian populations goods, sexual violence, victims of mines, military actions and displacement. The first component explained 67% of the variability. The geographical representation of the index by quintiles of intensity showed an unequal distribution of affectation, and the grouping of the most affected small areas into four conglomerates. TB mortality according to the ICI showed no differences between the quintiles among men (RR, 1998-2003= 1.2, 2004-2009 = 1.1, 2010-2015= 1.0). While, women showed higher mortality with the increased of mortality (RR, 1998-2003 = 1.8, 2004-2009 = 1.5, 2010-2015 = 1.6).

Conclusions: There is an unequal impact of the conflict at a small area level. Women living at the most affected areas showed higher TB mortality.

SOA-05-1051-31 Improving tuberculosis management in vulnerable populations: a case study of the National Referral Mental Health Hospital in Uganda

A Burua,[1] S Nakibuuka,[1] T Nsubuga Nyombi,[1] R Mugabe,[2,3] K Mutesasira,[1] A Nkolo,[1] S Turyahabwe,[4] [1]University Research Co., LLC (URC), Defeat TB Project, Kampala, Uganda, [2]Makerere University College of Health Sciences, Infectious Diseases Institute, Kampala, Uganda, [3]University Research Co. LLC, Defeat TB Project, Kampala, Uganda, [4]Ministry of Health, National Tuberculosis and Leprosy Control Program, Kampala, Uganda.
e-mail: aburua@urc-chs.com

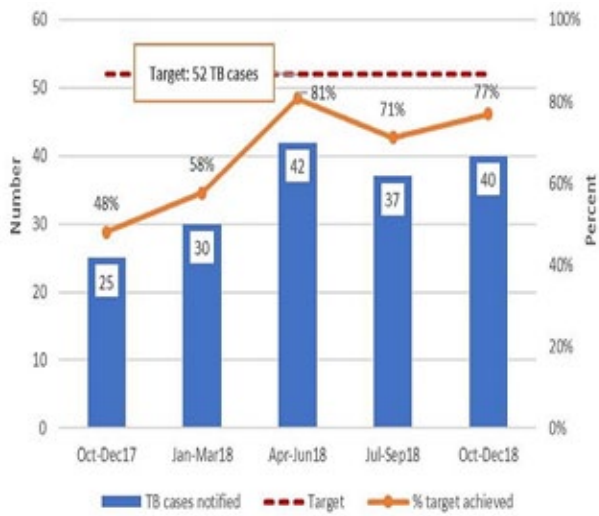
Background and challenges to implementation: Institutionalized mental patients are vulnerable to tuberculosis due to lack of self-awareness of the risk of TB and inadequate TB infection control practices. Management of TB is further complicated by poor adherence on treatment and loss to follow up. Butabika National Referral Mental Health Hospital notified 128 TB patients in 2017/18, which is 60% of the annual facility target of 208.

Intervention or response: USAID Defeat TB worked with the Quality Improvement team at Butabika Hospital to address gaps in TB management in mentally ill patients. A January 2018 hospital assessment showed gaps

in TB screening, inadequate utilization of TB screening tools and insufficient TB infection control. The facility team was oriented on TB screening and infection control, placed screening tools at various care points and enhanced health providers' screening skills through coaching. Clinicians received individualized competence building sessions on use of TB diagnostic algorithms to guide clinical decision making. To improve treatment outcomes, appointment systems were established, and documentation of TB patient information streamlined through centralizing discharge of TB patients in the outpatient clinic.

Results and lessons learnt: TB patients notified increased from 25 per quarter (Oct-Dec 2017) to 40 per quarter (Oct-Dec 2018); an increase of 30% of the quarterly facility target (figure 1). Treatment success rate improved from 55% to 75% for cohort of TB patients on treatment in Jan-Mar 2017 and Oct-Dec 2017 respectively. The lost to follow up however remained high (14%), impacting negatively on the treatment outcomes.

Conclusions and key recommendations: Enhancing health provider screening and diagnostic skills and using Quality Improvement to address gaps in clinic processes improves TB case identification and management. We recommend concerted efforts to increase TB awareness and management in mental institutions given the complexities of managing TB in these populations.



[Trends of TB case notification in Butabika National Referral Hospital for Mental Health]

SOA-05-1052-31 Healthcare provider behavioural, social and cultural issues contexts: how do DR-TB healthcare champions in South Africa influence programme implementation?

S Le Roux,[1] W Jassat,[2] L Dickson-Hall,[3] H Cox,[3] L Mitrani,[3] M Loveday,[4] A Grant,[5] J Black,[6] M Nicol,[3] M Moshabela,[7] [1]Unversity of Cape Town, Microbiology, Cape Town, South Africa, [2]University of the Western Cape, Public Health, Gauteng, South Africa, [3]University of Cape Town, Microbiology, Cape Town, South Africa, [4]Medical Research Council of South Africa, Drug Resistant Tuberculosis, Durban, South Africa, [5]London School of Hygiene & Tropical Medicine, Public Health, London, United Kingdom, [6]Livingstone Hospital, Microbiology, Nelson Mandela Bay, South Africa, [7]University of KwaZulu-Natal, Public Health & Nursing, Durban, South Africa.
e-mail: lindy.dickson-hall@uct.ac.za

Background: Literature has shown that champions positively influence the implementation of healthcare programs, however, the role of DR-TB champions in the South African context has yet to be examined. This study assesses the enablers and barriers of work undertaken by DR-TB champions and clarifies their level of influence within the healthcare system.

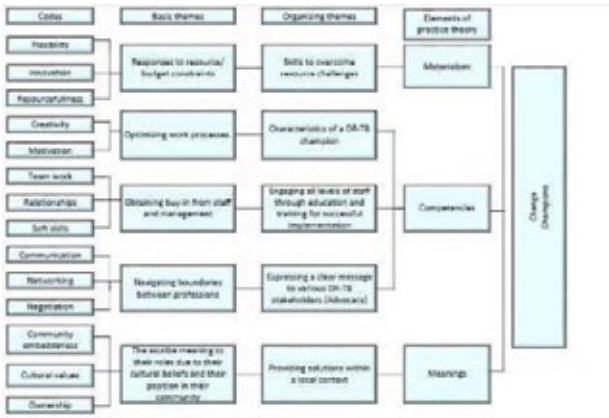
Methods: Interviews were collected in three stages across three provinces in South Africa. Initially, 31 interviews were conducted with key DR-TB stakeholders. Subsequently, 62 manager and clinician interviews were conducted to understand the implementation of DR-TB decentralization.

Finally, 7 interviews were conducted with staff involved in the local DR-TB programs at three decentralized DR-TB sites. A thematic analysis (Attride-Stirling, 2001) was utilized and a coding framework was created using QSR International's NVivo 12 software.

Results: Three types of ′champions′ were identified, based on their level of influence within the DR-TB program, namely 'change champions', 'fallen champions' and 'non-champions'. Their longevity and success within the healthcare system was explained by three elements defined in practice theories: materials, competencies and meanings (Shove et al, 2012). The dynamic interaction between materials (budget flexibility for the acquisition for additional staff and vital equipment), competencies (institutional knowledge, networking, negotiating, relationship building) and meanings (community embeddedness, moral obligation) altered the extent to which ′champions′ influenced the healthcare system. This dynamic interaction enabled or hindered the ′champion's′ creativity, which in turn affected their work quality and process.

Conclusions: 'Champions' flourish or struggle in response to DR-TB policy changes and may be creatively disruptive in driving change. By examining the elements of practice theory, differences were highlighted regarding the ′champion's′ level of influence in the implementation of a DR-TB program. Insights were provided as

to the barriers experienced by DR-TB ′champions′ and how they can be supported to optimize their efforts to improve the DR-TB program.



[Thematic framework illustrating the behavioral, social and cultural issues of DR-TB champions in SA.]

SOA-05-1053-31 Support: the miracle remedy against tuberculosis

M Biremon,[1] G Sydykova,[2] B Myrzaliev,[3] G Aytmurzaeva,[4] T Murzabekova,[3] A Djetigenova,[5] D Egemberdieva,[5] N Toktorboreva,[5] A Torobekova,[5] B Tilek Kyzy,[5] [1]KNCV Branch Office in the Kyrgyz Republic, Communication, Bishkek, Kyrgyz Republic, [2]KNCV Branch Office in the Kyrgyz Republic, Monitoring, Bishkek, Kyrgyz Republic, [3]KNCV Branch Office in the Kyrgyz Republic, Management, Bishkek, Kyrgyz Republic, [4]Republican Center for Health Promotion, Management, Bishkek, Kyrgyz Republic, [5]KNCV Branch Office in the Kyrgyz Republic, Case Management, Bishkek, Kyrgyz Republic. e-mail: gunta.dravniece@kncvtbc.org

Background and challenges to implementation: The Kyrgyz Republic is faced with a high burden of drug-resistant tuberculosis (DR-TB), worsened with the stark figure of one in four DR-TB patients lost-to-follow-up. Although the country adopted the newest WHO-recommended regimens and drugs, adherence remains an obstacle.

Intervention or response: In parallel to the case-management model introduced by USAID-funded Challenge TB, in January 2019 KNCV conducted a cross-sectional survey among patients on new DR-TB treatment regimens. Out of 700 patients enrolled, 170 were randomly selected for the survey; 163 participated in face-to-face interviews which included questions on challenges, stigma and coping strategies. Participation was voluntary, and informed consent was obtained from all respondents.

Results and lessons learnt: After side-effects (71% of respondents), the four most reported difficulties in treatment were related to social support: psychological challenges (44%), fear of stigma (33%), isolation from family (28%), and loneliness (26%). 80% of patients stated that family support was the most helpful factor in treatment. Patients were also asked if they agreed or disagreed with statements on stigma and discrimination, i.e. "Some people keep their distance from people with TB" (76% agreed), "Some people may not want to eat or drink with friends who have TB" (67% agreed) or "Some people are afraid of those with TB" (86% agreed). This demonstrates a very high level of perception of stigma among patients, which may cause isolation, depression, self-stigma and shaming.

Conclusions and key recommendations: Treatment for M/XDR-TB is long, compelling and painful. Making all possible efforts to ease treatment is necessary to ensure increased completion and success rates. The survey showed that non-medical factors - support of relatives and community - significantly matter to patients and can lift some of the burdens. Therefore, governments and programs should invest in increasing TB awareness, community engagement, empathy and understand that this battle against stigma is decisive in ending TB.

SOA-05-1054-31 Risk factors associated with unsuccessful outcome of tuberculosis (TB) treatment in a prison in Ecuador

F Chong,[1] F Perez,[2] D Marin,[3] [1]Ministerio de Salud Pública del Ecuador, Prevention and Control Strategies, Distrito de Salud 09D02, Guayaquil, Ecuador, [2]Panamerican Health Organization, Conmunicable Disease and Enviromental Determinants of Health Department, Washington, DC, United States of America, [3]Universidad Pontificia Bolivariana, School of Medicine, Medellin, Colombia. e-mail: felixchong@hotmail.com

Background: Ineffective compliance with national TB-control program goals and high percentage of unsuccessful treatment contributes to the perpetuation of TB transmission in Ecuadorean prisons. **Aim:** To estimate the incidence of unsuccessful TB treatment in a national prison and identify associated risk factors.

Methods: We analysed national surveillance data from the largest prison in Ecuador, located in the Guayas province, of a cohort of inmates diagnosed with TB between 2015 and 2016.Records without discharge status were excluded. The percentage of respiratory symptoms (RS), the TB incidence rate and the incidence of unfavorable condition at discharge were estimated. Factors associated with unsuccessful treatment were estimated with log-binomial regression.

Results: From a total of 59,846 medical consultations, 3% were identified with RS, of which 326 inmates had TB and 184 had TB at discharge. The TB incidence rate in the prison was 1,973 / 100,000 inhabitants while that of Ecuador was 31.9 and that of the province of Guayas 80.4. 80.4% of the inmates lacked susceptibility tests. The percentage of successful treatment was 70.7% (66.3% cured and 4.4% treatment completed) and 29.4% of unsuccessful outcome (12.5% loss to follow-up, 5.4% died, 1.1% treatment failed and 10.3% not

evaluated). HIV (RR:2.04 95%CI: 1.1 - 3.8) was associated with higher risk of unsuccessful outcome. Older age (RR:2.0 95%CI: 0.8 - 4.9), Pulmonary TB (RR:1.4 95%CI: 0.4 - 5.0) and a missing admission status (RR: 1.8 95% CI: 0.8 - 4.3) was positively associated with unsuccessful TB treatment outcomes.
Conclusions: The incidence of TB in the Guayas prison was higher than in the general population and the 90% treatment goal, established by WHO, was not met. The End TB-strategy program is currently not effectively applied at correctional facilities throughout Ecuador.

SOA-06-D2 Defining the TB epidemic in children to inform action

SOA-06-1055-31 Progressive burden of HIV-associated TB in children and adolescents during an era of increased ART use: data from six sub-Saharan African countries

A Kay,[1,2,3] J Bacha,[1,4,5] R Golin,[6] A DiNardo,[1,2] T Devezin,[1,2] D Dhillon,[1,2] S Ahmedov,[6] N Fida,[7] M Matshaba,[8] AM Mandalakas,[1,2] [1]Baylor College of Medicine, Pediatrics, Houston, TX, United States of America, [2]The Global Tuberculosis Program, Pediatrics, Houston, TX, United States of America, [3]Baylor Swaziland TB Center of Excellence, Pediatrics, Mbabane, Eswatini, [4]Baylor College of Medicine Children's Foundation, Pediatrics, Mbeya, Tanzania, United Rep., [5]The International Pediatric AIDS Initiative (BIPAI) at Texas Children's Hospital, Pediatrics, Houston, TX, United States of America, [6]United States Agency for International Development, Pediatric and Maternal Clinical Branch, Washington, DC, United States of America, [7]United States Agency for International Development, HIV/AIDS, Pretoria, South Africa, [8]Baylor College of Medicine Children´s Foundation-Botswana, Pediatrics, Gaborone, Botswana.
e-mail: alexander.kay@bcm.edu

Background: Tuberculosis (TB) is the leading cause of mortality in people living with HIV. Children and adolescents living with HIV (C/ALHIV) are up to 24 times more likely to develop TB compared to HIV-negative peers. Anti-retroviral therapy (ART) reduces risk of acquiring TB among adults, however limited data describes its protective effect in C/ALHIV.
There have been substantial gains in providing ART to people living with HIV (PLHIV); as of 2016, WHO recommends ART for all PLHIV, irrespective of age, immune status, or disease classification. This multi-site study describes the period prevalence of TB in C/ALHIV in relation to ART scale-up.
Methods: Patient data from 2013 to 2017 was analyzed from the electronic medical records at seven Baylor International Pediatric AIDS Initiative (BIPAI) Centres of Excellences (COEs): Botswana, Eswatini, Lesotho, Tanzania-Mbeya, Tanzania-Mwanza, and Uganda. Data was analyzed on C/ALHIV diagnosed with active TB disease (ages 0 - 18.99 years in Tanzania; ages 0 - 19.99 years at remaining sites). All sites used a standardized TB case definition, TB outcomes aligned with WHO guidelines, and ART in accordance with national guidelines at the time of ART initiation.
Results: Data was available on 1,217 C/ALHIV with HIV-associated TB, which encompassed 57,525 patient-years of follow-up. The average burden of disease was 2,017 TB cases/100,000 patient years. TB incidence varied across the clinic populations (range: 454 to 4,385 cases/100,000 patient years). For the majority of sites, as ART usage steadily increased, TB prevalence declined. COEs with lower prevalence of HIV-associated TB experienced less dramatic annual declines.
Conclusions: ART use is strongly associated with decreased TB prevalence among C/ALHIV yet the potential impact of this intervention may decline below a certain TB prevalence threshold. As ART continues to be scaled up throughout sub-Saharan Africa, innovative interventions will be needed to achieve TB elimination.

SOA-06-1056-31 High prevalence of tuberculosis infection in children living in households of MDR-TB patients

S Kim,[1] X Wu,[2] M Hughes,[2] A Mendoza-Ticona,[3] A Omoz-Oarhe,[4] G Churchyard,[5] S Swindells,[6] NS Shah,[7] A Gupta,[8] A Hesseling,[9] ACTG/IMPAACT A5 300/I 2003 PHOENIx Feasibility Study Team [1]Frontier Science Foundation, Biostatistics, Brookline, MA, United States of America, [2]Harvard School of Public Health, Biostatistics, Boston, MA, United States of America, [3]AC Impacta, San Miguel CRS, San Miguel, Peru, [4]Botswana Harvard AIDS Institute Partnership, Gaborone CRS, Gaborone, Botswana, [5]Aurum Institute, Head Office, Parktown, South Africa, [6]University of Nebraska Medical Center, Internal Medicine, Omaha, NE, United States of America, [7]Centers for Disease Control and Prevention (CDC), Global HIV & TB, Atlanta, GA, United States of America, [8]Johns Hopkins Bloomberg School of Public Health, Medicine, Baltimore, MD, United States of America, [9]Stellenbosch University, Desmond Tuttu TB Center, Stellenbosch, South Africa.
e-mail: skim@sdac.harvard.edu

Background: Few multinational, multisite studies have evaluated TB infection (TBI) status in child MDR-TB household contacts (HHCs).
Methods: From 10/2015-4/2016, the ACTG and IMPAACT networks conducted A5300/I2003, a cross-sectional feasibility study of MDR-TB patients and their HHCs, in high TB-burden countries in preparation for a randomized clinical trial. Among HHCs < 15 years of age without prevalent TB, we estimated TBI prevalence based on interferon gamma release assay (IGRA) (QuantiFERON Gold/Gold-in-Tube) status. Index case (IC), household, child and TB exposure characteristics

were evaluated for association with TBI. We combined collinear variables into composite measures then fit multivariable logistic regression models using generalized estimating equations.

Results: 304 children were enrolled at 14 sites across 6 countries. 283 (93%) had IGRA results, including 4 (1.4%) indeterminate. Of those with definite results, 160 (57% [95% confidence interval (CI): 50-64%]) had TBI, which increased with age: 50% [95%CI: 38%-61%], 58% [95%CI: 48%-68%], and 64% [95%CI: 52-74%] in ages < 5, 5 to < 10, and 10 to < 15 years, respectively. Multivariable models showed heterogeneity of TBI prevalence in HHCs. School-aged children (≥5 years) currently or ever in school were more likely to have TBI than children< 5 years or school-aged children without schooling. By IC-HHC relationship/sleeping arrangement, TBI increased from lowest to highest when the IC was not a parent and slept in a different room, was the parent or shared a room but not both, was a parent and shared a bedroom. HHCs had higher TBI prevalence if the IC reported current smoking. TBI prevalence varied by site/country but was not statistically significant.

Variable		Number IGRA+/ IGRA tested 160/279	Odds Ratio (95% Confidence Interval)	P
Index case smoking status	Current	41/58	2.3 (1.02, 5.0)	0.034
	Previous/never	119/221	1.0 reference	
HHC Age, Current or ever in school	Age <5 years	43/88	1.0 reference	0.013
	Age 5-<15, never in school	6/14	0.9 (0.3, 2.6)	
	Age 5-<15, currently or ever in school	111/177	2.4 (1.4, 4.2)	
IC-HHC Relationship, sleeping arrangement	Mother/father, same room	41/59	5.1 (2.4, 10.8)	0.002
	Mother/father, different room	20/32	2.4 (1.1, 5.6)	
	Other relationship, same room	35/57	2.6 (1.1, 5.7)	
	Other relationship, different room	64/131	1.0 reference	

[Multivariable logistic regression model adjusted for the age of TB case to predict positive IGRA status among HHC <15 years of age of MDR-TB cases]

Conclusions: Over half of children < 15 years of age living in households of MDR-TB patients had prevalent TBI. Screening childhood contacts for TB infection and disease remains critical to global TB prevention efforts, particularly those with higher exposure to index cases.

SOA-06-1057-31 The risk of tuberculosis disease in children after close tuberculosis exposure

L Martinez,[1] O Cords,[1] J Andrews,[1] Tuberculosis Observational Studies Consortium [1]Stanford University, Department of Infectious Disease and Geographic Medicine, Stanford, United States of America.
e-mail: leomarti@stanford.edu

Background: Millions of children are exposed to tuberculosis globally every year; however, the risk of disease progression in these children and the role of various public health interventions remains poorly understood.

Methods: We conducted a systematic review for cohort studies with individual-participant level data including children with close tuberculosis exposure. Baseline pediatric tuberculosis status and risk factors were assessed; children healthy at baseline were followed for tuberculosis progression. We estimated the odds of prevalent tuberculosis with a mixed-effects logistic model, and estimated hazard ratios for incident tuberculosis with parametric survival-time modeling including a random intercept for each study. The effectiveness of preventive therapy against incident disease was estimated through propensity score matching. We included analyses by age group, HIV, tuberculosis infection, BCG, and prior tuberculosis.

Results: We pooled participant-level data from 46 cohort studies and included 137,647 exposed children followed for 427,677 child-years. 2,093 pediatric tuberculosis cases were diagnosed (1,263 and 830 prevalent and incident cases). The two-year tuberculosis progression risk among infected children not receiving preventive therapy was 26% in children < 1-year-old and remained >20% until 5 years of age. In this group, progression risk decreased to 10%, 9%, and 11% at 5-9, 10-14, and 15-18 years old, respectively. Risk increased in children with HIV and positive tuberculin skin test at baseline. The effectiveness of preventive therapy was 63% (AHR, 0.37, 95% CI, 0.30-0.47) among all exposed children, and 85% (AHR, 0.15, 95% CI, 0.11-0.20) among infected children.

Conclusions: The risk of tuberculosis progression among exposed children is very high, especially in those < 5 years old. Over 65% of all cases were prevalent suggesting case-finding interventions should be prioritized.

SOA-06-1058-31 Drug resistance surveillance in children with confirmed tuberculosis in the era of Xpert MTB/RIF Ultra

HS Schaaf,[1] M Palmer,[1] M van der Zalm,[1] C Rautenbach,[2] C Bosch,[1] AC Hesseling,[1] E Walters,[1]
[1]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Cape Town, South Africa, [2]National Health Laboratory Service, Tygerberg Hospital, Cape Town, South Africa.
e-mail: hss@sun.ac.za

Background: To determine the prevalence of drug resistance among children with bacteriologically-confirmed tuberculosis (TB) in the context of routine use of Xpert MTB/RIF (Xpert) and Xpert MTB/RIF Ultra (Ultra).
Methods: Prospective surveillance was done from March 2017 through February 2019 at Tygerberg Hospital, Cape Town, South Africa. Drug susceptibility testing (DST) was done by line-probe assay (LPA, GenoType MTBDRplus) for isoniazid (INH) and rifampicin (RIF) on one isolate from every child (< 13 years) diagnosed with culture-confirmed TB. Further DST was done if RIF resistance was found. Xpert was done until February 2018 and was replaced by Ultra thereafter.
Results: 454 children, 231 (51%) boys, median age 26.5 months (IQR 11-65) had bacteriologically-confirmed TB. Of these, 361 (79.5%) were confirmed by culture. Fifty-seven (15.8%) had any INH or RIF resistance; 27 (7.5%) had multidrug-resistant TB (MDR-TB). Fluoroquinolone resistance was present in 6/27 (22%) MDR-TB cases. Ninety-three (20.5%) were positive by Xpert/Ultra only: 29/93 (31%) by Xpert, and 64/93 (69%) by Ultra, the latter of which 41/64 (64%) were trace-positive RIF-unsuccessful.
DST results are summarized in table 1. Of 228 Xpert/Ultra RIF DST results, 4 were discrepant with LPA. Of the 41 trace-positive Ultra results (median 2 negative cultures per child), 31 were managed as TB (9 with extrapulmonary TB) and 10 as TB infected only or without TB. Of cases only positive by Xpert/Ultra, 33/93 (35%) were on current treatment or had previous TB treatment. 443/454 (97.6%) children were tested for HIV, with 32/443 (7.2%) positive.

DST result (LPA on culture)	Number = 361 (%)	Comments
Susceptible to INH & RIF	304 (84.2)	
Any resistance to INH and/or RIF	57 (15.8)	
INH-resistant/RIF-susceptible	20 (5.5)	inhA=16 (80%); katG=4 (20%)
RIF-resistant/INH-susceptible	10 (2.8)	INH phenotypic DST susceptible
Multidrug-resistant (INH & RIF-resistant)	27 (7.5)	INH-resistance: inhA=17 (63%); katG=7 (26%); both mutations in 2, phenotypic DST resistance in 1
Xpert/Xpert Ultra	N = 93 (%)	
RIF-susceptible	48 (51.6)	Xpert=27; Ultra=21
RIF-resistant	3 (3.2)	Xpert=1; Ultra=2
RIF-unsuccessful	42 (45.2)	Xpert=1; Ultra=41

[Table 1: Drug-susceptibility test results of bacteriologically-confirmed tuberculosis in 454 children]

Conclusions: Prevalence of overall drug resistance remains high but stable compared to previous surveys at the same hospital. Ultra identified many culture-negative cases, but trace-positive results with unsuccessful RIF DST is difficult to interpret and needs further evaluation. Fluoroquinolone resistance in MDR-TB cases has implications for treatment and preventive therapy.

SOA-06-1059-31 Treatment outcomes of children with bacteriologically confirmed extensively drug-resistant TB in Ukraine

H Jenkins,[1] M Dolynska,[2] S Chiang,[3] M Taylor,[1] I Kuzin,[4] L Korinchuk,[4] Y Sheremeta,[2] CR Horsburgh,[5] N Rybak,[6] [1]Boston University School of Public Health, Biostatistics, Boston, MA, United States of America, [2]Bogomolets University, Department of Tuberculosis and Pulmonology, Kyiv, Ukraine, [3]Alpert Medical School of Brown University, Pediatrics, Providence, RI, United States of America, [4]National Center for Public Health, Monitoring and Evaluation, Kyiv, Ukraine, [5]Boston University School of Public Health, Epidemiology, Boston, MA, United States of America, [6]Alpert Medical School of Brown University, Medicine, Providence, RI, United States of America.
e-mail: tasharybak@gmail.com

Background: Confirmation of TB is harder in children because they are more likely to have extra-pulmonary TB and pauci-bacillary TB and have difficulties producing sputum. Therefore, confirmed diagnosis of extensively drug-resistant tuberculosis (XDRTB; TB that is resistant to at least a fluoroquinolone and an injectable drug) in children is rare; a recent meta-analysis of all available data identified only 37 children worldwide with confirmed XDRTB for whom treatment outcome data was available. Here, we aimed to summarize data on children in Ukraine diagnosed with XDRTB.
Methods: We used routinely collected data recorded in the Ukrainian online TB surveillance database ("eTB Manager"). This database was begun in 2013 and contains all individuals diagnosed with TB in Ukraine. We identified all children (<15 years) with bacteriologically confirmed XDRTB. We summarized their baseline and outcome data.
Results: We identified 37 children with confirmed XDRTB, of whom 54% were female. One third of these children were aged <2 years and half were aged <5 years. Ten (27%) had extra-pulmonary TB, none were HIV-infected, and only 30% had an identified contact with TB. Of 26 children with final outcome data, 23 (88%) had a favourable outcome (cured or completed treatment), while 2 (8%) died and one had treatment failure due to adverse reactions. One child transferred out (outcome unknown) and the remaining 10 are still on treatment.
Conclusions: Children with XDRTB can experience excellent outcomes, when correctly diagnosed. A large proportion (70%) of these children had no known TB contact highlighting the importance of further work needed to identify optimal strategies for screening chil-

dren at risk for TB. More work is also needed to estimate how many children in Ukraine are not being successfully diagnosed with XDRTB and thus experiencing far poorer outcomes than the children in this study.

SOA-06-1060-31 Remarkable outcomes in children and adolescents routinely treated for tuberculosis in the Netherlands, and factors associated with mortality and treatment default

F Gafar,[1] N van't Boveneind-Vrubleuskaya,[2] OW Akkerman,[3,4] B Wilffert,[1,5] J-WC Alffenaar,[5,6]
[1]University of Groningen, Groningen Research Institute of Pharmacy, Unit of PharmacoTherapy, -Epidemiology, and -Economics, Groningen, Netherlands, [2]Metropolitan Public Health Services, Department of Public Health TB Control, The Hague, Netherlands, [3]University of Groningen, University Medical Center Groningen, Department of Pulmonary Diseases and Tuberculosis, Groningen, Netherlands, [4]University of Groningen, University Medical Center Groningen, Tuberculosis Center Beatrixoord, Haren, Netherlands, [5]University of Groningen, University Medical Centre Groningen, Department of Clinical Pharmacy and Pharmacology, Groningen, Netherlands, [6]University of Sydney and Westmead Hospital, Faculty of Medicine and Health, School of Pharmacy, Sydney, NSW, Australia.
e-mail: f.gafar@rug.nl

Background: As one of the top-10 causes of death, tuberculosis (TB) has become a silent killer in children. Identifying factors associated with unfavourable outcomes would allow more focused interventions to support these patients once diagnosed. Thus, risk factors of mortality and treatment default in children and adolescents treated for TB were evaluated.
Methods: A retrospective cohort study using a nationwide surveillance database was performed in children and adolescents (≤18 years) routinely treated for TB in The Netherlands from 1993-2017. Univariate and multivariate logistic regressions were used to identify factors associated with treatment outcomes.
Results: Of 3301 children and adolescents diagnosed with TB over the study period, 90% were successfully treated (cured/completed), 5% defaulted and < 1% died during treatment. No treatment failure was recorded.
In multivariate analysis, children <5 years (aOR, 1.67; 95% CI, 1.07-2.60), miliary TB (aOR, 3.47; 95% CI, 1.56-7.75), malignant comorbidity (aOR, 20.26; 95% CI, 4.36-94.03), retreatment cases (aOR, 2.39; 95% CI, 1.15-4.96), single adverse drug reaction (ADR) (aOR, 1.90; 95% CI, 1.13-3.21) and multiple ADRs (aOR, 8.10; 95% CI, 3.97-16.55) were independently associated with mortality.
For treatment default, several factors were independently associated such as adolescents aged 15-18 years (aOR, 1.88; 95% CI, 1.24-2.87), illegal immigrants (aOR, 6.86; 95% CI, 2.63-17.91), living in urban area (aOR, 1.55; 95% CI, 1.08-2.23), single ADR (aOR, 1.87; 95% CI, 1.03-3.38), multiple ADRs (aOR, 7.17; 95% CI, 3.25-15.82), and treatment nonadherence (aOR, 8.16; 95% CI, 3.03-21.93).
Conclusions: We demonstrate a remarkable overall outcome in children and adolescents treated for TB. However, they faced a higher risk of death if they were under 5 years, had miliary TB, previously treated for TB, and developed ADRs during treatment. To reduce treatment default, special attentions should be given to adolescents, illegal immigrants, people living in urban area, nonadherent patients and those who developed ADRs during treatment.

SOA-06-1061-31 Increasing access to childhood TB services: the Katsina model

Y Adelakun,[1] A Yusuf Audi,[2] A Tijjani Habibu,[3] B Habibu,[4] [1]KNCV Tuberculosis Foundation, Programs, Katsina, Nigeria, [2]Katsina State Tuberculosis, Buruli Ulcer and Leprosy Control Program, Public Health, Katsina, Nigeria, [3]KNCV Tuberculosis Foundation, Programs, Kano, Nigeria, [4]General Hospital, Paediatrics, Katsina, Nigeria.
e-mail: yusufadelakuna@gmail.com

Background: Access to diagnostic services for children remains a major challenge to TB programs around the world. This study, undertaken across 17 local government areas (LGAs) in a state in northern Nigeria, examined the results of a free chest x-ray intervention on childhood TB case notification between January 2017 and December 2017.
Methods: In 2017, x-ray centers were mapped out by the state TB control team and the respective local government team based on client-burden across 17 LGAs. Large-scale community engagements and demand creation were then embarked upon with routine screening of children for basic TB symptoms and contact history, at the residence of local village heads by community volunteers and local government tuberculosis and leprosy supervisors. Buses were also provided to transport these children, aged between 0-14 years, from a central convergence point, in their respective LGAs to the x-ray centers. Clinicians reviewed these x-ray films for diagnosis and contact investigations were carried out afterwards.
The data generated during the intervention in 2017 across the 17 LGAs, was weighed against total data generated in 2016, to measure the effectiveness of the drive.
Results: A total 905 (457 males vs. 448 females) childhood TB cases were diagnosed across the 17 LGAs during the intervention period, compared to 155 in the previous year. This was a near six-fold increase. 61.6% (558) of these cases were aged 0-4 years (286 males vs. 272 females). Overall, of the 1232 childhood TB cases recorded across the 34 LGAs in the state in 2017, 73.4% came from 17 LGAs where the intervention was implemented.
Conclusions: Early diagnosis of childhood TB in communities is very important. However, increasing access to diagnostic services as well as further engagement

of community players, and purposeful advocacy visits should be strengthened. These are some of the factors responsible for the success of this intervention.

SOA-06-1062-31 Community-based intervention improves TB preventive treatment completion in children in Lesotho

Y Hirsch-Moverman,[1] AA Howard,[1] JE Mantell,[2] L Lebelo,[3] K Frederix,[3] K Yuengling,[1] A Hesseling,[4] S Nachman,[5] BL Maama,[6] W El-Sadr,[1] [1]MSPH at Columbia University, ICAP, New York, NY, United States of America, [2]NYS Psychiatric Institute and Columbia University, HIV Center for Clinical & Behavioral Studies, New York, NY, United States of America, [3]ICAP Lesotho, ICAP, Maseru, Lesotho, [4]Stellenbosch University, Desmond Tutu TB Centre, Cape Town, South Africa, [5]SUNY Stony Brook, Pediatric Infectious Diseases, Stony Brook, NY, United States of America, [6]Lesotho Ministry of Health, National TB Program, Maseru, Lesotho. e-mail: yh154@columbia.edu

Background: Child TB contact management (CCM) for household contacts is a proven strategy for TB case finding and for initiation of TPT to prevent progression to TB. However, CCM implementation is suboptimal in high TB/HIV burden settings. The PREVENT Study was a cluster randomized trial to evaluate the effectiveness of a community-based intervention (CBI) to improve CCM in Lesotho.

Methods: Ten clinics were randomized to CBI or standard of care (SOC). CBI included several interventions: nurse training and mentorship; health education for caregivers and patients by village health workers (VHW); adherence support with weekly messages and facility-based VHW; and multidisciplinary team meetings, where programmatic data were reviewed. Information on all adult TB cases ≥18 years registered during the study period, and their child contacts was retrieved from TB registers/cards. The primary outcome was completion of TPT. Generalized linear mixed models were used to test for differences between study arms.

Results: From 02/2016 through 06/2018, 547 children of 426 TB patients aged ≥18 years were noted in the contact tracing register, 399 children at CBI sites and 148 children at SOC sites. TB patients were 57% male, median age 39 (interquartile range [IQR] 32-56) and 81% completed treatment or were cured. Of 547 children, 17% were < 1 year, 29% 1-2 years, and 54% were >3 years, 48% were female, and 3% were HIV-exposed or -positive; with no significant difference between study arms. Five hundred one children were eligible and initiated TPT, 377/384 at CBI sites and 124/141 at SOC sites (98% vs. 88%, p< 0.0001). TPT completion was achieved by 82% (308/377) in CBI vs. 59% (73/124) in SOC (RR 1.38 95% CI 1.03-1.84; p=0.03).

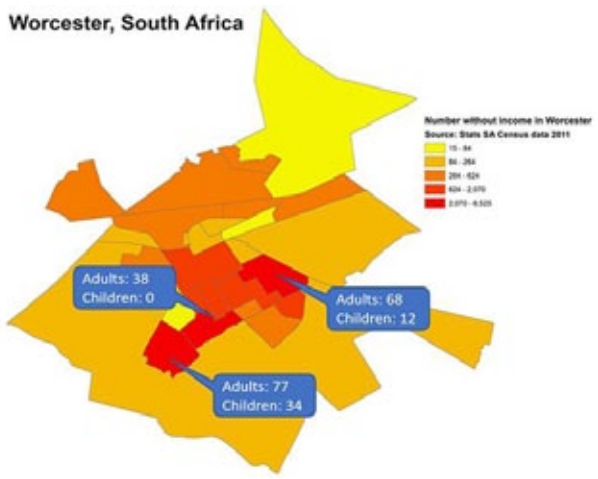
Conclusions: CBI significantly improved TPT completion among child TB contacts in Lesotho. The implementation and scale-up of this strategy can enhance child health by reducing TB incidence and deaths.

SOA-06-1063-31 A picture is worth a thousand words: combining the location of TB with social determinants of health to inform interventions to reduce TB among children

E Volschenk,[1] A van Zyl,[2] G Jagwer,[3] R Matji,[3] [1]University Research Co., LLC (URC), Monitoring, Evaluation and Learning, Pretoria, South Africa, [2]University Research Co., LLC (URC), Provincial Team, Pretoria, South Africa, [3]University Research Co., LLC (URC), Management, Pretoria, South Africa. e-mail: alicevz@urc-sa.com

Background and challenges to implementation: The USAID Tuberculosis South Africa Project supports the National Department of Health (NDOH) to improve the care and treatment of vulnerable populations, including children under the age of five years. In Worcester, a town in the Breede Valley sub-district in Western Cape province, 310 children were treated for TB in 2018, which comprises a third of the overall TB burden. To better address the high burden among children it is necessary to understand the context of where these children are being raised.

Intervention or response: To analyse the TB burden in Worcester, the project used ConnecTB, a mobile health (mHealth) application with geospatial technology to pinpoint patient locations on a map. The map showed TB clusters or hot spots indicating that in an area furthest from a health facility, 41% of TB patients were children. Additional maps of Worcester were then created using national census data on social determinants of health. When overlaid, high dwelling density, lack of income and lack of education correlated with high TB burdens for both adults and children.



[Map of Worcester showing TB burden per hot spot and number of people without income]

Results and lessons learnt: Understanding the social realities of TB hot spot areas informed planning for targeted interventions to address the TB burden in Worcester. Contact tracing initiatives focused on screening all households for TB patients at risk of spreading infec-

tion to children and three were initiated on treatment. A community orientated primary health care facility was set up in August 2018 to ensure ease of access to primary healthcare services and is currently providing support to 37 TB patients under the age of five

Conclusions and key recommendations: Creating geolocation maps to show TB hotspots is only the first step in understanding reasons for high TB burdens in specific areas. Additional data such as social determinants of health must also be mapped and analysed to inform interventions for impact.

SOA-06-1064-31 Caregivers' and health workers' perceptions on the effects of caregiver-child separation during long-term hospitalisation for MDR-TB: a qualitative study in the Western Cape, South Africa

KA Meyerson,[1] G Hoddinott,[1] A Garcia-Prats,[1] M Tomlinson,[2] [1]Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, [2]Faculty of Medicine and Health Sciences, Stellenbosch University, Department of Global Health, Cape Town, South Africa. e-mail: meyersonk@sun.ac.za

Background: There are an estimated 32 000 incident cases of multidrug-resistant tuberculosis (MDR-TB) in children globally each year. In the Western Cape, South Africa, approximately 60-100 children are diagnosed with MDR-TB each year. Due to the complexity of treatment including the use of daily injectable medications, MDR-TB treatment is often delivered during extended hospitalisation. Currently, long-term hospitalisation entails caregiver-child separation, which has been shown to cause behavioural problems in children.

Methods: We explored caregivers' and health workers' perceptions of the effects of caregiver-child separation during long-term hospitalisation for MDR-TB treatment. We conducted 19 semi-structured, in-depth interviews with health workers and caregivers of children who were receiving treatment for MDR-TB. All interviews were audio-recorded, transcribed and translated verbatim. We used thematic analysis to organise and interpret the data.

Results: We identified three major themes:

(i) MDR-TB treatment was a distressing experience;

(ii) children's behavioural states during and post- hospitalisation included excessive crying, aggression, hyperactivity, and withdrawal;

(iii) caregivers' and health workers' used behavioural management strategies such as deception, threat, and the prioritisation of biomedical health over psychological health.

Conclusions: This study highlights the challenges that children, caregivers and health workers experienced in the context of caregiver-child separation during MDR-TB treatment. These challenges intersected with predisposing factors related to the social adversity that families affected by childhood TB experience. Children's behavioural states during MDR-TB treatment could therefore be considered adaptive responses to the cumulative stress of MDR-TB treatment and social adversity. Caregivers and health workers used the most effective strategies available to them to manage paediatric illness, in a context with constrained resources. Future research should develop and evaluate an intervention, co-constructed with the community, to reduce the negative effects of caregiver-child separation during MDR-TB treatment in the Western Cape and other developing countries. Additionally, TB programmes should prioritize community-based delivery of MDR-TB treatment to children.

SOA-06-1065-31 Predictors of incomplete evaluation among paediatric household contacts of pulmonary tuberculosis patients in Kampala, Uganda: a secondary analysis

G Lee,[1] AJ Meyer,[1] S Kizito,[2] A Katamba,[3] JL Davis,[1] M Armstrong-Hough,[1,4] [1]Yale School of Public Health, Epidemiology of Microbial Diseases, New Haven, CT, United States of America, [2]Makerere University College of Health Sciences, Uganda TB Implementation Research Consortium, Kampala, Uganda, [3]Makerere University College of Health Sciences, Clinical Epidemiology Unit, Kampala, Uganda, [4]New York University, College of Global Public Health, New York, NY, United States of America. e-mail: giylee95@gmail.com

Background: Contact investigation is an active approach to identifying new TB cases by screening contacts of known patients for symptoms and risk factors. This is particularly important for child contacts of TB patients because young children are at higher risk of progressing to severe disease compared to adults. Moreover, children are unable or unlikely to travel to clinics for evaluation independently, so their access to TB evaluation may depend on the adults in their household. We sought to evaluate the association between individual- and household-level characteristics and reaching a clinic for TB evaluation among children.

Methods: We carried out a prospective cohort study including participants from both the intervention and control arms of a pragmatic, household-randomized trial in Kampala, Uganda. We used generalized estimating equations with logistic regression to estimate the association of individual- and household-level characteristics with reaching a clinic for TB evaluation among children.

Results: Of 196 contacts under 5 years who were referred for evaluation, 25 (13%) appeared at a clinic by day 60. Of 48 contacts 5-14 years who were referred for TB evaluation, 19 (40%) appeared by day 60. In children under 5, controlling for age and household head's level of education, presence of TB symptoms (adjusted risk ratios (aRR) 2.6, 95% CI 1.14-6.01, p=0.024) and house-

hold income (aRR 1.2, 95%CI 1.11-1.36, p< 0.001) were significantly associated with reaching a clinic for evaluation by day 60.
Conclusions: Most children referred for TB evaluation did not reach a clinic within 60 days. Children in higher-income households and children with symptoms evident to parents were more likely to appear at a clinic than children in lower-income households or those without recognized symptoms. Further research is needed to identify barriers to pediatric evaluation among low-income households, strategies for facilitating clinic visits for asymptomatic children, and interventions to increase completion of pediatric TB evaluation.

SOA-08-C3 Different approaches to combating DR-TB

SOA-08-1075-31 Replacement of second line injectable agents with bedaquiline in longer regimens for multidrug-resistant tuberculosis

N Ndjeka,[1] JR Campbell,[2] F Conradie,[3] D Menzies,[2]
[1]National Tuberculosis Control Program, Department of Health, Pretoria, South Africa, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]University of the Witswatersrand, Clinical HIV Research Unit, Johannesburg, South Africa. e-mail: ndjeka@esnet.co.za

Background: New World Health Organization (WHO) guidelines on the treatment of multidrug-resistant tuberculosis (MDR-TB) recommend a backbone of bedaquiline, linezolid, and moxifloxacin/levofloxacin. Second line injectables (SLI) are no longer recommended as a primary treatment option. In South Africa, bedaquiline has already been used in place of SLI. We evaluated differences in treatment outcomes among similar MDR-TB patients treated with bedaquiline vs. SLI.
Methods: Included patients began treatment in 2014-2015, were registered in the national electronic MDR database, were susceptible to SLI, were treated with an individualized longer (intended duration ≥18 months) regimen, and received at least 90 days of treatment. A case-control approach, with replacement, matched patients receiving SLI and no bedaquiline to patients receiving bedaquiline and no SLI. Exact matching was done for fluoroquinolone resistance, acid fast bacilli smear positivity, HIV, previous treatment, linezolid use, and moxifloxacin/levofloxacin use. Nearest neighbor (caliper distance = 0.02) based propensity score matching was done for age and number of companion drugs from each WHO drug grouping. End-of-treatment outcomes were compared between groups using risk differences (RD) and associated 95% confidence intervals (95%CI).
Results: In total, 358 patients (179 matched pairs) treated for a median (interquartile range, IQR) duration of 19.9 (15.4-23.3) months were included. The median (IQR) age of patients was 41 (31-48) years, 266 (74%) were HIV-positive, and 190 (53%) received concomitant linezolid. Success (cure or treatment completion) among patients receiving SLI was 45.3% and among patients receiving bedaquiline was 69.3% (RD 24.0%; 95%CI 14.1% to 34.0%). Notably, treatment failure was 10.1% (95%CI 3.8% to 16.4%) lower among patients receiving bedaquiline.
Conclusions: In South Africa, patients with similar characteristics treated with regimens that differed only for SLI and bedaquiline use, fared much better when they received bedaquiline. It is of critical importance to ensure MDR-TB patients have access to this medicine.

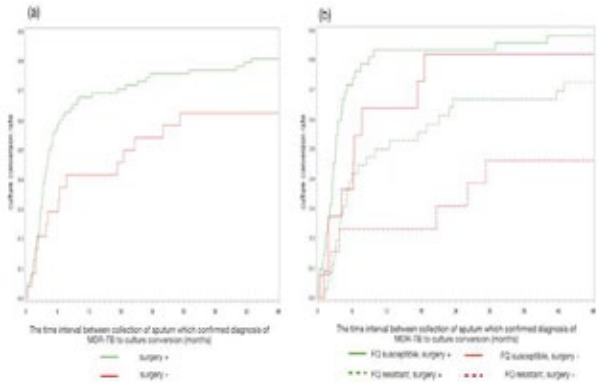
SOA-08-1076-31 Impact of surgical intervention on time to culture conversion among MDR-TB patients in Taiwan

PH Lee,[1] CH Liu,[1] PC Chan,[1] YT Peng,[1] YF Huang,[1]
[1]Division of Chronic Infectious Diseases, Centers for Disease Control, Taipei, Taiwan.
e-mail: leepinhui@gmail.com

Background: Surgery may be used alongside MDR-TB regimen to increase treatment success. Taiwan MDR-TB Consortium (TMTC) was established in 2007 to provide patient-centered care with high treatment coverage. We assess the impact of surgical intervention on the time interval of culture conversion among MDR-TB patients in Taiwan.
Methods: We conducted a retrospective cohort analysis of pulmonary MDR-TB patients who were enrolled into TMTC and suitable for surgical intervention from 2007 to 2018 from TB registry. Evaluation of surgery would be indicated for MDR-TB patients who did not achieve culture conversion after 8 months of enrollment or need to reduce intractable lung tissues to improve prognosis through TMTC quarterly review committee. We analyzed treatment outcomes and the time interval from sputum collection that confirmed MDR-TB diagnosis to culture conversion among patients who were eligible for elective surgery.
Results: There were 224 patients eligible for evaluation of surgical intervention. After excluding those who were not suitable for partial lung resection or transferred out (n=122), seventy-eight patients received surgery and 24 patients refused operation. Patients who received surgery tend to be new patients (43.6% vs. 33.3%, p=0.516) and had cavitation (69.2% vs. 58.3%, p=0.322). We found that 44% of those who received surgery had received operation within 6 months after initiating second-line drugs treatment. The median time from sputum collection to culture conversion in patients who received or refused surgery was 4.5 and 19.6 months, respectively (figure 1). Patient who received surgery had higher treat-

ment success rate (76.9% vs. 54.2%, p=0.04). Patients with fluoroquinolone (FQ) susceptible mycobacterium isolates had significantly shorter time interval of culture conversion than those who had FQ resistant (aHR: 2.1, 95% CI: 1.38 - 3.19).

Conclusions: Surgical intervention with MDR-TB regimen tend to shorten time interval of culture conversion that was significantly affected by fluoroquinolone resistance in eligible patients.



[Figure 1.
(a) Time interval of culture conversion, by receiving surgical intervention or not (log rank test, p-value = 0.078)
(b) Time interval of culture conversion, by receiving surgical intervention and fluoroquinolone resistance (log rank test, p-value = 0.001)]

SOA-08-1077-31 Delamanid and greater than six months of bedaquiline for RR-TB has promising treatment outcomes in a high HIV prevalence programmatic setting in South Africa

A Reuter,[1] E Mohr,[1] H Cox,[2] V De Azevedo,[3] G Ferlazzo,[4] V Mudaly,[5] L Trivino-Duran,[6] [1]Medecins Sans Frontieres, DR-TB, Khayelitsha, South Africa, [2]University of Cape Town, Division of Medical Microbiology, Department of Pathology & Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa, [3]City of Cape Town Department of Health, Primary Health Care Health Department, Cape Town, South Africa, [4]Medecins Sans Frontieres Southern Africa Medical Unit, TB & DR-TB, Cape Town, South Africa, [5]Provincial Department of Health- Western Cape, Health Programmes, Cape Town, South Africa, [6]Medecins Sans Frontieres, Coordination Office, Cape Town, South Africa.
e-mail: msfocb-khayelitsha-tbdoc@brussels.msf.org

Background: Bedaquiline (BDQ) has been newly recommended as a core drug in rifampicin-resistant tuberculosis (RR-TB) treatment; delamanid (DLM) is a group C drug due to limited evidence. We describe safety and treatment outcomes for RR-TB treatment regimens containing DLM and >6 months of BDQ in Khayelitsha, South Africa.

Methods: This was a retrospective cohort study of patients receiving DLM and >6 months of BDQ as part of a RR-TB regimen between November 2015 and August 2018. We report on sputum culture conversion (SCC), serious adverse events (SAEs), and final treatment outcomes.

Results: Overall, 40 patients were enrolled; 22 (55%) were males, the median age at treatment initiation was 34 years (interquartile range [IQR] 27-41), and 25 (63%) were HIV-positive with a median CD4 count of 170 cells/mm^3 (IQR 61-269). Thirty (75%) patients had RR-TB with fluoroquinolone resistance; 26 (65%) were culture positive at the time of DLM initiation and SCC at month 6 was 69%. Twenty three (58%) patients had both BDQ and DLM extended >6 months; 17 (42%) had only BDQ extended. The median time on BDQ and DLM for this cohort was 15.4 months (IQR 12.6-18.5) and 12.1 months (7.1-13.9), respectively. Overall, 22 SAEs were reported among nine (23%) patients; four of these SAEs were assessed as possibly related to BDQ and DLM. QTcF prolongation was noted in one patient (525 milliseconds) at month 7 of treatment (no permanent discontinuation of drugs). Sixteen patients had final treatment outcomes; 13 (82%) were successfully treated, 1 (6%) died, 1 experienced treatment failure (6%), and 1 (6%) was transferred-out.

Conclusions: Final outcomes in this group of RR-TB patients who received DLM and >6 months of BDQ, most of whom had fluoroquinolone resistance and advanced HIV were excellent with a favorable safety profile. Access to DLM and >6 months of BDQ should be scaled-up.

SOA-08-1078-31 Ambulatory based bedaquiline treatment for drug-resistant TB patients at Government Hospital, Mumbai, India

A Iyer,[1] D Shah,[2] V Oswal,[3] S Mankar,[3] N Sutar,[3] S Ravi,[1] M Das,[1] S Kalon,[1] G Ferlazzo,[4] P Isaakidis,[4] [1]Médecins Sans Frontières (MSF) / Doctors without Borders, Medical, Mumbai, India, [2]City TB Office, Tuberculosis, Mumbai, India, [3]Revised National Tuberculosis Control Programme, DR-TB OPD, Shatabdi Hospital, Mumbai, India, [4]Médecins Sans Frontières (MSF) Southern Africa Medical Unit, Medical, Cape Town, South Africa.
e-mail: dtomhbmc@rntcp.org

Background: In India, Bedaquiline (BDQ), a new TB-drug, has recently been considered for routine-use in Multi-drug resistant tuberculosis (MDR-TB) treatment, as internationally recommended. Administration is now allowed at ambulatory level. However, during initial roll-out of national BDQ conditional-access-program, in 2016-2018, DR-TB patients eligible for BDQ received first two-weeks of treatment under hospitalization. Shatabdi hospital, Mumbai, was among the first decentralized DR-TB sites in India to pilot ambulatory treatment with BDQ-based regimen. The current study doc-

uments the initial programmatic experiences of providing ambulatory BDQ based DR-TB treatment including early safety and efficacy results.
Methods: This is a retrospective cohort study of patients with DR-TB initiated on ambulatory BDQ based treatment between June-Dec 2018 at DR-TB OPD, Shatabdi hospital, Mumbai, where National TB programme (RNTCP) Mumbai provides diagnosis, treatment and care to DRTB patients with support of Médecins Sans Frontières (MSF), in terms of additional human resources. Analysis was conducted in Apr-2019.
Results: A total of 84 patients were initiated on treatment. The median age was 24 years (Interquartile range: 19-28) and 65% (55/84) were females. None was co-infected with HIV. Majority 54 (64%) had MDR + Fluroquinolone-resistance, while 22 (26%) extensively-drug-resistance (XDR-TB); 6 (7%)=MDR-TB; 2 (2%) = MDR+Injectable resistance. 21 patients completed 6-months, of whom 20 (95%) had culture-conversion. 24 received 3-month treatment, and all (100%) culture-converted. 36 were yet to complete 3-months treatment at time of analysis. One was lost-to-follow-up. Two died during treatment; the fatal-outcome was attributed to advanced clinical-condition of patients and not to drug-related serious-adverse-event (SAE).
Conclusions: The encouraging high-rate of culture-conversion, with no major reports of adverse-events suggests effectiveness and safety of ambulatory administration of DR-TB regimens including BDQ. TB programmes must devise similar decentralised, innovative 'patient- centered' strategies for patients with DR-TB, to enhance access and scale-up of BDQ based DR-TB treatment.

SOA-08-1079-31 Examining the efficacy of the short MDR-TB regimen: alternative analyses from the STREAM trial

P Phillips,[1] S Ahmed,[2] S Meredith,[2] ID Rusen,[3] A Nunn,[2] STREAM collaboration [1]University of California, Medicine, San Francisco, CA, United States of America, [2]UCL, MRC Clinical Trials Unit, London, United Kingdom, [3]Vital Strategies, Research and Development, New York, NY, United States of America.
e-mail: patrick.phillips@ucsf.edu

Background: STREAM Stage 1 was a randomised phase III clinical trial. Participants with rifampicin-resistant TB from South Africa, Ethiopia, Vietnam and Mongolia received either the 9-11 month standardized 'Short' regimen or locally-used standard of care 'Long' regimen that followed 2011 WHO guidelines. The Short regimen was shown to have non-inferior efficacy and comparable safety in the primary outcomes. In this presentation we report on secondary efficacy outcomes and further examine the efficacy of the 9-11 month MDR-TB regimen.
Methods: The primary efficacy outcome was re-classified according to the likelihood that it was a Failure or Relapse (FoR) event on a four-point scale: Highly Likely, Likely, Unlikely, and Highly Unlikely. This classification did not depend on treatment allocation, although done after trial completion. A further five alternative programmatic outcomes included WHO DR-TB treatment outcomes, WHO outcomes modified to include relapse, two other published DR-TB treatment outcome definitions, and durable cure at end of follow-up irrespective of changes or restart of treatment.
Results: In 383 participants in the modified-ITT analysis, the risk difference of cure between regimens did not exceed 1.3% in favour of the Long regimen in any of the five outcomes with the upper bound of the confidence interval never exceeding 11%. These results are therefore consistent with the primary efficacy results from the trial. In a time-to-outcome analysis, the hazard of FoR (Highly likely/Likely vs. Unlikely/Highly unlikely) was 2.19 (95% CI 0.90, 5.35) higher for the Short regimen. Re-defining FoR (Highly Likely vs. all other groups combined) increased this to 3.53 (95% CI 1.095, 11.87), although sensitivity analyses accounting for non-informative censoring reduced the treatment effect.
Conclusions: Alternative programmatic outcome definitions for MDR-TB gave results consistent with the primary efficacy outcome. However, post-hoc analyses from the STREAM trial suggest increased risk of FoR in the Short regimen as compared to the Long regimen.

SOA-08-1080-31 What are we missing in analyses of tuberculosis treatment outcomes? A systematic review of methods used to control for time-dependent confounding

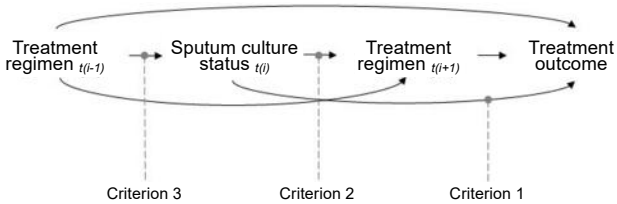
CA Rodriguez,[1] KTL Sy,[2] CD Mitnick,[1] MF Franke,[1] [1]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [2]Boston University School of Public Health, Department of Epidemiology, Boston, MA, United States of America.
e-mail: carly_rodriguez@hms.harvard.edu

Background: Bacteriologic response and toxicity are important prognostic factors in the decision to switch multidrug-resistant tuberculosis (MDR-TB) treatment. These factors may function as time-dependent confounders, defined as a time-varying risk factor for poor treatment outcome (criterion 1), that can predict a regimen change (criterion 2) and is a result of the current treatment regimen (criterion 3) (Figure).
Time-dependent confounding can introduce substantial bias if not appropriately controlled for during analysis. We examined if methods to control for time-dependent confounding were used in longitudinal studies of TB or MDR-treatment.
Methods: We conducted a systematic search in Pubmed of terms related to TB AND time-varying confounding, causal inference, and methods to control time-dependent confounding. We screened abstracts, excluding those

that were not on TB, included TB but were principally on HIV, or did not reference methodologies of interest. We assessed full texts for whether the methodologies were applied to control for time-dependent confounding in studies of TB treatment on TB outcomes.

Results: Our search yielded 55 papers. We excluded 34 (62%) abstracts and assessed the full text of 21 (38%) studies. Of these, 13 studies used a method; however, all were focused on research questions in HIV. We did not find any studies assessing the effect of TB treatment on a TB outcome that implemented a method to control for time-dependent confounding.

Conclusions: Methods to contend with time-dependent confounding have not been applied in TB. This may be due to a dearth of cohorts collecting longitudinal data on potential confounders, thus precluding the ability to conduct appropriate analyses. The repercussions of this bias would be substantial: observational data has provided much of the guidance for MDR-TB, which affects 550,000 people annually. Longitudinal data on time-dependent confounders is critical to improving the validity of evidence guiding TB treatment and guaranteeing optimal treatment options for patients.



[Figure. Time-dependent confounding at time i (t(i)), where i represents a specified time point in treatment]

SOA-08-1081-31 Salvage treatment of patients with poor outcomes on the shorter MDR-TB regimen is complicated but possible

U Khan,[1] M Alam,[2] S Islam,[2] A Hossain,[2] N Arefin,[3] S Ahmed,[4] PY Khan,[5] [1]IRD Global, endTB, Dubai, United Arab Emirates, [2]IRD Bangladesh, endTB, Dhaka, Bangladesh, [3]National TB Control Program, MBDC, Dhaka, Bangladesh, [4]IRD Pakistan, endTB, Karachi, Pakistan, [5]IRD Global, endTB, Karachi, Pakistan.
e-mail: uzma.khan@ird.global

Background: The World Health Organization continues to recommend the shorter MDR-TB regimen as part of MDR-TB treatment guidelines despite the downgrading of several constituent drugs whilst restricting the use of group A drugs, such as bedaquiline (Bdq) to 6 months.

We present findings from patients enrolled in the "endTB" observational cohort in Bangladesh who had prior treatment exposure to the shorter MDR-TB regimen for the period when the endTB project was the only source of access to Bdq- or delamanid (Dlm)-containing regimens.

Methods: We enrolled patients in a prospective, observational study at a central MDR-TB treatment site in Dhaka from April 2016 to September 2018. A clinical committee evaluated patients for eligibility for treatment with Bdq- and/or Dlm-containing regimens. Routine clinical data including medical and treatment history, examination, investigations (diagnostic and for monitoring), adverse events and treatment outcomes were collected on a purpose built, open source electronic medical record system. Data was analyzed using STATA software.

Results: 280 patients were enrolled: 159(56.8%) patients had prior exposure to the shorter MDR-TB regimen (of any duration) prior to starting treatment with Bdq- and/or Dlm-containing regimen. Of these 31(19.5%) had prior poor treatment outcomes on the shorter MDR-TB regimen. Restricting further analysis to this group: 22(71.0%) received either prolonged treatment with Bdq or Dlm or concomitant use of Bdq and Dlm or both prolonged concomitant use of Bdq and Dlm. 21(67.7%) patients were culture-positive at baseline, of these 20(95.2%) had culture converted at 6 months.

Conclusions: Restriction on the duration of use and combination of Bdq and Dlm needs to be urgently reviewed and addressed to ensure effective drugs are used early and are available for the full duration of MDR-TB treatment as required. Further operational research on all-oral modified shorter MDR-TB regimens is needed to supplement evidence from MDR-TB clinical trials.

SOA-08-1082-31 Pilot of weekly ECHO model videoconferencing system in Mozambique to review complex drug-resistant TB cases

C Mutaquiha,[1] I Manhiça,[1] P Zindoga,[1] C Mbate Mutemba,[1] M Sumalgy,[2] J Creswell,[3] ZZ Qin,[3] B Struminger,[4] R Chiau,[5] J Cowan,[5,6] [1]Mozambique Ministry of Health, National TB Program, Maputo, Mozambique, [2]Mozambican Ministry of Health, Information, Technology and Communication Department, Maputo, Mozambique, [3]Stop TB Partnership, TB REACH, Geneva, Switzerland, [4]University of New Mexico Health Sciences Center, Project ECHO, Albuquerque, NM, United States of America, [5]Health Alliance International, TB, Maputo, Mozambique, [6]University of Washington, Department of Global Health, Seattle, WA, United States of America. e-mail: claudia.c.mutaquiha@gmail.com

Background and challenges to implementation: Mozambique has one of the highest rates of both TB (551 cases per 100,000) and MDR-TB (8,800 cases annually) in 2017 per WHO estimates.

Intervention or response: As part of a TB REACH Wave 5 project the Mozambican National TB Program (NTP) and Health Alliance International piloted The ECHO model™ - a well-established evidence and case-based telementoring education and training platform using the Zoom videoconferencing sofware designed to strengthen the capacity of community providers to offer best-practice care in their local context. Five peo-

ple attended a weeklong ECHO replication training. In early 2018 Videoconferencing equipment was procured and installed at 2 hubs in Maputo and in 3 provincial health departments. Fifty iPad tablets with monthly data plans and Zoom videoconferencing software were procured and distribute to high-volume MDR-TB health centers.

Results and lessons learnt: The NTP team implemented weekly DR-TB Clinical Conferences using the ECHO Model and Zoom videoconferencing software in May 2018 and invited health facilities to submit summaries of complex MDR-TB cases eligible for individualized regimens. During the following eleven months the NTP hosted 34 DR-TB ECHO videoconferences with a range of 5-20 meeting participants, the majority using the iPad tablets and 3G data connection. Participants have included individuals from all 11 provinces, but most clinical cases were from Southern Mozambique.

Over the first year 131 DR-TB clinical cases were discussed and of these individualized regimens containing bedaquiline, delamanid and both bedaquiline/delaminid were recommended for 73, 12 and 30 patients respectively. Major challenges included configuration of the videoconferencing system and occasional challenges with data speeds using 3G connections for the tablets.

Conclusions and key recommendations: This project demonstrated that weekly DR-TB clinical conferences using The ECHO model™ are possible in Mozambique, even over 3G internet, and facilitated access to individualized regimens. The project is being scaled nationally with support from the World Bank.

SOA-08-1083-31 Shorter treatment regimen for multidrug-resistant tuberculosis: first outcomes in Kazakhstan

N Osmanova,[1] R Kusainova,[2] M Kuspekova,[3] E Pravednaja,[3] K Tabagabylova,[4] A Zhumanijazova,[5] N Zekeshov,[6] G Dravniece,[7] S Pak,[1] M Idrissova,[1]
[1]KNCV TB Foundation, Representative in Central Asia, Almaty, Kazakhstan, [2]Regional TB Center, MDR-TB Ward, Petropavlovsk, Kazakhstan, [3]Regional TB Center, MDR-TB Ward, Pavlodar, Kazakhstan, [4]Regional TB Center, MDR-TB Ward, Kyzylorda, Kazakhstan, [5]Regional TB Center, MDR-TB Ward, Mangystau, Kazakhstan, [6]Regional TB Center, MDR-TB Ward, Uralsk, Kazakhstan, [7]KNCV TB Foundation, Technical Unit, The Hague, Netherlands.
e-mail: nadira.osmanova@kncvtbc.org

Background and challenges to implementation: In Kazakhstan the NTP has attained some success in restraining further increases of TB incidence since 2004; however, multi drug resistant tuberculosis (MDR-TB) remains a growing challenge to controlling TB. Since the 2000s, a conventional longer therapy (20-24 month) was used for all MDR-TB patients.

Intervention or response: Since October 2017, NTP with the support of the USAID Challenge TB Project (CTB) led by KNCV, started preparations for the programmatic implementation of new drugs and regimens using TB patient triage approach. The approach includes clinical evaluation to determine the rifampicin resistant TB (RR-TB) patient's risk of resistance or intolerance of key second line drugs, and bacteriological testing of a pre-treatment specimen to determine the strain's resistance to fluoroquinolones (FQ) and second line injectables (SLI).

Results and lessons learnt: During April-December 2018, 115 (35%) RR-TB patients started shorter treatment regimen in five pilot sites. Baseline testing coverage using genotype MDRTBsl was 65,2%. Out of 115 patients (65,3% male, 34,7% female, aged range 25-45 years) 76% patients experienced at least one adverse event (AEs).

Nineteen AEs of clinical significance have been recorded so far (e.g., dyspepsia, toxic hepatitis, QT prolongation, headache, and skin rash) of that dyspepsia prevailed compared with other recorded AEs. Analysis showed that most of AEs were recorded at the second month of treatment. All of them were successfully managed without stopping the guilty drugs.

Among 25 patients enrolled in April-May 2018, 24 (96%) successfully completed treatment; one patient died due thromboembolism.

Conclusions and key recommendations: Although these are just preliminary results, the experience in Kazakhstan shows that with the proper evaluation of eligibility criteria, the efficiency of STR is good under programmatic conditions, even in a country with a high level of resistance to FQs and SLIs. Timely detection and treatment of AEs prevented development of serious AEs and allowed continuing treatment without interruptions.

SOA-08-1084-31 Adherence to MDR-TB treatment of patients receiving standardised short MDR-TB treatment in Mozambique

M Bastard,[1] L Molfino,[2] C Mutaquiha,[3] M Arago Galindo,[2] P Zindoga,[3] I Manhiça,[3] B Rusch,[4] A Telnov,[5] [1]Epicentre, Research, Geneva, Switzerland, [2]Médecins Sans Frontières (MSF), Medical, Maputo, Mozambique, [3]Ministry of Health, National TB Program, Maputo, Mozambique, [4]Médecins Sans Frontières (MSF), Operations, Geneva, Switzerland, [5]Médecins Sans Frontières (MSF), Medical, Geneva, Switzerland.
e-mail: mathieu.bastard@geneva.msf.org

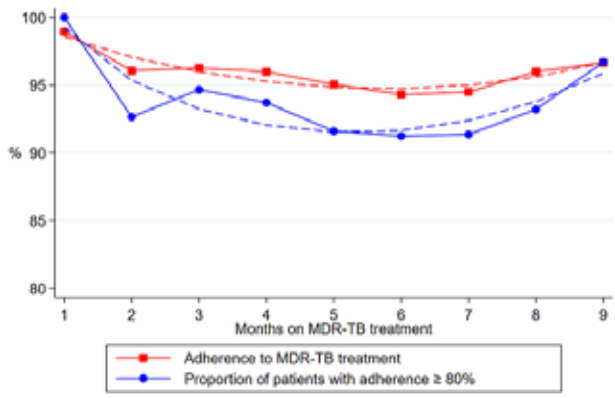
Background: Adherence to treatment is a strong predictor for treatment success. However, it is often poorly documented in multidrug-resistant Tuberculosis (MDR-TB) and few studies are looking at adherence to treatment over time.

Methods: A prospective cohort study was conducted in Maputo, Mozambique, to evaluate the efficacy of the standardized short MDR-TB treatment. Adherence to treatment, defined as the proportion of days fully observed over days prescribed, was collected monthly under DOT. We described and explored the difference in

the evolution of adherence over time on treatment between HIV-positive and HIV-negative using multivariate mixed-effect model.

Results: Of the 162 patients started short MDR-TB regimen, 58% were males, median age was 32 [IQR 25-40] and 104 (64.2%) were HIV-positive. Mean adherence was constantly greater or equal to 95% during the whole treatment and proportion of patients with an adherence ≥80% was greater than 90% despite a slight decrease during treatment (Figure). In adjusted analysis, the proportion of patients with adherence ≥80% was similar over time between HIV-positive and HIV-negative patients (aOR=0.75, 95%CI 0.22-2.57; interaction with time aOR=1.03, 95%CI 0.76-1.38). A slightly higher proportion of patients with adherence ≥80% was found among females (aOR=4.08, 95%CI 1.07-15.53). In addition, an average adherence ≥80% was strongly predictive of treatment success (positive predicted value 86.8%, 95%CI 79.7-92.1%).

Conclusions: This study shows that adherence to MDR-TB treatment was constantly high during the whole course of treatment both for HIV-positive and HIV-negative patients and that an adherence ≥80% is strongly predictive of treatment success. Efforts to educate patients on treatment adherence is still necessary to ensure good treatment response.



[Adherence]

SOA-09-D9 Achieving UHC: understanding and eliminating catastrophic patient costs in TB care

SOA-09-1085-31 National tuberculosis patient cost survey in Taiwan: design, implementation, and preliminary results

H-K Tseng,[1] P-W Chu,[2] K-Y Liu,[3] S-L Yang,[2] C-Y Chiang,[4] H-Y Chang,[5] B Chen,[6] H-Y Lo,[2] Y-F Huang,[2] H-H Lin,[7] [1]National Taiwan University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan, [2]Taiwan Centers for Diseases Control, Division of Chronic Infectious Diseases, Taipei, Taiwan, [3]National Taiwan UniversityUniversity, Medicine, Taipei, Taiwan, [4]Taipei Municipal Wanfang Hospital, Chest Medicine, Taipei, Taiwan, [5]National Health Research Institutes, Institute of Population Health Sciences, Taipei, Taiwan, [6]National Yang-Ming University, Institute of Public Health, Taipei, Taiwan, [7]National Taiwan University University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan. e-mail: threebriers@gmail.com

Background: Patients with tuberculosis (TB) and their family often incur direct and indirect costs related to the illness. Universal health coverage (UHC) promises to alleviate TB-related costs through reducing medical costs. To document the magnitude of household-level economic burden and to examine the cost-mitigation policy of UHC in Taiwan, we conducted the first national TB patient cost survey.

Methods: We conducted a national cross-sectional survey, adapting the WHO protocol of TB patient cost survey. Among total 5539 TB patients under anti-TB treatment in July of 2018, three waves of samples (632, 646, and 230) were selected from national TB registry using simple random sampling.

All patients with multi-drug-resistant TB (MDR-TB, n=145) were deliberately sampled. Retrospective data on income, medical costs, non-medical costs, and time loss were collected.

Results: Of the 1508 selected patients, 1293 were valid and 548 (480 non-MDR-TB and 68 MDR-TB) participated in the survey. The response rate was 42%; households from metropolitan areas had the lowest rate of participation. Of these 548 participants, 392(72%) were male; 118(22%) were in intensive treatment phase, and the average age was 65. There was a 13% decrease in the average monthly household income (pre-morbid: US$1639, post-morbid: US$1431). TB-affected households reported a loss of work days (29%), and 8% households resorted to loans or sold assets as a coping strategy.

Conclusions: In this national cost survey using simple random sampling, low response rate presented a challenge for home-based interview. Substantial financial burden was still observed in TB-affected households in this high-income setting with well-functioning UHC.

Further analysis is required to estimate the proportion of households experiencing catastrophic costs and the main drivers of the total costs.

SOA-09-1086-31 Catastrophic costs could worsen tuberculosis treatment outcome: a prospective cohort study in Indonesia

A Fuady,[1,2] TAJ Houweling,[1] M Mansyur,[2] E Burhan,[3] JH Richardus,[1] [1]Erasmus MC University Medical Centre Rotterdam, Public Health, Rotterdam, Netherlands, [2]Universitas Indonesia, Community Medicine, Jakarta, Indonesia, [3]Universitas Indonesia, Respiratory and Pulmonology, Jakarta, Indonesia.
e-mail: a.fuady@erasmusmc.nl

Background: The incidence of catastrophic costs due to tuberculosis (TB) is high. Yet, there is a paucity of evidence on the impact of catastrophic costs on TB treatment outcome and adherence. This study aimed to assess whether, and at which threshold, catastrophic costs worsen TB treatment outcome and adherence among TB-affected households in Indonesia.
Methods: During July-September 2016, we interviewed adult TB patients who had undergone TB treatment in 19 primary health centers in Indonesia. One-year after the interview, we followed-up their treatment outcome and adherence, and calculated total costs incurred during the treatment course. Treatment outcome was defined as successful (completed treatment or cured) and unsuccessful (died, failed, or defaulted). Adherence was defined as poor if a patient's treatment period exceeded 14 days or more than the expected end of treatment date or were lost-to-follow up.
Results: We had follow-up data for 252 of the 282 patients (89%) interviewed in 2016. Of these, 18 (7%) patients had unsuccessful treatment and 39 (15%) had poor adherence. Total costs as a proportion of annual household income was not statistically significantly different between patients with successful and unsuccessful treatment outcome (P=0.350), nor between patients with good and poor treatment adherence (P=0.702).
However, the incidence of catastrophic costs was strongly associated with unsuccessful outcome (RR=3.32, 95% CI=1.13-9.69, P=0.029) when using a threshold of 30% of annual household income. Treatment outcome was also affected by job loss (RR=3.87, 95% CI=1.34-11.22, P=0.013) which was partly mediated by catastrophic costs (indirect effect=0.37, 95% CI=-0.36-1.09, $Z_{Mediation}$=0.991, P=0.322).
Conclusions: Along with job loss, experiencing catastrophic costs during TB treatment could worsen TB treatment outcome. The WHO's target of eliminating the incidence of catastrophic costs, as well as the incidence of TB itself, requires innovations by incorporating job and income security programs into comprehensive TB elimination strategies.

SOA-09-1087-31 Proportion of tuberculosis-affected households experiencing catastrophic costs due to TB in Uganda: main cost drivers

W Muttamba,[1] L Mugenyi,[1] C Batte,[1] A Nkolo,[2] S Turyahabwe,[3] F Mugabe,[3] P Lochoro,[4] IG Baena,[5] B Kirenga,[1] [1]Makerere University Lung Institute, Makerere University, Kampala, Uganda, [2]University Research Co., LLC (URC) & Center for Human Services (CHS), Defeat TB Project, Kampala, Uganda, [3]National Tuberculosis and Leprosy Control Programme, Ministry of Health, Kampala, Uganda, [4]Doctors with Africa, CUAMM, Kampala, Uganda, [5]World Health Organization, Geneva, Switzerland.
e-mail: muttamba@gmail.com

Background: Tuberculosis (TB) patients incur large costs related to illness. Other costs are incurred while seeking and receiving health care. Such costs create access and adherence barriers which affect health outcomes and increase transmission of disease. Until the survey, the proportion of households incurring catastrophic costs and the main drivers of these costs were unknown.
Methods: A Cross sectional survey with retrospective data collection and projections was conducted in 2017. A total of 1,178 multidrug resistant (MDR) TB (44) and Drug sensitive (DS) TB patients (1134), 2 weeks into intensive or continuation phase of treatment were consecutively enrolled across 67 randomly selected TB treatment facilities.
Results: Of the respondents, 62.7% were male, median age was 35 years, 55.5% were HIV positive and 3.7% had MDR TB. For each TB episode, patients on average incurred in costs of USD 396 for a DS-TB episode and USD 3722 for an MDR TB episode. Up to 48.5 % of households used any of the three coping strategies (borrowing, using savings or selling assets) to mitigate against these costs. More than half (53.1%) of TB affected households experienced TB-related costs above 20% of their annual household expenditure, with the main cost cost drivers being non-medical expenditures such as travel, nutritional supplements and food.
Conclusions: Despite "free" health care in public health facilities, over half of Ugandan TB affected households experience catastrophic costs. Roll out of social protection interventions such as insurance schemes, and enforcement of legislation on social protection through multisectoral action plans with Ministry of health/ National TB program involvement would palliate these costs.

SOA-09-1088-31 Cost of tuberculosis care: is it catastrophic in a programmatic setting? Evidence from a coastal city in Karnataka, India

A Kibballi Madhukeshwar,[1] V Chandra Shekar,[2]
[1]Yenepoya Medical College, Yenepoya (Deemed to be University), Community Medicine, Mangalore, India, [2]Yenepoya (Deemed to be University), Community Medicine, Mangalore, India. e-mail: docakshay@gmail.com

Background: The End TB Strategy aims to reduce the catastrophic costs due to Tuberculosis (TB) to zero by 2035 among patients and their households. We looked into the direct and indirect costs of treatment and the proportion of patients' households experiencing catastrophic expenditure due to TB under programmatic settings.
Methods: A longitudinal study with three interview points was carried out among 61 newly diagnosed TB patients registered in Mangaluru tuberculosis unit during April to June 2017. A diary was given to each patient to record the cost incurred and a mobile call reminder every 15 days to reiterate this. Tool to Estimate TB Patient's Costs of the Stop TB Partnership was used to collect the data. Data collected was analysed using IBM SPSS for Windows, Version 23.0. Costs were reported as median values. Kruskal-Wallis test and Pearson's Chi-square test were used for statistical analyses.
Results: Median total cost incurred by the patients with during the course of TB treatment was INR 20952 (IQR 14146 - 33046). There was no cost incurred towards diagnostic tests or drugs during the treatment. The direct costs were mostly related to food expenses during seeking care and hospitalization. Indirect cost (one fourth of total) was mostly attributed to decreased income/ loss of wages. Hospitalisation ($p< 0.001$) was found to be associated with increased costs. Thirty seven (60.66%) households experienced catastrophic costs. Eleven patients (18%) resorted to coping strategies.
Conclusions: Despite free diagnostic and treatment services under national TB program, newly diagnosed patients spent a considerable amount towards TB care. Three out of five patients experienced catastrophic expenditure. Involvement of patients' charter in provision of food vouchers, empanelment of tertiary care hospitals to provide hospitalization care and need based social security mechanisms should be evolved by the national TB program.

SOA-09-1089-31 Patients' perception of economic costs of tuberculosis in a low incidence country, Italy: a qualitative research. National Institute for Infectious Diseases ´Spallanzani´, Rome, Italy

S Pittalis,[1] RM Zagarella,[2] GA Gualano,[3] P Mencarini,[3] F Palmieri,[3] C Caporale,[2] E Girardi,[1] [1]National Institute for Infectious Diseases 'Spallanzani', Clinical Epidemiology Unit, Rome, Italy, [2]National Research Council - Section of Rome, Institute of Biomedical Technologies, Rome, Italy, [3]National Institute for Infectious Diseases 'Spallanzani', Respiratory Infectious Diseases Unit, Rome, Italy.
e-mail: enrico.girardi@inmi.it

Background: WHO´s End tuberculosis (TB) Strategy aims to eliminate the potentially devastating economic effects of TB on affected households. Little is known on the economic burden of the disease on patients in low burden countries with universal health coverage.
Methods: A qualitative approach was employed to explore patients' perception on TB costs for them and their household. Twenty-five in-depth semi-structured narrative interviews of patients diagnosed with TB in the last two years were conducted at National Institute for Infectious Diseases "Spallanzani" in January-February 2019. Clinical and demographic data were collected. Interviews focused on: socioeconomic determinants; diagnostic-therapeutic-pathway; knowledge of the disease; perception of direct and indirect TB costs. A content qualitative discourse analysis is ongoing (NVivo software).
Results: A qualitative analysis suggests different perceptions of the costs, needs and challenges faced by our TB patients, according to the heterogeneous epidemiological characteristics (Table 1).
Most of patients reported direct medical and non-medical costs (consultations, medicines, tests, procedures, travel and accommodation) in the prediagnostic period, especially those experiencing a diagnostic delay. Patients reporting long waiting lists at public health facilities faced out-of-pocket expenses for lab tests and radiological procedures in the private sector during the treatment phase.
Patients with a temporary job contract or working in the black market, especially those foreign born, reported indirect costs, income and job loss or missed opportunities, in the whole period from symptoms onset to hospitalization and afterwards. Asylum seekers reported prolonged stay in migrant reception structures because of TB.
Few patients perceived as significant the impact of TB social protection interventions.
Almost all the patients reported low knowledge of the disease and shared fear of stigma and discrimination.
Conclusions: Qualitative research has the potential to identify TB care barriers thorough the patients' voice. Implementing surveys to document TB patient costs in Italy can inform policies for TB prevention and care.

Characteristics		Total N = 25
Sex	Male	18 (72%)
Mean age, years (range)		42 (20-86)
Country of origin	Italy	11 (44%)
	Romania	5 (20%)
	Bangladesh	2 (8%)
	Gambia	2 (8%)
	Other (Albania, Eritrea, Sudan, Mauritania, Brazil)	5 (20%)
Employement	Employed (permanent contract/private business/temporary activities)	11 (44%)
	Student	1 (4%)
	Retired	2 (8%)
	Inactive or black market	7 (28%)
	Asylum seeker	4 (16%)
Highest International Standard Classification of Education level	Secondary or above	13 (52%)
	Lower secondary	9 (36%)
	Primary education	3 (12%)
Site of TB disease	Pulmonary (1 with pleura; 1 with bones and lymph nodes; 1 with larynx; 1 with meningoencephalitis)	21 (84%)
	Extrapulmonary (3 lymph nodes; 1 bones)	4 (16%)
TB Case definition	New cases	24 (96%)
	Bacteriologically confirmed	19 (76%)
Median diagnostic delay, months (interquartile range)		3 (2-8)
Antituberculosis treatment	Treatment success	8 (32%)
	Treatment ongoing: intensive phase	2 (8%)
	Treatment ongoing: continuation phase	15 (60%)

[Patients' characteristics. Qualitative research on tuberculosis (TB) costs. Rome, Italy, 2019.]

SOA-09-1090-31 Social impact of tuberculosis illness in Zimbabwe

M Ngwenya,[1] C Sandy,[2] C Zishiri,[3] R Ncube,[3] D Pedrazzoli,[4] N Mlilo,[3] C Timire,[3] [1]World Health Organisation, Tuberculosis, Harare, Zimbabwe, [2]Ministry of Health and Child Care, Tuberculosis, Harare, Zimbabwe, [3]The Union Zimbabwe, Tuberculosis, Harare, Zimbabwe, [4]World Health Organisation, Tuberculosis, Geneva, Switzerland. e-mail: dr.c.sandy@gmail.com

Background: Tuberculosis (TB) affects the poorest and most vulnerable people and communities, worsening existing levels of income and wealth, perpetuating poverty as well as decreasing the probability of completing testing and treatment. To document the costs incurred by TB patients and the social impact of the disease, in order to guide policies to address barriers to TB treatment access and adherence, Zimbabwe conducted a survey in 2018.

Methods: A nationally representative cross-sectional survey with random cluster sampling among TB patients at 60 public health facilities across Zimbabwe.

Results: Data from a weighted sample of 900 survey participants were analysed. Payments for TB care led to a significant increase in the proportion of households that live below the poverty line at the time of survey compared to pre-TB diagnosis, from 71% to 81%. Patients in the lowest income quintile and multi-drug resistant TB (MDR-TB) patients were found most at risk. Over half (51.6%) of the patients reported that there were unable to pay for TB care from their income alone, and had to rely on borrowing (21.4%) or selling assets (12.3%) or both (17.9%). Up to 62.3% of the poorest experienced dissavings. About a third (28.1%) of the survey participants experienced social exclusion, 5% interrupted schooling, and 27% of respondents reported that they lost their job as a consequence of TB. Coverage of social welfare payments after TB diagnosis was 1.2% with the wealthiest benefiting more than the poorest (2.4% vs 0.5%).

Conclusions: TB-affected people in Zimbabwe were poor and TB illness made them even poorer. The coverage of social protection is very low and TB patients resort to either borrowing and selling assets to finance TB treatment. The government needs to introduce equitable social protection for people suffering from TB in the form of food, transport vouchers, support against social exclusion and income loss.

SOA-09-1091-31 Tuberculosis illness-related catastrophic costs in Zimbabwe

M Ngwenya,[1] C Sandy,[2] C Zishiri,[3] R Ncube,[3] N Mlilo,[3] D Pedrazzoli,[4] C Timire,[3] [1]World Health Organisation, Tuberculosis, Harare, Zimbabwe, [2]Ministry of Health and Child Care, Tuberculosis, Harare, Zimbabwe, [3]The Union Zimbabwe, Tuberculosis, Harare, Zimbabwe, [4]World Health Organisation, Tuberculosis, Geneva, Switzerland. e-mail: dr.c.sandy@gmail.com

Background: Zimbabwe is a high tuberculosis (TB) burden country which has suffered from economic and humanitarian crises for much of the last two decades. Zimbabwe subscribes to the global End TB Strategy target of achieving zero TB-affected households facing catastrophic costs due to TB. In order to monitor progress towards this milestone and to inform national efforts to eliminate catastrophic costs for TB patients, Zimbabwe conducted a survey to assess the magnitude and nature of costs incurred by TB patients during care seeking and treatment, in line with WHO's recommendations.

Methods: A nationally representative cross-sectional survey with random cluster sampling among TB patients at 60 public health facilities across Zimbabwe. Data was collected using an electronic structured questionnaire and analysed using Stata Ver. 15. Statistical analysis accounted for unequal sampling.

Results: Data from a weighted sample of 900 patients were analysed (49; 5.5% MDR-TB). The median expenditure per TB episode was US$1,247. This was three times higher for MDR-TB patients (P-value = 0.001). The largest cost driver was non-medical costs (51%), followed by lost income (36%). Catastrophic costs affected 80% of patients (90% and 79% for MDR-TB and drug-susceptible patients, respectively). The main cost drivers before diagnosis were medical costs while during treatment, it was mainly nutritional supplements and income loss.

Conclusions: TB-affected households suffer catastrophic costs, despite free diagnosis and treatment policy for TB in Zimbabwe. Catastrophic expenditure was mainly driven by medical costs before diagnosis, while during treatment, it was nutritional supplements and income loss. There is an urgent need to accelerate implementation of the proposed roadmap for national health insurance to ensure universal health coverage to mitigate against catastrophic expenditure. Additionally, there is need to curb against income loss due to TB disease and to understand the type, motivation and source of nutritional supplements that are accessed by TB patients.

SOA-09-1092-31 Implementation of cash incentive scheme for patients with tuberculosis in Vadodara, India: a study on coverage and association with treatment outcome

B Patel,[1] J Kathiresan,[2] C Palanivel,[3] M Vijayageetha,[3] K Mehta,[1] D Solanki,[1] B Modi,[4] C Zala,[5] P Dave,[6] H Shewade,[7] [1]GMERS Medical College, Community Medicine Department, Vadodara, India, [2]Velammal Medical College, Department of Community Medicine, Madurai, India, [3]Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Preventive and Social Medicine, Puducherry, India, [4]GMERS Medical College, Community Medicine Department, Gandhinagar, India, [5]Vadodara Municipal Corporation, City TB Centre, Vadodara, India, [6]Government of Gujarat, Public Health, Gandhinagar, India, [7]The Union, South East Asia Office, New Delhi, India. e-mail: drbharatpatel1@gmail.com

Background: Government of India has started a direct benefit cash incentive transfer (DBT) scheme for patients with TB to provide nutrition support and encourage completing the treatment. Scheme provides incentive of 500 INR per month to the notified patients with TB for the entire duration of anti-TB treatment directly in their bank account.The study was done with objectives to evaluate the coverage of DBT scheme and to compare the treatment outcomes among recipients and non-recipients of cash incentive.
Methods: This retrospective record based study included records of all TB patients notified from April to September 2018 and initiated on first line anti-TB drugs. Data was extracted from nikshay portal of city TB centre, Vadodara. Analysis done with EpiData analysis and EpiInfo software. Statistics used were means, proportions, chi-squared test and binary logistic regression.
Results: A total of 2583 patients with TB were notified within 6 months of implementation of DBT scheme, of which 1562 (60%) were from public sector. Partial and complete cash incentive was received by 134 (5.2%) and 266 (10.3%) patients respectively. Among non-recipients of cash incentive three-fourth did not having bank account, more so in private sector ($p< 0.05$). Receipt of partial or complete cash incentive was proportionately more among males, 20-39 year aged, residing within Vadodara city, non-reactive HIV serostatus, re-treatment and extra-pulmonary TB patients compared to their counterpart. Receipt of cash incentive was found to be significantly associated with successful outcome (OR 0.23; 95% CI 0.09 to 0.60) after adjusting for age, sex, place of residence, HIV serostatus and treatment sector.
Conclusions: Cash incentive for patients with TB is associated with successful treatment outcome. However, coverage of the DBT scheme was found to be very low in this study which can be addressed by special provisions from government to open the bank accounts of patients with TB.

E-POSTER SESSION (EP)

EP-01-C7 Person-centred care for improved experiences, services and outcomes

EP-01-100-31 Sentenced to life: exceeding the TB 90% target in resource-limited correctional facilities in South Africa

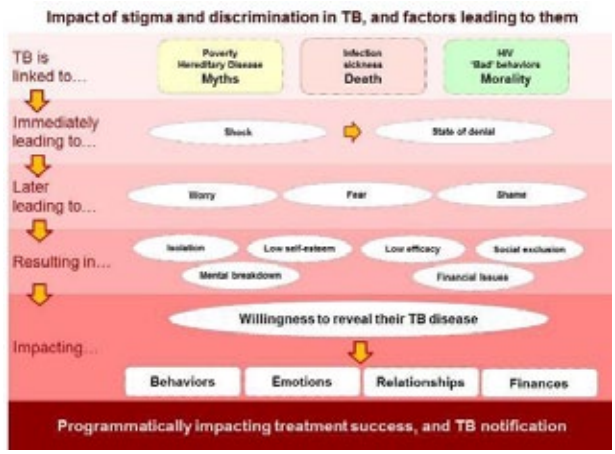
S Govender,[1] S Maseko,[1] T Leseka,[1] A Govender,[1] N Ngozo,[1] P Mandindi,[1] R Oliphant,[1] T Lechuti,[1] J Mohammed,[1] M Busenga,[1] [1]Right to Care, Programmes, Pretoria, South Africa. e-mail: sibusiso.maseko@righttocare.org

Background: South Africa is one of the leading countries in Africa addressing the issue of TB, HIV and STIs in Prison settings in a comprehensive manner through the implementation of its own Health care policies, National Strategic Plan for HIV and AIDS, STIs and TB and WHO guidelines. A comprehensive prevention package (CPP) through the Global Fund for AIDS, TB and Malaria (GFATM) was implemented across 40 Correctional Facilities in the Free State/Northern Cape and Kwa-Zulu Natal Regions. A targeted integrated TB,HIV, STI data collection tool was developed. We analyzed data for the TB cascade measured against the 90-90-90 strategy.
Methods: Patient level data was collected at the point of service using the CPP tool by counsellors. Clients screened as TB presumptive had on-the-spot sputum collected by the counsellor or Enrolled Nurse, and was subsequently isolated for Infection Prevention Control. All MTB Gene-Xpert (GXP) results received were triaged and referred immediately to the nurse for TB Treatment Initiation. All services were documented on standardised stationery, including TB HIV Integrated System (T.H.I.S). Data was captured daily on a tally sheet and T.H.I.S, and aggregated monthly on a standardized reporting template. A retrospective, desktop data analysis was conducted.
Results: Between April 2018 - February 2019, 88,254/90,828 (97%) of newly admitted offenders were screened for TB. 2,574 offenders were not screened due to release/bail. 3,608/3,763 (96%) of Presumptive TB clients received GXP testing with a 9% (n=341) TB positivity rate. 98% (n=334) of TB diagnosed patients were successfully initiated on treatment.
Conclusions: Adequate and trained human resources can result in achieving the 90-90-90 TB targets. A review of the current health staff establishment in DCS is warranted to ensure continuous provision of services and routine monitoring and review of data enables improved quality of services.

EP-01-102-31 Understanding stigma associated with tuberculosis: unravelling a silent barrier to TB care in India

O George,[1] K Chadha,[1] A Bhanot,[1] [1]Abt Associates Inc., IDD, New Delhi, India. e-mail: oommen.geo@gmail.com

Background: Stigma is a phenomenon where someone with a socially discredited attribute is rejected, and disqualified from social acceptance. Stigma in TB is pervasive and tends to be latent, manifesting when the disease becomes known. Stigma is added baggage, and a barrier to effective TB management.
Methods: A multi-fold methodology was used to understand stigma associated with TB in India. This included desk research on stigma, and of health-related anti-stigma media campaigns; focus group discussions with TB-affected and vulnerable groups; in-depth interviews with healthcare providers; technical discussions with stakeholders; and experiential insights. Findings were synthesized using a socio-ecological model of influence to understand how stigma influences people connected to persons with TB, including close family and friends, and others, whose behaviors adversely impact those affected.
Results: The main reasons for stigma are: fear of infection, and belief that TB never goes away, eventually leading to death; fear that TB causes financial ruin; myths and misconceptions on how TB spreads; and prevalent socio-behavioral norms. Stigma results in vicious cycles of isolation, social exclusion, poverty, low self-esteem, and compromised efficacy. It drives persons with TB to hide the disease, programmatically impacting treatment success and TB notification. Stigma affects men and women differently. Stigmatizing attitudes are high in India, and independent of knowledge regarding TB. Current dissemination is mainly medical, inadequately addressing stigma.



[Impact of stigma and discrimination in TB, and factors leading to them]

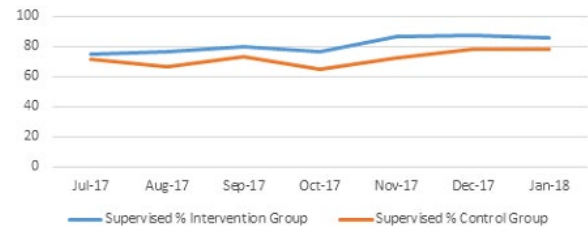
Conclusions: Collaborative efforts are needed to remove root causes of stigma and inspire positive deviance to influence people in the socio-ecological model. Manage-

ment of TB needs to be socially and medically balanced, complementing and influencing each other. Stigma reduction, addressed using a gender approach, makes TB services equitable and empowering. Adopting a vision of 'Stigma-free TB Care' is a step towards the realization of India's goal of TB elimination, with zero catastrophic costs, and optimal acceptance and utilization of RNTCP services.

EP-01-103-31 Animated counselling videos for significantly improved treatment adherence by disadvantaged tuberculosis patients in India

S Batra,[1] S Batra,[2] S Ahuja,[3] D Saxena,[3] [1]Operation ASHA, Technology, New Delhi, India, [2]Operation ASHA, Development, New Delhi, India, [3]Operation ASHA, Operations, New Delhi, India.
e-mail: sonali.batra@opasha.org

Background: Operation ASHA employs Community Health Workers (CHWs) to carry out detection and treatment of Tuberculosis (TB) patients. The CHW's are trained in-depth on all aspects of TB and they are supposed to impart their knowledge to the patients and their family members during counselling. However, there was no method of getting to know whether the CHWs are actually performing their job well or not prior to this study.
Methods: We made a series of 12 counselling videos lasting 3-4 minutes each on all aspects of TB such as effect of missed doses, how to handle side effects etc. Then, we integrated these videos into an application which was loaded on to the Android tablet that is carried by all our CHWs.
We made the workflow such that the videos cannot be fast forwarded or skipped to next before they are shown. There is time allotted after every video for the CHW to add his inputs. Also, on the back end we keep track of the videos that are played, the time durations as well as the time duration of the CHW input.
The hypothesis was that this would increase the adherence to the TB treatment protocol among patients. We conducted a RCT (Randomized Control Trial) to test this hypothesis. We formed an intervention group of 1150 patients and a control group of 1429 patients in 8 cities of India. The trial lasted for 7 months. Only the patients in the intervention group were shown the videos.
Results: At the end of the trial, we found that the adherence of the intervention group was 8.88% higher (82.27% compared to 73.39%) on an average.
Conclusions: 8.88% higher adherence of patients in the intervention group is a significant improvement which proves our hypothesis that animated counselling videos can increase adherence among patients to the TB treatment protocol.



[Monthly Difference Between Control And Intervention Group]

EP-01-104-31 Treatment outcomes of tuberculosis patients on video-observed treatment: prospective country cohort study

A Skrahina,[1] H Hurevich,[2] D Falzon,[3] E Ilyasova,[4] V Akulov,[4] D Klimuk,[5] V Grankov,[6] M Dara,[7] [1]The Republican Scientific and Practical Center for Pulmonology and TB, Clinical Dept, Minsk, Belarus, [2]The Republican Scientific and Practical Center for Pulmonology and TB, Clinical Dep, Minsk, Belarus, [3]World Health Organization, Global TB Programme, Geneva, Switzerland, [4]The Republican Scientific and Practical Center of Medical Technologies, Informatization, Management and Economics of Public Health, Communicable Diseases, Minsk, Belarus, [5]The Republican Scientific and Practical Center for Pulmonology and TB, Monitoring and Evaluation Dept, Minsk, Belarus, [6]World Health Organization, Country Office, Minsk, Belarus, [7]World Health Organization, Regional Office for Europe, Copenhagen, Denmark.
e-mail: alena.skrahina@gmail.com

Background: Video observed treatment (VOT) for tuberculosis (TB) has demonstrated its advantages over conventional directly observed treatment (DOT) in terms of patients' acceptability and treatment adherence. In February 2015, Belarus Ministry of Health, with support from the World Health Organization (WHO), piloted VOT for TB patients in the capital, Minsk. Following a pilot project VOT was expanded countrywide with Global Fund support in October 2016.
Methods: TB patients were provided with smartphones equipped with custom-built software for video recording and transmission, internet access, and instructions on use by trained clinic staff. The Belarus national TB programme (NTP) captured outcomes of VOT treatment prospectively on the countrywide electronic TB register.
Results: Between October 2016 and April 1, 2019, 748 TB patients across the country were recruited: median age 37 years (range:18-69); 61,5% male; 55% employed, 5% students, 34% unemployed, 5% on maternity leave, 1% on military service; 336 (45%) had drug susceptible TB (DS-TB), (33) 4% - rifampicin monoresistant TB, and 379 (51%) M/XDR-TB (MDR-TB - 20%; pre-XDR-TB - 17%; XDR-TB - 14%), 272 (72%) M/XDR-TB patients were on regimens containing new and repurposed TB drugs. Final treatment outcomes were recorded in 317. DS-TB treatment outcomes (215

patients): treatment success - (99%), treatment failure - 1 (0,5%), lost to follow up - 1 (0,5%). M/XDR-TB treatment outcomes (90 patients): treatment success - 78 (86%), treatment failure - 3 (4%), death - 2 (2%), lost to follow up - 7 (8%).
Conclusions: Our data demonstrate excellent treatment outcomes using VOT among patients with DS-TB and M/XDR-TB. The experience gained can promote further expansion of this approach particularly in light of system transition from in-hospital to out-patient based TB care.

EP-01-105-31 "They are inconveniencing us": exploring the need for patient-centred approach to messaging on tuberculosis treatment adherence in the Free State Province, South Africa

N Moodley,[1] A Saimen,[1] N Zakhura,[2] D Motau,[3] G Setswe,[1] S Charalambous,[4] C Chetty-Makkan,[1]
[1]The Aurum Institute, Implementation Research Division, Johannesburg, South Africa, [2]Free State Department of Health, TB Directorate, Mangaung, South Africa, [3]Free Sate Department of Health, Management, Mangaung, South Africa, [4]The Aurum Institute, Science Office, Johannesburg, South Africa. e-mail: asaimen@auruminstitute.org

Background: Non adherence to tuberculosis (TB) treatment contributes to the staggering TB epidemic in South Africa. It is unclear whether treatment interruption stems from poor understanding by patients or from inadequate health education by clinicians. We explored clinician and patient perspectives on the gaps in patient-centred approaches including TB messaging that influence TB treatment adherence.
Methods: This exploratory, qualitative study took place between January and May 2018 at three health facilities in the Mangaung District, Free State Province, South Africa. We conducted semi-structured in-depth interviews (IDI) with a sample of 15 clinicians (2 doctors; 13 nurses) managing TB and seven known loss-to-follow up (LTFU) TB patients. Clinical outcome of LTFU was derived from the TB registers. The IDI guide explored social, cultural and educational aspects of managing TB disease. Audio-recorded interviews were conducted in Sesotho, Setswana and English. Saturation of themes were reviewed during the study procedures. Audio-recordings were transcribed prior to analysis. Manual coding and a grounded theory approach using content analysis was used.
Results: Fourteen females and eight males were interviewed (mean participant age 42 years; SD13.8). Health education that was given to patients during their standard of care clinic visits did not translate into improved clinical outcomes. Patients felt that they were not given the opportunity to be constructively involved in their health management and expressed a need for individual counselling. Many clinicians felt that improving patient's knowledge on TB treatment would reinforce adherence. Clinicians concurred that their medical management lacked the psychosocial dimension to enhance treatment adherence.
Conclusions: Understanding the socio-cultural interface between clinician and patient could improve TB outcomes. Successful management of TB hinges on patient-centred care, clear communication and innovative strategies to convey TB messaging to patients and the community.

EP-01-106-31 Patient-centred community-based multidrug-resistant TB care through community-based volunteers in Yangon, Myanmar: a mixed methods study

AP Phyo,[1] S Saw,[1] KT Soe,[1] S S Majumdar,[2] KS Win,[3] MK Thu,[4] ST Aung,[4] [1]Ministry of Health and Sports, Department of Medical Research, Yangon, Myanmar, [2]Burnet Institute, Health Security, Melbourne, NSW, Australia, [3]Myanmar Medical Association, MDR-TB Project, Yangon, Myanmar, [4]Ministry of Health and Sports, Department of Public Health, Nay Pyi Taw, Myanmar. e-mail: aung.p.phyo37@gmail.com

Background: Myanmar is a high burden multidrug-resistant tuberculosis (MDR-TB) country with known hotspots in Yangon. The national TB program has decentralized treatment to patient-centered MDR-TB care model through community-based volunteers (CBVs) in Yangon since 2014. With the objectives to describe the treatment outcomes of patient-centered community-based MDR-TB (CBMDR-TB) care from 2015-16 and to explore the perspectives of patients receiving care, this study was done in Yangon in 2017-2018.
Methods: Mixed-methods study involving a retrospective cohort study using routine programmatic data and focus group discussions (FGDs) with adult patients receiving care.
Results: There were 2636 MDR-TB patients enrolled in Yangon during 2015-2016 of which 81% were provided patient-centered CBMDR-TB care. The treatment success rate (TSR) for 2015 cohort was 80% and 16% died. For 2016 cohort, 84% was in care and 13% died. Lost to follow-up (LTFU)was 3% and 2%, respectively. The patients in the 25-54 year and ≥ 55 year old age groups were about 2 times and 9 times more likely to have unfavorable outcomes than < 25 year old age group. HIV-positive patients had a significantly higher risk of unfavorable outcomes. Through FGDs, 3 main themes emerged; services received, services needed by MDR-TB patients, their perceptions towards the care model. The majority of the patients had positive perspectives towards the model and valued monetary support most.
Conclusions: CB MDR-TB care by CBVs in Yangon was perceived majority of the patients positively and demonstrated good acceptability with high TSR and low LTFU. Similar treatment outcomes to 2012-14 are maintained as the care model decentralizes from facil-

ity based to clinic-based and to home-based care. The death rate, however, remains high and requires further investigation. Our study shows low rates of LTFU and supports continuation of the model in Myanmar. This should be coupled with future research on effectiveness, feasibility and cost.

EP-01-108-31 Putting communication back into tuberculosis care: implementing an interpersonal communication and counselling model to strengthen management of tuberculosis in South Africa

ZL Dlamini,[1] G Jagwer,[2] R Matji,[2] P Mabota-Rapholo,[3]
[1]University Research Co., LLC - South Africa, Clinical and Diagnostics, Pretoria, South Africa, [2]University Research Co., LLC - South Africa, Management, Pretoria, South Africa, [3]University Research Co., LLC - South Africa, Strategic Communication, Pretoria, South Africa.
e-mail: zamanid@urc-sa.com

Background and challenges to implementation: KwaZulu-Natal province records the highest incidences of tuberculosis (TB), drug-resistant TB (DR-TB) and HIV in South Africa. The USAID TB South Africa Project developed and implemented an interpersonal communication and counselling package to strengthen capacities of healthcare professionals to support patients to adhere to treatment in uMkhanyakude district, KwaZulu-Natal.
Intervention or response: The model's approach includes training healthcare providers to improve communication with patients. Training is presented through a module that favours role-plays. A checklist of 39 communication behaviours, including positive verbal and non-verbal language, psychosocial and medical assessment, treatment education, discussion of psychosocial factors that might impact adherence and treatment goals is included in the module. These behaviours are used to assess counselling practice and form part of a peer mentoring approach. After observation of role plays, feedback is provided.
Results and lessons learnt: A total of 42 healthcare providers from seven healthcare facilities benefitted from intensive capacity building and mentoring sessions over three months. Following training, 52 patients were counselled by trained care providers during a two-week period using the checklist. Peer-to-peer observation to assess the quality of counselling provided to 17 of the 52 patients who consented to the exercise were conducted. It was found that although patients' TB and TB treatment knowledge increased and was reinforced during counselling, medical history was not correctly taken and there were gaps in discussing, recording psychosocial factors that may affect adherence and treatment goals.
Conclusions and key recommendations: Peer observation and mentoring are key to ensuring that treatment communication and adherence counselling is standardized in areas where TB, DR-TB and HIV burdens are high and patients' treatment regimens include many drugs taken over long periods. It is important to routinely observe counselling sessions to improve practice and quality of TB care. This also improves patient-healthcare worker relations. consideration should be made to scale up the intervention.

EP-01-109-31 Adherence to national tuberculosis guidelines among private practitioners in Indonesia: preliminary results from a mystery patient study in Bandung

P Hadisoemarto,[1,2] N Afifah,[1] D Fattah,[1] B Lestari,[1,2] A Salindri,[1] P Hill,[3] B Alisjahbana,[1,4] Tuberculosis Working Group Infectious Disease Research Center Faculty of Medicine Padjadjaran University
[1]Padjadjaran University, Tuberculosis Working Group, Faculty of Medicine, Bandung, Indonesia, [2]Padjadjaran University, Department of Public Health, Faculty of Medicine, Bandung, Indonesia, [3]University of Otago, Dunedin School of Medicine, Centre for International Health, Department of Preventive and Social Medicine, Dunedin, New Zealand, [4]Hasan Sadikin Hospital, Internal Medicine, Bandung, Indonesia.
e-mail: panji.fortuna@unpad.ac.id

Background: Private physicians (PP) have been associated with a lower quality of tuberculosis care. This study aimed to evaluate their clinical decisions in managing pulmonary tuberculosis cases in outpatient settings.
Methods: Observational study using standardized tuberculosis patients (SP) posing as unannounced mystery patients. We developed four cases: (A) patient with classic tuberculosis-associated complaints; (B) case (A) presenting negative microscopy result; (C) case (A) presenting positive microscopy result; and (D) case (A) with recent history of tuberculosis treatment default. SP presented these cases to randomly selected PP (all cases) and community health centers (CHC, cases A and D only) in Bandung and recorded their interactions on a standardized form. Following the national guideline, correct decisions were defined as: (A) referral for sputum examination, (B) referral for chest x-ray and/or prescription of antibiotics, (C) prescription of anti-tuberculosis drugs, and (D) referral for rapid molecular examination.
Results: We trained and sent 12 mystery patients to 320 general practitioners (GP, success rate/SR 70.9%), 32 internist and pulmonologist (SR 89.1%), and 30 CHC (SR 100.0%). GP correctly managed 32.1%, 62.3%, 70.7%, and 38.2% of cases A, B, C, and D, respectively. Specialists correctly managed 18.8%, 55.6%, 66.7%, and 9.1%, respectively. In comparison, CHC correctly managed 86.7% and 40.0% of cases A and D. For cases A and D, the majority of PP requested chest x-ray (GP: 65.7%, specialists: 85.2%, CHC: 6.6%), while request for sputum examination only was low (GP: 7.4%, specialists: none, CHC: 85.0%). Further, eight out of sixteen anti-tuberculosis drugs regimens prescribed by PP were incorrect.

Conclusions: The majority of PP did not follow the national guideline for tuberculosis care. There was a clear preference for chest X-ray over sputum examination; incorrect TB drug prescriptions and the use of irrational antibiotics are of concerns. Re-educating private practitioners on tuberculosis management may be warranted.

EP-02-D7 Finding the "missing" cases: TB, HIV, hepatitis and depression

EP-02-110-31 Development and validation of a prediction model for systematic screening of active tuberculosis among people living with HIV

C-C Yang,[1] Y-J Shih,[1] H Ayles,[2] P Godfrey-Faussett,[3] M Claassens,[4] H-H Lin,[1] [1]National Taiwan University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan, [2]London School of Hygiene and Tropical Medicine, Zambart, Department of Clinical Research, Lusaka, Zambia, [3]London School of Hygiene & Tropical Medicine, Department of Clinical Research, London, United Kingdom, [4]Stellenbosch University, South Africa, Desmond Tutu Tuberculosis Centre, Department of Paediatrics and Child Health, Cape Town, South Africa. e-mail: r06849005@ntu.edu.tw

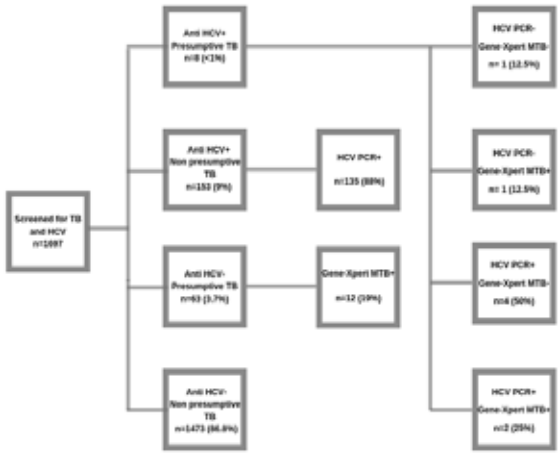
Background: WHO recommends that people living with HIV (PLHIV) should be systematically screened for tuberculosis (TB)-related symptoms. However, the low specificity of the screening tool and the substantial following cost of TB diagnosis cause a heavy burden to resource-constrained areas. A prediction model for TB screening among PLHIV was developed and converted to a scoring system, aiming to provide a simple and less costly strategy with better performance than the conventional screening strategy based on any TB symptoms.
Methods: The study population was based on a 2010 TB prevalence survey in the Zambia/South Africa Tuberculosis and AIDS Reduction (ZAMSTAR) trial. Only individuals with HIV were included in the analysis. The dataset was divided into two parts according to participants' countries for model development (South Africa) and external validation (Zambia). The outcome was prevalent culture-confirmed TB. The potential predictors included TB symptoms, TB risk factors, and previous TB history. The model was built on multivariable logistic regression and selected through stepwise backward elimination based on Akaike Information Criterion. A scoring system was then converted from the model.
Results: The predictors selected in the final model and the corresponding scores are shown as follows: gender(1), weight loss(1), ever drink(2), current cough(2), and chest pain(1). In the training dataset, the area under the curve (AUC) of the scoring system was 0.652 (95%CI: 0.602-0.701), which was higher than the performance of any TB symptoms (AUC 0.568, 95%CI: 0.524-0.612, p-value: 0.00009422). The AUC of the scoring system and any TB symptoms in the Zambian dataset was 0.768 (95%CI: 0.714-0.822) and 0.725 (95%CI: 0.681-0.769) respectively (p-value: 0.1078).
Conclusions: The scoring system for TB screening presented better performance than any TB symptoms in the training dataset and showed slightly increased discrimination in the validation dataset. Future cost-effectiveness analysis should be conducted to provide options with different score cutoffs for resource-constrained settings.

EP-02-111-31 Active screening for hepatitis C (HCV) among people screened for tuberculosis (TB) in a high-burden setting

A Hasnain,[1] S Shah,[1] S Khowaja,[2] U Khan,[3] [1]Indus Health Network, Global Health Directorate, Karachi, Pakistan, [2]IRD Global, Program Development, Karachi, Pakistan, [3]IRD Global, Infectious Diseases, Dubai, United Arab Emirates. e-mail: saira.khowaja@ird.global

Background and challenges to implementation: Pakistan has the 2nd highest burden of HCV and 4th highest burden of TB worldwide. Existing health services manage both diseases as "vertical programs".This approach is not patient-centered and duplicates cost of services in resource limited settings, hence leaving the health structure weak and vulnerable to new challenges.
Intervention or response: In January 2019, we piloted an integrated approach to provide access to rapid HCV testing at an existing mobile van deployed to screen for TB utilizing a chest x-ray based algorithm with further testing by GeneXpert. The van serves a catchment population of 1.5 million people and is linked to TB and HCV treatment services at a tertiary care center, the Indus Hospital (TIH), in Karachi, Pakistan. All patients with no prior evidence of HCV were screened using rapid anti-HCV diagnostic kits. Seropositive HCV cases were referred for reflex HCV PCR testing.
Results and lessons learnt: 1697 patients were screened for TB and HCV with a mean age of 38 years (range: 15 -70 years). Most people screened were young (25%) females (52%). 71 (4%) were presumed to have TB, 8 (11%) were serologically positive for HCV and 6 (75%) of these were also PCR positive. Only 2 (2.8%) patients were confirmed to have active TB and HCV co-infection. Among those non-presumptive for TB, 153 (9.0%) were serologically positive for HCV and 135 (88%) of them were also PCR positive (See Figure 1). All patients with active disease (PCR positive) were referred for treatment.
Conclusions and key recommendations: Early results from screening a sub-population at risk of TB and HCV show higher rates of seroprevalence and active disease

indicating a need for more evidence-based research to:
a) develop strategies that integrate TB and HCV services and;
b) further data on cost-effective approaches in high burden, resource limited settings that can be implemented at scale.

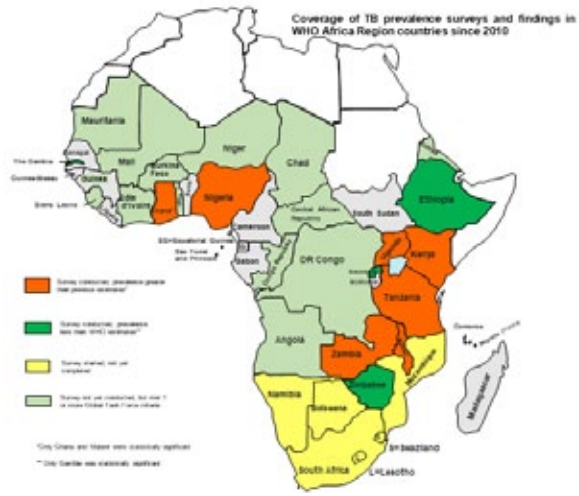


[Figure 1 - Results of TB and HCV screening]

EP-02-112-31 Towards ending TB in Africa: the urgent need for investment in disease burden measurement

F Mavhunga,[1] W Nkhoma,[2] J Iragena,[1] M Gasana,[1] H Lago,[3] [1]World Health Organization, African Region (Afro), TUB, Brazzavile, Congo, [2]World Health Organization, African Region (Afro), TUB, Harare, Zimbabwe, [3]World Health Organization, African Region (Afro), HIV, TB and Hepatitis, Brazzavile, Congo. e-mail: mavhungaf@who.int

Background and challenges to implementation: One key target of the End TB Strategy is an 80% reduction in TB incidence by 2030, compared to 2015. TB prevalence surveys (TBPS) provide a good measure of TB disease burden, but many countries in the African region rely on estimates computed and published by WHO. There's however been progress; 11 African countries have completed their TBPS, and an additional 5 are at various stages of implementation. Key lessons learnt from these surveys are being utilised to catalyse the TB response in the countries; and can inform disease burden measurement in other countries and scale up of the regional TB response.
Intervention or response: We reviewed the overall regional progress and conducted a geo-mapping of the surveys that have been conducted, highlighting how the prevalence compared to previous WHO estimates, with a view to exploring opportunities for applying the results obtained from these surveys to the rest of the region.
Results and lessons learnt: Eleven countries in the African region have conducted TBPS since 2010, while 5 are underway. Of the 11 surveys, 7 (64%) (2 statistically significant) found point prevalence higher than previous WHO estimates, while the rest (36%) found lower prevalence (1 statistically significant). There's no obvious discernible pattern to reliably extrapolate the findings to other countries. The majority of the surveys are in East and Southern African countries, with limited coverage in West and Central Africa, where 13 countries met at least one criterion for justifying prevalence surveys (**see map**).
Conclusions and key recommendations: Conclusions: TBPS are revealing the magnitude of Africa's TB burden, with the point prevalence generally higher than previous WHO estimates. There is however paucity of precise disease burden data in some sub-regions. Achieving the End TB Strategy targets requires better estimates of disease burden in the region as a whole; there is therefore need for urgent investment in TB burden measurement in Africa.



[Coverage of TB prevalence surveys and findings in WHO Africa Region countries since 2010]

EP-02-113-31 The effect of age and sex on tuberculosis case notification rates in South Africa, 2004-2016

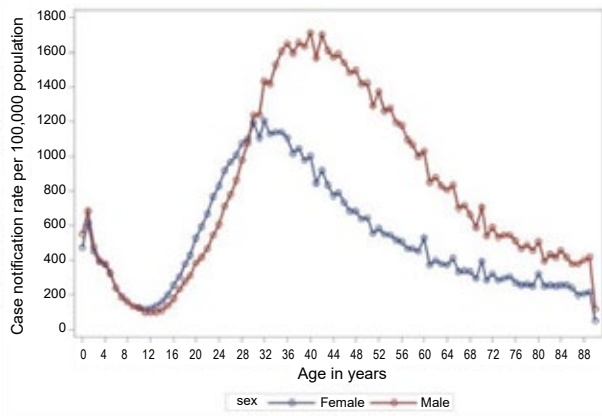
M Osman,[1] K Du Preez,[1] JA Seddon,[1,2] R Dunbar,[1] A Welte,[3] AC Hesseling,[1] P Naidoo,[4] [1]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Cape Town, South Africa, [2]Imperial College London, Department of Paediatrics, London, United Kingdom, [3]Stellenbosch University, SACEMA, Stellenbosch, South Africa, [4]Bill and Melinda Gates Foundation, TB Program, Seattle, WA, United States of America. e-mail: muhammadbinyusuf@gmail.com

Background: Globally, 64% of incident tuberculosis (TB) is estimated to occur in males, consistent with prevalence surveys which have suggested that men are more affected by TB than women. In South Africa, the high prevalence of HIV and the high risk of TB among the HIV-infected populations raise concerns about the

emerging burden of TB disease particularly in young women. We describe the burden of routinely reported TB by age and sex.

Methods: This a retrospective analysis of the South African TB treatment cohort using data from the drug-susceptible electronic TB register for 2004-2016 and the Thembisa model for population denominators. We described the total number of TB patients, the ratio of males-to-females and the case notification rates (CNRs) as the number of notified TB patients per age and sex specific populations for each year.

Results: Between 1 January 2004 and 31 December 2016, 4,479,164 newly registered TB patients were recorded in the national electronic TB register, with an overall male:female ratio of 1.2. The male:female ratio declines from birth and is less than 1 between 10 and 29 years of age, reflecting the increased burden in females. The male:female ratio increases thereafter and peaks at 2 (between 50 and 55 years). The CNR increases in children from birth to 1 years of age and appears slightly higher in males and then declines through childhood. Female CNRs start increasing from 10 years of age, earlier than males, and peak (1,205/100,000) 10 years before the male peak (1,712/100,000).



[South African case notification rate (2004-2016) by age and sex per 100000 population]

Conclusions: In South Africa although the overall burden of TB is greater in males than females, from adolescents to early adulthood the burden of disease is more significant in females. We have also identified an earlier increase and peak in female TB CNRs, possibly driven by high rates of HIV-infection in this group.

EP-02-114-31 A prospective mass tuberculosis screening evaluation of 89,704 diabetic patients in Jiangsu Province, China

Q Liu,[1,2] N You,[1] P Lu,[1] L Zhu,[1] W Lu,[1] [1]Center for Disease Control and Prevention of Jiangsu Province, Department of Chronic Communicable Disease, Nanjing, China, [2]Nanjing Medical University, Department of Epidemiology, Nanjing, China. e-mail: liuqiaonjmu@163.com

Background: China has amongst the highest rates of tuberculosis and diabetes globally. Despite this, the prevalence and clinical characteristics of tuberculosis in diabetes patients remains poorly-characterized in China.

Methods: In 2017, the National Basic Public Health Service Diabetes Patients Physical Examination Project was conducted in 38 township community health service centers in Jiangsu Province, China. Physical examinations were conducted and included fasting blood glucose, liver and kidney function, chest radiographic examinations, lifestyle, among others.

We then linked the electronic diabetes system with the Tuberculosis Management Information System to link active tuberculosis patients.

Our main study outcome was prevalent tuberculosis, defined as tuberculosis diagnosed within 8 months of the physical examination.

Results: In this survey, 89,704 diabetes patients were enrolled in this study. Mean age was 65 years (SD, ±9.8) and 34,463 (38.4%) were male.160 tuberculosis patients were diagnosed (prevalence, 178.4/100000). Mean fasting blood glucose was 8.12 in all patients and 8.86 in diabetes-tuberculosis patients. On multivariate analysis, female (aOR 0.45, 95% CI 0.31-0.642), quiting smoking (aOR, 3.76, 95% CI 2.05-6.94), and body mass index ≥24 (aOR, 0.58, 95% CI 0.42-0.81) were statistically associated with prevalent tuberculosis. Age and fasting glucose levels was not associated with disease.

Conclusions: We demonstrated the feasibility of a large provincial-wide tuberculosis screening program among almost 90 thousand diabetic patients. The prevalence of tuberculosis among diabetes patients was 2-fold higher than the general population in our province suggesting the need for active tuberculosis screening.

EP-02-115-31 Improving reporting rates of TB diagnostic and treatment units in the National HMIS Reporting System

P Tumwesigye,[1,2] T Kiyemba,[1] T Nsubuga-Nyombi,[3] A Nkolo,[4] [1]University Research Co. LLC- USAID Defeat TB Project, Monitoring, Evaluation & Learning, Kampala, Uganda, [2]National TB and Leprosy Program, Ministry of Health, Monitoring & Evalution, Kampala, Uganda, [3]University Research Co. LLC- USAID Defeat TB Project, Quality Improvement, Kampala, Uganda, [4]University Research Co. LLC- USAID Defeat TB Project, Project Lead, Kampala, Uganda. e-mail: tkiyemba@urc-chs.com

Background and challenges to implementation: In October 2017, the USAID Defeat TB Project started to strengthen TB care service delivery in Uganda with emphasis on the capital, Kampala, Wakiso and Mukono. This mandate includes improving reporting on TB care services. The average report submission rate was 75% for all three districts for the July-September 2017 reporting period. This was attributed to limited attention given to quarterly reporting in the DHIS2 platform since District & TB Leprosy Supervisors (DTLS) focused, compiled and reported independent reports to the National TB and Leprosy Program; leading to lower reporting rates in the national DHIS2 platform. DHIS2 is the official Ministry of Health reporting platform.

Intervention or response: To close this gap, the project worked with the National TB & Leprosy Program (NTLP) to change the reporting channel from a DTLS reporting system which fostered a single submitted district report to web-based electronic system (DHIS2.) that required individual TB Diagnostic and Treatment Units (DTU) to report. The project supported the DTLS and Health Sub-District TB focal persons to train TB focal persons at each DTU to report into DHIS2. District TB performance review meetings were held to further enhance data cleaning and entry skills.

Results and lessons learnt: By September 2018, there was a 23% increase (from 75% to 97%) in submission of reports as shown below.

		July - Sept 2017		July - Sept 2018	
Name	Expected Reports	Actual Reports	Percent	Actual Reports	Percent
Kampala District	71	45	63%	67	94%
Mukono District	26	24	92%	26	100%
Wakiso District	82	65	79%	80	98%
Total	179	134 (2,220 notified)	75%	173 (2,841 notified)	97%

[Report Submission Rates for Kampala, Wakiso and Mukono Districts]

Conclusions and key recommendations: Focus on a single reporting system coupled activities directed towards improving health worker knowledge for TB data compilation plus regular data review improves report submission rates. It is also critical to adopt a single national reporting system for the best system strengthening results.

EP-02-116-31 Innovative approach to TB case finding in Muslim communities in northern Nigeria: the experience of "Uwargida" (Housewife) Community TB Care Initiative

AAb Dikko,[1] U Sani,[2] A Habibu,[3] BM Yakasai,[4] B Nsa,[2] I Aliyu,[5] U Emperor,[6] [1]KNCV Challenge TB, Programmes, Kano, Nigeria, [2]KNCV Challenge TB, Programmes, Abuja, Nigeria, [3]KNCV-Challenge TB, Programmes, Kano, Nigeria, [4]Ministry Of Women Affairs and Social Development, Social Development, Kano, Nigeria, [5]Kano State Ministry of Health Tuberculosis and Leprosy Control Programme, Public Health and Disease Control, Kano, Nigeria, [6]National Tuberculosis and Leprosy Control Programme, Public Health and Disease Control, Abuja, Nigeria. e-mail: abdurrazaq.dikko@kncvtbc.org

Background and challenges to implementation: TB treatment coverage in Nigeria has remained at 24% with an estimated incidence of 219/100,000 population (2018 Global TB report). The intervention is aimed at improving TB case finding and treatment adherence in Hausa Fulani predominantly Muslim communities in northern Nigerian.

Intervention or response: The Uwargida community TB care initiative adopted a household approach by empowering a senior house wife in a polygamous home to identify and refer those family members, neighbors and friends who are found to have presumptive TB to a DOTS center. One hundred housewives from one hundred communities were selected through community-based organization (CBOs) in 5 local government areas in Kano state. These women were provided with skills and knowledge on identification of presumptive TB, appropriate referral and treatment support for TB patient in the community to ensure adherence. Courier services were engaged to transport sputum specimen from DOTS clinics to designated GeneXpert laboratories. National community TB recording and reporting tools were used by the housewives to document presumptive TB referred. Hijab outfits were provided to the housewives for recognition and acceptance in families and neighborhood within the communities. Advocacy and community sensitization were made to traditional and community leaders and officials of the Ministry for Women Affairs.

Results and lessons learnt: From July 2018 to March 219 a total of 13,235 presumptive TB cases were identified by the housewives and appropriately referred to the DOTS Centres in their communities. 8549 (64%) were tested and 294 new TB cases were detected and commenced on appropriate TB treatment. This contributed an increase of 11% in total TB cases detected in the LGAs.

Conclusions and key recommendations: Household units can be effectively and efficiently utilized to improve TB case finding in traditional Muslim communities in Northern Nigeria. The intervention can likely be effectively implemented in other traditional Muslim communities of Sub-saharan countries.

EP-02-117-31 Engaging private practitioners for early HIV screening and treatment initiation of tuberculosis (TB) patients in Mumbai, Maharashtra

J Thakker,[1] S Gupta,[1] V Jondhale,[1] AA Sayyed,[2] P Mahesh,[3] R Gandhi,[1] A Hegde,[1] R Chopra,[1] P Koiri,[1] S Vijayan,[1] [1]PATH, Global Health, Mumbai, India, [2]Maharshtra Janavikas Kendra, Public Health, Mumbai, India, [3]Alert India, Public Health -TB, Mumbai, India. e-mail: jthakker@path.org

Background and challenges to implementation: India with estimated 2.8 million TB patients, has documented 87,000 HIV co-infected cases of which 12,000 (14%) died. Although there is a policy on 100% screening of TB patients for HIV, there is lack of documentation of the patients in private sector. During 2014-17, PATH implemented a Private Provider Interface Agency (PPIA) model which notified >65,000 TB patients by engaging private healthcare providers in Mumbai. As a pilot, within this project in 2016, private providers were sensitized to screen TB patients for HIV and refer them to public sector for confirmation of diagnosis and further continuum of care.
Intervention or response: All TB patients notified by private providers in engaged facilities were screened for HIV at private laboratories through a reimbursement model between the laboratories and subcontracted CBO. A dedicated cadre of Link Counsellors (LCs) supported the patients in care cascade to ensure linkages for treatment initiation and retention. Public sector providers were trained to fast track TB patients for HIV confirmation and treatment. Thus, if TB patient is screened HIV reactive, the LCs facilitates confirmation of diagnosis at the ICTC and same day treatment initiation at ART centers.
Results and lessons learnt: Out of 12,535 TB patients notified from 135 private facilities, 9,098 (75%) were screened for HIV. Of these, 262 were TB-HIV co-infected patients (2.9% HIV positivity). 79 (30%) were already on ARV treatment; and of the 183 newly diagnosed patients, 157 (85%) were confirmed for HIV and 147 (94%) were linked to ART centres. The average time taken for linkage to the public sector ICTC was 5 days and 7-14 days for treatment initiation.
Conclusions and key recommendations: The intervention demonstrated early HIV screening of TB patients in private sector and linkage public sector for timely treatment and provided a platform to engage with the government for scaling up HIV case finding in high-burden TB districts.

EP-02-118-31 Reducing TB burden among women through gender-sensitive programming

S Muhib,[1] AB Zahirzai,[1] MK Seddiq,[2] N Ahmadzada,[2] [1]ACREOD, TB, Kabul, Afghanistan, [2]NTP, TB, Kabul, Afghanistan. e-mail: acreod@gmail.com

Background and challenges to implementation: Women carry higher (57%) burden of TB then men in Afghanistan whilst socio-culturalThe TB REACH initiatives funded a project that focused on engaging school age girls in TB screening to respond women/girls' challenges in access to TB care services in remote high TB burdened villages.
Intervention or response: The intervention began in coordination/consultation with governmental sectorial departments, community leaders and girls' schools in-charges and training of 650 school-aged girls. The schoolgirls conducted the screening in 60 TB high burdened villages in Kabul province, and they linked presumptive TB patients to MobileTB services for chest X-ray, sputum collection and ultimately GeneXpert test. Moreover, Imams of mosques were continuously engaged in sharing TB messages to Jummah prayer worshipers in the respective villages.
Results and lessons learnt: During Oct 17-Dec 2018, 182,404 women in villages were screened by schoolgirls. 13,722 presumptive TB patients were identified and 12,640 referred. 68% (8,555) of the referred attended mobile TB services and 59% (5,007) of them were confirmed presumptive, who re-screened by medical doctor. 79 % (3,973) of women/girls consented to have a chest X-ray and 54% (2,719) were able to provide sputum samples for GeneXpert test that resulted in the diagnosis of 188 bacteriologically confirmed, 168 clinically confirmed and in total 356 all forms TB. The intervention reduced restrictions for women in accessing TB services due to involvement of the religious scholars and community leaders as part of the project implementer, female staff as service provider, having services closer to their residential areas. However, 32% of women, who were referred to mobile TB team, didn't attend the services, possibly due to stigma attached to TB, physical conditions or managing housework.
Conclusions and key recommendations: In Afghanistan, women are one of TB key affected population. Women gender specific interventions enable TB program to further reach women with TB.

EP-02-119-31 Overcoming the challenges of electronic TB data entry in internet network constrained areas using e-TB Manager Offline Mobile Application

H Akande,[1] A Adeoti,[1] O Chijioke-Akaniro,[2] B Tifase,[1] A Lawanson,[3] B Assefa,[4] P Suarez,[5] [1]Management Sciences for Health, Health Program Group, Abuja, Nigeria, [2]National Tuberculosis & Leprosy Control Program, Monitoring & Evaluation, Abuja, Nigeria, [3]National Tuberculosis & Leprosy Control Program, Programs, Abuja, Nigeria, [4]Management Sciences for Health, Health Program Group, Addis Ababa, Ethiopia, [5]Management Sciences for Health, Health Program Group, Arlington, VA, United States of America. e-mail: hakande@msh.org

Background and challenges to implementation: In 2016, an electronic management information system for TB cases, called e-TB Manager, was launched in Nigeria. DOTS officers in high-burden facilities and TB local supervisors (TBLS) managed TB cases from presumptive to confirmed and until completion of treatment on the tablet provided. Using the web portal requires stable internet, users in internet network-constraint areas found it difficult to enter and manage cases on the system due to unstable internet connection, which resulted in the delay of timeliness uploaded data.

Intervention or response: USAID-funded Challenge TB (CTB) project supported the development of the e-TB manager offline mobile android application after consultation with NTP and other stakeholders. This application enables users to enter case data and manage them without internet connection. Once connected to internet, the data will be synchronize to the server. The goal of this effort is to optimize the use of electronic TB case management, address internet issues in network-constrained areas, and ultimately eliminate the use of paper-based TB registers for case management and reporting.

CTB conducted training for TBLS in fourteen CTB states between May - August 2018.While NTP conducted the remaining sixteen states and the capital city to complete the training of 370 DOTS officers and 774 TBLS across the country.

Results and lessons learnt: Offline mobile data entry accounts for 8.1% of the total upload at baseline (February 2018) compared to 56.8% at end line (December 2018) (Figure 1).

[Comparison of new TB case data entry on Web portal and Offline mode mobile app.]

In September and December 2018, cases uploaded through offline mode surpassed cases uploaded through the web portal.

Conclusions and key recommendations: e-TB offline mobile implementation in Nigeria helped strengthen TB case data entry in internet network-constraint areas. Stakeholders should leverage this application to optimize electronic TB case management in areas with unstable or no internet network across the country.

EP-03-C12 Fighting back: keeping the tobacco industry at bay

EP-03-120-31 Cigarette industry and bidi-related myths: a case study from Sri Lanka

S Kandeepan,[1] MN Perera,[1,2] H Wijesooriya,[1] C Perera,[1] S Lakmal,[1,3] I Fernando,[1,3] P Dineshkumar,[1,4] M Rajasuriya,[1,5] [1]Faculty of Medicine, University of Colombo, Centre for Combating Tobacco, Colombo, Sri Lanka, [2]Faculty of Medicine, University of Kelaniya, Public Health, Kelaniya, Sri Lanka, [3]Alcohol and Drug Information Centre (ADIC), Strategic Intervention Programme, Colombo, Sri Lanka, [4]Alcohol and Drug Information Centre (ADIC), North and East Programme, Colombo, Sri Lanka, [5]Faculty of Medicine, University of Colombo, Psychiatry, Colombo, Sri Lanka. e-mail: sathuri92@gmail.com

Background: Ceylon Tobacco Company (CTC), a subsidiary of British American Tobacco, owns 99% of the cigarette market in Sri Lanka. Further, CTC is directly involved in the complete production process of cigarettes: tobacco cultivation, cigarette manufacturing and distribution to retailers. Globally tobacco industry is known to use false arguments to protect their business. This study aimed to explore "the beedi issue" highlighted in public information domains and its potential association with the cigarette industry.

Methods: Investigative research techniques were used. Publications in the TobaccoUnmasked website, documents from the Truth Tobacco Documents library related to Sri Lanka, and local media reports that mentioned 'beedi' were analysed using a mixed inductive-deductive thematic analysis method.

Results: Twenty seven articles and documents were identified from 1983, highlighting a range of beedi related issues against increasing cigarette tax. All were based on either an unreviewed 'survey report' or an 'expert opinion'. The main stated argument was the alleged diversion of consumers to beedi due to increase of cigarette tax, an assumption not supported by scientific evidence. Minister of Finance used the same argument to oppose the ban on single stick cigarettes sales in 2018. Beedi use has been constantly low during the past two decades according to national statistics and scientific research.

CTC annual reports published their own research that reported exponentially high proportional beedi use rates (around 40%) among smokers compared to contemporarily published scientific research (< 8%). Media reports quoted beedi rates given by CTC supporting the argument against cigarette tax increase.
Conclusions: Cigarette industry in Sri Lanka has been involved in propagating myths related to beedi, misleading successive governments and the public for the past 35 years, negatively influencing tobacco control policies and actions.

EP-03-121-31 Performance of FTND in assessing dependence among tobacco users in Indian settings

P Jena,[1] S Das,[2] [1]Kiit Deemed to be University, School of Public Health, Bhubaneswar, India, [2]Central Institute of Psychiatry, Nursing, Ranchi, India.
e-mail: drpratapjena@gmail.com

Background: Two important components of Fagerstrom test for Nicotine Dependence (FTND) i.e. cigarette per day (CPD)use, and time to first cigarette (TTFC) are less reliable in Indian settings considering lower average CPD and simultaneous use of myriad variety of tobacco products. In this context this study explores the performance of FTND in Indian settings.
Methods: A cross sectional survey was carried out in Cuttack District using a adapted and composite tool of Global Adult Tobacco Survey, FTND Scale and international Classification of Disease (ICD) 10th edition clinical criteria. Both dependence measures were compared with its outcome measures like quit intention and quit attempt. Only exclusive cigarette users were considered for analysis. A ROC curve was plotted to identify best cut off points for FTND score in correctly identifying tobacco dependence as identified by ICD-10 criteria.
Results: The burden of moderate to high nicotine dependence (FTND score≥5) was 32.3% and tobacco dependence was 35.7%. The concordance between them was 73.5%. In cigarette-only use setting, moderate to high dependence was explained 33.5% of no quit attempt (p=.124) and 14.5% of no quit intention (p=.029). ICD-10 dependence criteria could significantly differentiate between no quit intention and definite quit intention as well as between quit attempt and no quit attempt. The ROC-curve analysis suggested the FTND score of 3 can have sensitive of 91.5% and specificity of 87.5% in identifying clinical tobacco dependence.
Conclusions: The study suggest lowering of FTND criteria to categorize dependence level in India setting which may be attributed to the lower mean CPD use in Indian context. However considering increase in CPD use from 2009 to 2016 as indicated in GATS surveys, the result may be interpreted with caution. Further study is required to validate FNTD in Indian context.

EP-03-122-31 Capacity building in generating greater media attention on tobacco control: current trends in tobacco-related media coverage in Bangladesh

AK Azad,[1] M Hossein,[1] [1]PROGGA, Tobacco Control Program, Dhaka, Bangladesh.
e-mail: azad.bd1971@yahoo.com

Background and challenges to implementation: Traditional media outlets in Bangladesh play vital roles in raising mass awareness and influencing policymakers on different issues. But, tobacco control issues are yet to get ample media attention despite 1,26000 tobacco-related deaths annually. On this predicament, PROGGA initiated its earned media initiative in 2010 to develop stronger media support-base through capacity building of journalists on important tobacco control policies including tobacco control legislation and tobacco taxation. It trained over 350 journalists working nationwide in different media outlets. The trained journalists are followed up regularly to focus tobacco control related media pieces on their respective media. Consequently, training with regular follow-ups has had a significant impact on tobacco control issue and media coverage increase supporting ongoing tobacco control advocacies in Bangladesh. The study demonstrates impacts of capacity building initiative in generating greater media attention on tobacco control issues based on media monitoring information and analysis.
Intervention or response: A comparative analysis of media coverage on tobacco control issues for a week (29 May to 4 June) marking World No Tobacco Day of 2011, 2012, 2013, 2014, 2015, 2016 and 2017 is compared to find the impact of capacity building and regular follow up with trainees.
Results and lessons learnt: The study witnesses a massive change in number of media pieces on tobacco control issues over the years - it was 330 in 2011 and reached to a ceiling of 1746 in 2017. Remarkably, the media pieces dealt in various issues related to advocacy priority (i.e. tobacco control legislation and taxation). The trend continues. The figure shows upsurges in number of reports, features/ articles, editorial etc. in 2017 compared to 2011.
Conclusions and key recommendations: In spite of various constraints, PROGGA's earned media initiative has resulted in considerable impact on generating greater media attention for important tobacco control advocacy in Bangladesh.

EP-03-123-31 Mobilising organised media support for tobacco control policy advocacy in Bangladesh

MS Alam,[1] A Zubair,[2] [1]PROGGA, Tobacco Control Program, Dhaka, Bangladesh, [2]PROGGA, Tobacco Control and other Programs, Dhaka, Bangladesh.
e-mail: shahed.progga@gmail.com

Background and challenges to implementation: Tobacco control was traditionally marginalized in Bangladesh society. The trend reversed recently due to emergence of organized Journalists' platform called 'Anti-Tobacco Media Alliance' (ATMA). The Alliance got over 350 journalists from print, electronic and broadcast media - involved in both reporting tobacco control issues and advocating for stronger tobacco control policies. The present illustration shares how an organized media support played a vital role in tobacco control policy advocacy in Bangladesh particularly for law amendment and tobacco taxation.
Intervention or response: PROGGA facilitates ATMA members - representing major media outlets- through series of trainings on tobacco control issues. The trained journalists felt necessity of an organized platform that created the Alliance. PROGGA, the ATMA secretariat, continued its interactions with member journalists round the year to make it an integral part of the mainstream tobacco control movement in Bangladesh.
Results and lessons learnt: ATMA has become one of the key drivers in stronger tobacco control legislation formulation processes. Whenever the process experienced barriers at different stages, the Alliance of the journalists has always appeared as an organized force in fighting those barriers. Besides, reporting in respective media, the journalists as a group organized different events to draw attention of policymakers and public on the need for moving the process of stronger tobacco control law forward. Similarly, for increasing tobacco taxes, the Alliance has been very vocal particularly before and after announcement of national budget. Finally, all the ATMA activities for stronger tobacco control legislation and demand for higher tobacco taxation received lots of media attention and substantial policy buy-in.
Conclusions and key recommendations: The earned media environment created by Anti-Tobacco Media Alliance contributed significantly in advancement of tobacco control advocacy in Bangladesh.

EP-03-126-31 How multinational tobacco companies are targeting school children in Africa

L Sessou,[1] B Sim-Yassah,[2] C Ayong,[1] [1]African Tobacco Control Alliance, Communications, Lome, Togo, [2]African Tobacco Control Alliance, Programs, Lome, Togo.
e-mail: sessou@atca-africa.org

Background and challenges to implementation: In Africa, multinational tobacco companies are aggressively engaged in marketing their deadly products with a view to increase consumption and profits at a time when sale of these products is decreasing in developed countries. Vulnerable groups like children are being systematically targeted to create a new generation of young smokers who could eventually replace those lost in rich countries and those who die due to tobacco-related conditions.
Intervention or response: Civil society organisations in eight African countries conducted a study to understand the marketing practices of BAT, PMI and other tobacco companies around primary and secondary schools. These countries were Benin, Burkina Faso, Cameroon, Madagascar, Nigeria, Sierra Leone, Uganda, and Zambia. Interviewing and observational techniques were used to collect data. It also included high-quality pictorial evidence of tobacco industry activities around the schools.
Results and lessons learnt: The study reveals that tobacco multinational tobacco companies are using five main strategies to target African children, namely:

- High density of cigarette sale outlets around schools
- Sale of single cigarettes
- Sale of flavoured cigarettes
- Advertising and promotion
- Non-compliance with existing laws

In Zambia, for example, it was found that there were 672 tobacco sale outlets around the 30 schools surveyed. In Madagascar, 297 tobacco sale outlets were found around the 20 schools surveyed.
Conclusions and key recommendations: Africa is likely to become the epicentre of the tobacco epidemic in the not-too-distant future if the tobacco industry is not contained in its attempts to make Africa its next frontier. There is an urgent need for governments in Africa to domesticate the WHO FCTC by adopting and implementing comprehensive tobacco control policies aimed at protecting its populations and especially vulnerable groups like children.

EP-03-127-31 Assuring sustainability of funding for tobacco control by using taxation is possible: an example from Chad

D Elhadj Adam,[1] N Mbairo,[2] S Yaya,[3] [1]The Union, Tobacco Control, Ndjamena, Chad, [2]Ministry of Health, Tobacco Control, Ndjamena, Chad, [3]Chadian Consumers Association, Tobacco Control, Ndjamena, Chad. e-mail: dadam@theunion.org

Background and challenges to implementation: Many African developing countries are facing several challenges for implementating the FCTC. Lack of internal funding is one of principle challenges. Chad has done significant progress in the implementation of the FCTC but since the adoption of FCTC in 2006, tobacco control activities has been funded more by partners. Sustainability of funding is the challenge of this country who engaged to faithing tobbacco during the 6 last years. Different strategies and actions for internal funding have been used and started to produce interesting results.

Intervention or response: Raising taxes on tobacco, one action of MPower of the WHO has triple main benefits:
1) to reduce consumption of tobacco and tobacco-related burden of disease and deats, and
2) to raise revenue for the state budget
3) to provids internal funding for tobacco control activities.

Two studies on funding tobacco control by using taxation have been done. The data collected strengthened capacity building of the staff of Ministry of Health, Finance, civil society and parliamentarians on taxation and on advocacy for using taxation for funding tobacco control.

Each of the steakeolders including government used theses evidences in their advocacy, lobby for a common goal of introducing a tax dedicated to tobacco control and others deseases.

Results and lessons learnt: As results, the Parliament has adopted in the national Budget of 2019, a specific tax of 100 XAF (0,17usd) per cigarette pack dedicated to the Health (30% to tobacco control and 70% for NCDs HIV, and Health coverage).

Conclusions and key recommendations: The new specific tax increased the price of cigarett pack for 18% and offer a sustainability funding to tobacco control and other diseases. This successful achievement of Chad is an excellent example for African countries for assuring the sustainability funding of tobacco control.

It is also, a good example of collaboration between Government, experts, parliament and civil society.

EP-03-128-31 Tobacco use among patients suffering from non-communicable diseases: results from two districts of Punjab

G Bhatt,[1] S Goel,[2] N Kaur,[3] [1]PGIMER, School of Public Health, Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research (PGIMER), Community Medicine and School of Public Health, Chandigarh, India, [3]Goverment of Punjab, Health and Family Welfare, Chandigarh, India. e-mail: garimabhatt.90@gmail.com

Background: Tobacco use is a major preventable and modifiable behavioural risk factor for Non Communicable Diseases (NCDs), leading to around 7 million deaths worldwide. The objective of this study was to assess tobacco use among patients suffering from non communicable diseases attending NCD clinic in two districts of Punjab.

Methods: It was a cross sectional study conducted between May to September 2018 in SAS Nagar and Fatehgarh districts of Punjab. The adult patients, aged 30 years and above, suffering from any NCD (Diabetes, Cardiovascular diseases, Stroke, Cancer, Chronic Respiratory Diseases, Hypertension) and attending NCD clinics at district level were enrolled. Using p =50% and d=3%, a resultant sample size of 1068 was calculated. Thereafter, these patients were administered pre tested questionnaire by the researcher to assess tobacco use after obtaining their informed consent.

Results: So far, data for 837 participants has been analyzed of which 29.03 % have diabetes, 41.81% have hypertension, 2.86% have COPD, 0.95 % reported CVD and 23.6% had both Diabetes as well as Hypertension. Of these, 9.8% Diabetics, 10.2% Hypertensives, 91.6% COPD, 25% CVD and 3.03 % of (Diabetics + Hypertensives) are reported tobacco users.

Conclusions: These NCD patients who are tobacco users as well provide an opportunity to the health care providers at NCD clinic to impart a tobacco cessation intervention which will help them quit. The tobacco cessation services should be an integral part of duties of a health care provider at NCD clinics.

EP-03-129-31 Evolution of tobacco and marihuana consumption during pregnancy in low SES populations in Uruguay

R Magri,[1] MF Fleming,[2] E Ostrander,[3] A Baldwin,[4] N Hayes,[5] M Martinez,[6] P Cabral,[7] [1]Universidad de la Republica de Uruguay, Obstetrics, Montevideo, Uruguay, [2]Northwestern University, Family Medicine, Chicago, IL, United States of America, [3]Northwestern University, Feinberg School, Chicago, IL, United States of America, [4]USDTL, Research, Chicago, IL, United States of America, [5]Northwestern University, Psychology, Chicago, IL, United States of America, [6]Universidad de la Republica de Uruguay, Facultad de Odontologia, Montevideo, Uruguay, [7]Universidad de la Republica de Uruguay, School of Sciencies, Montevideo, Uruguay.
e-mail: magri.raquel@gmail.com

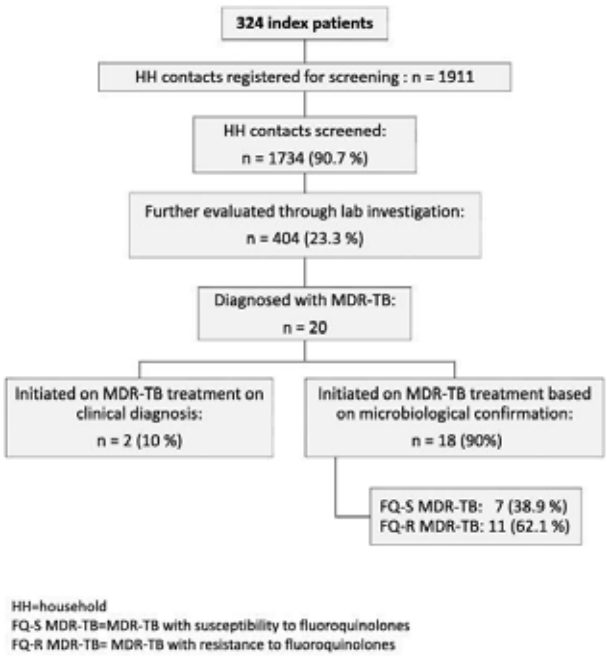
Background: Tobacco and marijuana used during pregnancy act negatively on the mother and the fetus. Tobacco is the second most consumed substance in Uruguay. 28.1% of women of childbearing age in the general population smoke tobacco and 6.4% use marijuana.
Since the Marijuana law 2013, the state regulates its market, production and marketing, although the campaigns and measures have highlighted the risk associated with the use of both.
In Montevideo, tobacco consumption in pregnant women of low and middle income has been studied with surveys and biomarkers. The results showed a tobacco consumption between 41.3% in 2005, 30.8% in 2007, 38.8 * in 2009 and 1.5% of marijuana consumption in 2005, 1.4% in 2009 and 0.4% in 2011.
Methods: In our current study during 2017, 233 women with similar SES (low and middle) were interviewed in a public hospital after giving birth and were asked about tobacco and marihuana use during pregnancy and about preventive education provided by their health care providers.
Results: The results showed that 10.7% of those mothers continued smoking tobacco daily and 6.3% smoked marijuana during pregnancy. Although tobacco decreased consumption, marijuana raised it.Surprisingly, only 27.9% of these women reported receiving education about substance use prevention during their antenatal visits.
Conclusions: There seems to be an information gap provided to vulnerable populations, such as pregnant women. These preliminary findings suggest that tobacco and marijuana use continues to be a serious public health problem in Uruguay despite the greater focus on campaigns and should be enhanced on vulnerable populations and at education schools such as Medical, Social, Dental, Nursing and others at different levels.

EP-04-D6 TB epidemiology and prevention interventions

EP-04-130-31 High prevalence of multidrug-resistant tuberculosis among household contacts in a high TB-burden setting

S Ahmed,[1] P Khan,[2] Z Ali,[1] S Adnan,[3] J Singh,[3] U Khan,[2] [1]Interactive Research and Development (IRD), endTB, Karachi, Pakistan, [2]Interactive Research and Development (IRD), Global, endTB, Karachi, Pakistan, [3]Indus Health Network (IHN), Global Health Directorate (GHD), Karachi, Pakistan. e-mail: saman.ahmed@ird.global

Background: Household contact investigation of multidrug-resistant tuberculosis (MDR-TB) patients is an integral component of MDR-TB care. However, in Pakistan poor literacy rate, lack of accessible TB screening facilities, and social stigma, as well as health system deficits act as barriers to the scale up of contact investigation.
We present the findings of contact investigation undertaken as part of routine programmatic implementation in Pakistan.
Methods: We collected contact screening data of 329 patients with MDR-TB (index patients) initiated on treatment with Bedaquiline or Delamanid containing regimens at 3 MDR-TB treatment sites in Pakistan from May 2016 to Sep 2018. All members living within the same residential boundary wall as the index patient were defined as contacts. Screening included an initial verbal symptom screen, followed by further evaluation through lab investigations.
Results: Of the 329 MDR-TB index patients started on Bedaquiline- or Delamanid-containing regimens during the study period, contact registry was completed for 324 (98.4%) individuals. 1911 contacts were registered, median number of contacts per index of 5 (IQR=6). Of these, 1734 (90.7%) were screened (see Figure 1: Household contact screening flow).
20 contacts were diagnosed with MDR-TB disease, of whom 18 (90%) were microbiologically confirmed with a full drug-resistance (DR) profile. All 18 contacts were found to have the same DR profile as the index patient. The overall estimated prevalence of MDR-TB disease was 1153 per 100,000 population screened.
Conclusions: Prevalence of MDR-TB disease in contacts was found to be extremely high highlighting the urgent need for the implementation of contact investigation in our setting. Significant household transmission is underscored by the concordance of drug resistance profile between index patients and contacts. Earlier detection of disease in contacts through contact investigation not only benefits contacts but also their communities through a reduction in transmission.



[Figure 1: Household contact screening flow]

EP-04-131-31 Resistance to Mycobacterium tuberculosis infection among household contacts of MDR TB patients

D Baliashvili,[1] N Gandhi,[1] S Kim,[2] A Gupta,[3] G Churchyard,[4] S Swindells,[5] A Hesseling,[6] M Hughes,[2] S Shah,[7] ACTG 5300/IMPAACT I 2003 PHOENIx Feasibility Study Team [1]Emory University, Rollins School of Public Health, Department of Epidemiology, Atlanta, GA, United States of America, [2]Harvard T.H. Chan School of Public Health, Department of Biostatistics, Boston, MA, United States of America, [3]Johns Hopkins University, Center for Clinical Global Health Education, Division of Infectious Diseases, Baltimore, MD, United States of America, [4]Aurum Institute, Health Research, Parktown, South Africa, [5]University of Nebraska Medical Center, Department of Internal Medicine, Omaha, NE, United States of America, [6]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Tygerberg, South Africa, [7]Centers for Disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Atlanta, GA, United States of America. e-mail: dbalias@emory.edu

Background: Although risk factors for Mycobacterium tuberculosis (Mtb) infection and progression to disease have been identified, studies suggest that some individuals may be "resistant" to Mtb infection. This hypothesis is based on observations that 10-50% of household contacts (HHC) of tuberculosis (TB) patients remain negative on tuberculin skin test (TST) and interferon gamma release assays (IGRA), despite substantial exposure to an index case. We determined the proportion of HHCs who may be "resistant" to Mtb infection despite high TB exposure.

Methods: We conducted a cross-sectional study from 10/2015-4/2016 at 16 study sites in 8 countries (Botswana, Brazil, Haiti, India, Kenya, Peru, South Africa, and Thailand). Adult pulmonary MDR-TB index cases and their HHCs were enrolled. HHCs underwent testing for Mtb infection by TST and/or IGRA. We calculated an exposure score based on demographic and clinical measures identified in previous studies, then categorized into three groups (Figure). Contacts were categorized as resistant to infection if both TST and IGRA were negative (0 mm induration, <0.35 IU/ml, respectively), and they had high exposure.

[Components of TB exposure score and classification scheme]

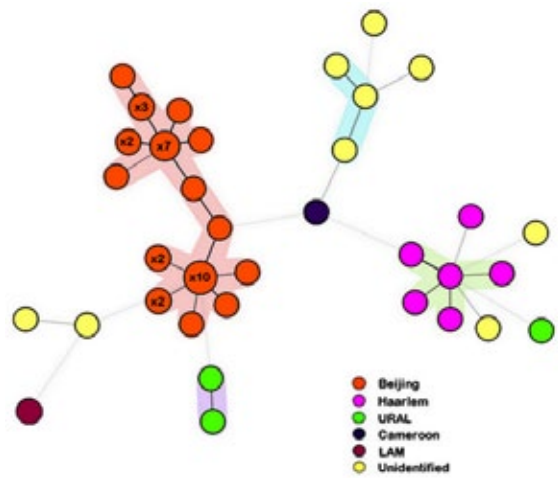
Results: We enrolled 1018 HHCs of 284 index cases; 305 (30%) were < 15 years old and 683 (67%) had both TST and IGRA results available. Among these, 140 (20.5%) were negative on both tests, 212 (31%) had discordant results, and 331 (48.5%) were positive on both tests. Among HHCs with both tests, 178 (26%) had low, 288 (42.2%) medium and 217 (31.8%) high exposure. Among 217 HHCs with high exposure, 42 (19%) were resistant to Mtb infection: 4 (9%) were HIV-positive, 20 (48%) were < 15 years old.

Conclusions: Nearly 1 in 5 HHCs remain uninfected despite high exposure to TB. Further analyses focused on identifying immunologic factors associated with resistance to TB infection in this population could contribute to developing effective preventive measures against TB.

EP-04-132-31 Molecular epidemiology of Mycobacterium tuberculosis strains among in-hospital TB patients in Kyiv Oblast, Ukraine

M Dolynska,[1] T Dukhlii,[2] G Dolynskyi,[1] HE Jenkins,[3] NR Rybak,[4] CR Horsburgh,[5] V Petrenko,[1] [1]National Medical O.O. Bogomolets University, Department of Tuberculosis, Kyiv, Ukraine, [2]Kyiv Oblast TB Hospital, Laboratory, Kyiv, Ukraine, [3]Boston University School of Public Health, Biostatistics, Boston, MA, United States of America, [4]Warren Alpert Medical School of Brown University, Infectious Disease, Providence, RI, United States of America, [5]Boston University School of Public Health, Epidemiology, Biostatistics & Medicine, Boston, MA, United States of America.
e-mail: dolynskamaria@gmail.com

Background: Ukraine is among five countries with the largest multidrug-resistant tuberculosis (MDR-TB) burden with estimated 28% of new cases, and 48% re-treatment cases with MDR-TB. Nosocomial MDR-TB transmission can jeopardize TB treatment outcomes. TB treatment is still mainly hospital-based with an average in-hospital TB treatment duration of 92 days.
Methods: 55 isolates of M.tuberculosis were collected in January-April, 2018 from 31 patients with new cases and 24 patients with re-treatment cases of sputum culture-positive pulmonary TB, in Kyiv Oblast TB Hospital, Ukraine. 15-loci set of variable number tandem repeat (VNTR)-mycobacterial interspersed repetitive units (MIRUs) were used for analysis. For strain comparison, we used the number of markers with different alleles divided by the number of markers with a cutoff of 0.2 corresponding to, at most, a three-locus difference. Clusters as defined by genotypes sharing a selectable maximum locus difference are highlighted in the Minimum Spanning Tree, shown in Figure 1; each color represents a separate lineage, clusters are shaded. The circle diameter corresponds to the number of identical genotypes.



[Figure 1. Minimum Spanning Tree constructed by VNTR- MIRU 15-loci]

Results: Patients' age ranged from 17 to 79 years old (median 47), with 84% male and 16% female. 45 (84%) patients had MDR TB. 35 isolates were clustered into the largest cluster belonged to Beijing family and consisted of two subclusters with 10 and seven identical genotypes, smaller clusters consisting of five (Harlem), three (URAL), and two unidentified isolates. 10 singletons were detected, among which LAM, URAL and Cameroon lineages were identified.
Conclusions: The high clustering rate among in-hospital patients suggests nosocomial transmission. Detailed contact tracing will be needed to identify how TB is spreading among these patients. Reduction of time in hospital by moving sooner to outpatient management and improvement of infection control measures in the hospital can both contribute to preventing such transmission.

EP-04-133-31 Estimating long-term tuberculosis reactivation rates in Australian migrants

K Dale,[1,2] J Trauer,[1,3] P Dodd,[4] R Houben,[5,6] J Denholm,[1,7] [1]Victorian Tuberculosis Program, Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia, [2]University of Melbourne, Department of Microbiology and Immunology, Melbourne, VIC, Australia, [3]Monash University, School of Public Health and Preventive Medicine, Melbourne, VIC, Australia, [4]University of Sheffield, School of Health and Related Research, Sheffield, United Kingdom, [5]London School of Hygiene and Tropical Medicine, TB Modelling Group, TB Centre, London, United Kingdom, [6]London School of Hygiene and Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom, [7]The University of Melbourne, Department of Microbiology and Immunology, Melbourne, VIC, Australia. e-mail: katie.dale@mh.org.au

Background: The risk of progression to tuberculosis (TB) disease is greatest soon after infection, yet disease may occur many years or decades later. However, rates of TB reactivation long after infection remain poorly quantified. Australia is a low-TB incidence setting and most cases occur among migrants. We explored how TB rates in Australian migrants varied with time from migration, age and gender.
Methods: We combined TB notifications in census years 2006, 2011 and 2016 with time and country-specific estimates of latent TB prevalence in migrant cohorts to quantify reactivation rates.
Results: During the census years 3,246 TB cases occurred among an estimated 2,084,000 migrants with latent-TB. There were consistent trends in reactivation rates, which appeared to be dependent on both time from migration and age. Reactivation rates were lower in cohorts with increasing time from migration until at least twenty years from migration, and on this background there also appeared to be increasing rates during youth (15-24 years of age), and in those aged 70 years and above.

Within five years of migration, annual reactivation rates were approximately 400 per 100,000 (uncertainty interval [UI]: 320-480), dropping to 170 (UI: 130-220) and 110 (UI: 70-160) from five-to-ten and ten-to-twenty, then sustaining at 60-70 per 100,000 up to sixty years from migration. Rates varied depending on age at migration.
Conclusions: Reactivation rates appeared to show dependency on both time from migration and age. This approach to quantifying reactivation risk will enable evaluation of the potential impact of TB control and elimination strategies.

EP-04-134-31 Prevalence and determinants of tuberculosis infection in young people across 14 communities in Zambia and South Africa

M Amofa-Sekyi,[1] L Mureithi,[2] M Ruperz,[3] B Kosloff,[1,3] A Schaap,[1,3] R Vermaak,[2] C Sisam,[2] R Hayes,[4] H Ayles,[1,5] K Shanaube,[6] on behalf of the TREATS Study Team [1]Zambart, Research Directorate, Lusaka, Zambia, [2]Health Systems Trust, Health Systems Research Unit, Cape Town, South Africa, [3]London School of Hygiene and Tropical Medicine, Clinical Research, London, United Kingdom, [4]London School of Hygiene and Tropical Medicine, Infectious Disease, Epidemiology, London, United Kingdom, [5]London School of Hygiene and Tropical Medicine, Infectious and Tropical Disease, London, Zambia, [6]Zambart, Research Directorate, Zambart, Zambia.
e-mail: modupe@zambart.org.zm

Background: HPTN071 (PopART) was a cluster randomized trial conducted in 21 Zambian and South African (SA) communities. Between 2013-2017, the intervention (population-level TB screening combined with universal HIV testing and treatment) was implemented in 14 communities. TREATS (TB Reduction through Expanded Antiretroviral Treatment and TB Screening) is being conducted to evaluate the impact of the intervention on TB outcomes in 7 intervention and 7 control HPTN071 communities. We report on the baseline prevalence and determinants of tuberculosis infection (TBI) in a cohort of young people (YP) aged 15-24.
Methods: At enrollment, information on TB/HIV risk factors and TB symptoms were collected from all consenting participants; symptomatic individuals had sputum tested using GeneXpert MTB/RIF. All were offered HIV antibody testing. TBI was defined as a positive QuantiFERON-TB Gold-Plus assay (QFT-G+) using manufacturer's thresholds. Factors associated with TBI were determined using multivariate logistic regression, adjusted for age, gender, HIV status and community.
Results: We enrolled 4148 YP (64% Zambia; 36% SA), females were 2318 (55.0% Zambia; 57.5% SA). HIV prevalence was 5.1% in Zambia vs 3.1% in SA. QFT-G+ indeterminate results were obtained in 3.7% (98/2654) in Zambia and 1.3% (19/1494) in SA.
Overall TBI prevalence was 44% (1809/4148), Zambia 33.0% (876/2654) and SA 62.4% (933/1494). Gender and HIV status were not associated with TBI in either country. In Zambia prevalent TBI was associated with age [aOR 1.51, 95%CI 1.25-1.83] and being a household contact [aOR 1.91, 95% CI1.39-2.64] (table 1).In South Africa prevalent TBI was only associated with being a household contact [aOR 1.56, 95% CI 1.06- 2.29].

Characteristic (*Indeterminate results not included in this analysis) († In SA analysis was performed only where HIV status of the participant was known N=934)	Zambia: N=2556	Zambia: QFT-G+ Positive* (%)	Zambia: aOR (95%CI)	Zambia: Likelihood Ratio test (p-value)	SA: N=1478	SA: QFT-G+ Positive* (%)	SA: aOR (95%CI)	SA: Likelihood Ratio test (p-value)
Age(in years): 15-19	1,381	417 (30.2%)	1	<0.001	759	466 (61.4%)	1	0.108
20-24	1,175	459 (39.1%)	1.51 (1.25, 1.83)		719	471 (65.5%)	1.2 (0.94, 1.53)	
Sex: Male	1,141	382 (33.5%)	1	0.934	628	408 (65%)	1	0.545
Female	1,415	494 (34.9%)	0.99 (0.81, 1.2)		850	529 (62.2%)	0.86 (0.67, 1.12)	
HIV Status: Negative	2,418	826 (34.2%)	1	0.408	889†	575 (64.3%)	1	0315
Positive	133	47 (35.3%)	0.93 (0.61, 1.42)		45†	23 (51.1%)	0.5 (0.25, 1.01)	
TB Contact: No contact	2,180	709 (32.5%)	1	<0.001	1,097	682 (62.2%)	1	0.38
Contact	148	56 (37.8%)	1.30 (0.87, 1.94)		180	110 (61.1%)	0.87 (0.58, 1.29)	
Contact but on treatment for more than two weeks	228	111 (48.7%)	1.91 (1.39, 2.64)		201	145 (72.1%)	1.56 (1.06, 2.29)	

[Factors associated with tuberculosis infection in Zambia and South Africa]

Conclusions: Prevalence of TB infection in this young cohort is high. Twice as many YP in SA were infected with TB as compared to Zambia. TBI increased with being a household contact in both countries, and with age in Zambia.

EP-04-136-31 Evidence for administrative controls reducing Mtb transmission in health settings: a systematic review

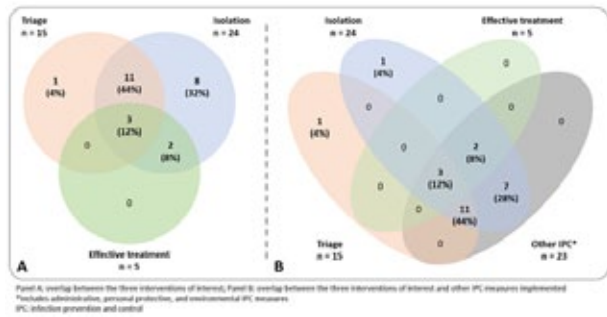
AS Karat,[1] M Gregg,[2] HE Barton,[3] M Calderon,[4] J Ellis,[5] I Govender,[1] RC Harris,[1] M Tlali,[6] DAJ Moore,[1] KL Fielding,[1] the LSHTM TB Centre Systematic Review Group [1]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom, [2]London School of Hygiene & Tropical Medicine, Department of Health Services Research and Policy, London, United Kingdom, [3]University College London Hospitals NHS Foundation Trust, University College Hospital, London, United Kingdom, [4]Universidad Peruana Cayetana Heredia, Medicine, Lima, Peru, [5]University College London Hospitals NHS Foundation Trust, Hospital for Tropical Diseases, London, United Kingdom, [6]University of Cape Town, Centre for Infectious Disease Epidemiology and Research, School of Public Health and Family Medicine, Cape Town, South Africa. e-mail: katherine.fielding@lshtm.ac.uk

Background: Mycobacterium tuberculosis (MTB) transmission is common in health facilities, but evidence is limited for the effectiveness of infection prevention and control (IPC) measures. This World Health Organization (WHO)-commissioned systematic review asked: do triage and/or isolation and/or effective treatment of tuberculosis (TB) disease reduce MTB transmission in health care settings?

Methods: A librarian searched 22 databases, including MEDLINE, EMBASE, Web of Science (final search 30/11/2017). Bias assessments were conducted at study level and at outcomes level using Grading of Recommendations Assessment, Development and Evaluation (GRADE). Data heterogeneity prevented meta-analysis. Countries were classified as high or low TB burden based on lists published by WHO in 2016. Outcomes included latent TB infection (LTBI) and TB disease incidence.

Results: 14,765 records were hand-sifted; 25/44 included articles reported primary research: 19/25 (76%) from low TB burden settings and 24/25 (96%) in hospitals. 23 (92%) studies implemented multiple IPC measures including administrative controls and personal protective equipment for health care workers (HCWs); changes to ventilation and other environmental controls; and broader administrative controls. Effects of individual measures, therefore, could not be disaggregated (Figure). 19 studies reported LTBI incidence among HCWs (16 low TB burden): absolute risk reductions ranged from 1%-21%; crude incidence rate ratios ranged from 0.2-1.1. Five studies reported TB disease incidence among HCWs: four (high TB burden) showed slight or no reduction and one (low TB burden) showed a moderate reduction. Two studies reporting TB disease incidence in HIV-positive in-patients (low TB burden) described absolute reductions of 6%-29%.

Conclusions: IPC measures appeared to reduce MTB transmission, but evidence for the effectiveness of individual or combined administrative measures was indirect and of low quality. Data are needed from high TB burden and primary care settings. Harmonising study designs and reporting frameworks will permit formal data syntheses and facilitate policymaking informed by quality evidence.



[Venn diagrams showing overlap between interventions implemented in the 25 studies included]

EP-04-137-31 Detection of M. tuberculosis in the environment as a novel tool for identifying high-risk locations for tuberculosis transmission

R Verma,[1] K Middelkoop,[2] N Degner,[1] F Moreira,[1,3] A da Silva Santos,[3] L Martinez,[1] S Patil,[1] R Wood,[2] J Croda,[4,5] J R.Andrews,[1] [1]Stanford University School of Medicine, Infectious Diseases and Geographic Medicine, Stanford, CA, United States of America, [2]Desmond Tutu HIV Centre, Desmond Tutu HIV Centre, Cape Town, South Africa, [3]Federal University of Grande Dourados, Postgraduate Program in Health Sciences, Dourados, MS, Brazil, [4]Federal University of Mato Grosso do Sul, Postgraduate Program in Infectious and Parasitic Diseases, Campo Grande, MS, Brazil, [5]Oswaldo Cruz Foundation, Oswaldo Cruz Foundation, Campo Grande, MS, Brazil. e-mail: vrenu@stanford.edu

Background: Understanding where tuberculosis transmission occurs is critical to devising prevention strategies; however, it has been challenging to study transmission patterns directly given complex mobility patterns of individuals, the long infectious duration of TB cases, and the reliance on detecting M. tuberculosis from individuals at one time point. We sought to determine whether M. tuberculosis could be detected in environments where individuals with TB are present, as a new means for characterizing infectiousness and transmission risk.

Methods: We collected environmental swab samples from several high-risk environments: prisons in Mato Grosso do Sul, Brazil, TB clinics and hospital wards and public minibus-taxis in Cape Town, South Africa and TB isolation rooms in a hospital in California, USA, along with "low-risk" control environments (non-TB households, offices) in each setting. We performed real-time PCR using two dual-labeled TaqMan probes (IS6110 and RD9) to detect and quantify Mycobacterium tuberculosis in the environmental samples.

Results: We detected M. tuberculosis in: 7 of 70 (10%) samples from prisons; 5 of 30 (16.6%) samples from TB clinics and hospital wards; and 22 of 56 (39.2%) samples from TB isolation rooms in hospitals, compared with 1 of 80 (1.25%) swab in lower-risk environments (households and offices).
No samples (0 of 24) were positive in public transit. M. tuberculosis DNA copy numbers were high (24 - 4,300 CFU/swab) in hospital rooms and prisons (80-57,000 CFU/swab).
Conclusions: M. tuberculosis is detectable in environments where individuals with active TB are present, and is rarely detected in low-risk environments, suggesting this could be used as a novel tool to identify high-risk environments for transmission and evaluate the effectiveness of prevention strategies.

EP-04-138-31 Risk of TB in healthcare workers compared with the general population: systematic review and meta-analysis

M Calderon,[1] N McCreesh,[2] A Endo,[3] J Falconer,[4] RC Harris,[3] AS Karat,[3] DAJ Moore,[3] KL Fielding,[3] the LSHTM TB Centre Systematic Review Group
[1]Universidad Peruana Cayetana Heredia, Medicine, Lima, Peru, [2]London School of Hygiene & Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [3]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom, [4]London School of Hygiene & Tropical Medicine, Library and Archives Service, London, United Kingdom. e-mail: nicky.mccreesh@lshtm.ac.uk

Background: This World Health Organization-commissioned systematic review aimed to estimate the risk of latent tuberculosis infection (LTBI) or active TB disease in health care workers (HCWs) compared with the general population.
Methods: Four major bibliographic databases were searched for studies reporting incidence/prevalence of LTBI and TB disease in HCWs and the general population. Pairs of reviewers independently selected, extracted, and assessed risk of bias. Discrepancies were resolved by consensus.
Results: 3,256 records were assessed; 41 were eligible primary research articles of which 12 measured LTBI prevalence, two LTBI incidence, and 28 TB disease incidence.
Ten studies (six in high TB burden countries [HTBC]) reported LTBI prevalence using unadjusted effect estimates (combined odds ratio [OR] 2.04 HCWs vs general population [95% confidence interval [CI] 1.73-2.40; I^2 39.3%]). Three studies in HTBC reported an adjusted estimate (OR 1.61 [95% CI 1.35-1.93; I^2 0%]).
Two studies (HTBC) reported LTBI incidence: one reported percentage difference of conversion in 1.1% (95% CI−1.0-3.2) and one reported an additional 13.2 conversions per 1000 person-years at risk (95% CI -6.5-20.0) among medical/nursing students.
20/28 studies reporting TB disease incidence (Table) contributed to random-effects meta-analysis of unadjusted combined rate ratios [RR], giving RR 4.32 (95% CI 2.36-7.91; I^2 98.6%) in eight HTBC and RR 1.28 (95% CI 0.67-2.42; I^2 99.4%) in 12 low TB burden countries (LTBC). Four studies (all LTBC), reported an adjusted RR (RR 1.29 [95% CI 0.82-2.03; I^2 77.1%]).

Low/high TB burden setting	Number of studies	Fixed effects meta-analysis		Random effects meta-analysis		I^2, %
		Unadj RR	95% CI	Unadj RR	95% CI	
Overall	20	1.34	1.29-1.39	2.05	1.22-3.46	99.5
High	8	3.00	2.83-3.17	4.32	2.36-7.91	98.6
Low	12	0.80	0.76-0.83	1.28	0.67-2.42	99.4

CI: confidence interval; RR: rate ratios; Unadj: unadjusted; I2: percentage of variation across studies that is due to heterogeneity; TB: tuberculosis

[Summary of meta-analyses based on unadjusted RRs (20 studies) comparing TB disease in healthcare workers versus the general population]

Conclusions: HCWs had double the odds of prevalent LTBI compared with the general population, overall and when stratified by HTBC and LTBC. LTBI incidence studies were scarce, but available studies showed more incident conversion in the HCW population. Active TB incidence was four times higher in HCWs in HBTC, though this should be interpreted with caution due to large between-study heterogeneity.

EP-05-C8 Active Case finding in key populations

EP-05-140-31 Is active case finding an effective strategy to reduce catastrophic costs for TB treatment in Nepal?

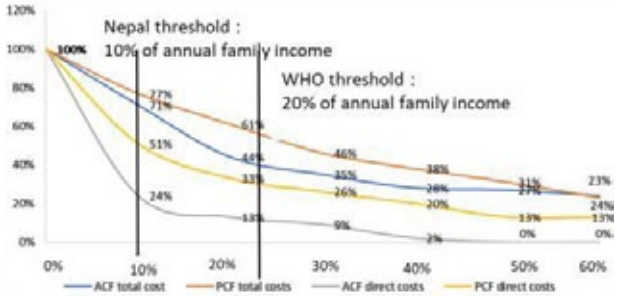
K Dixit,[1] S Acharya,[1] GR Budhathoki,[1] SC Gurung,[1] R Dhital,[1] B Rai,[1] B Subedi,[2] K Shah,[3] M Caws,[4] N Teixeira,[4] [1]Birat Nepal Medical Trust, Public Health, Kathmandu, Nepal, [2]Health Office, Pyuthan, Public Health, Pyuthan, Nepal, [3]Nick Simon Institute, Public Health, Kathmandu, Nepal, [4]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom. e-mail: kritika.dixit07@gmail.com

Background: The Nepal tuberculosis (TB) program is identifying people with TB (PWTB) through active and passive case finding (ACF and PCF) strategies to increase case notifications. The program also set a goal in line with END TB strategy that by 2020 no TB affected families will suffer catastrophic costs (CC).The potential role of ACF through national TB Programmes in reducing CC for patients has not been determined.
Methods: We conducted a cross-sectional study from July to August 2018 in Pyuthan and Bardiya districts of Nepal to compare costs during pre-treatment and inten-

sive phase among PWTB diagnosed through either PCF or ACF strategies.50 PWTB diagnosed by ACF and 50 by PCF between 2 weeks to 3 months of their treatment initiation and ≥18 years were recruited in the study and interviewed using the WHO costing tool. A sensitivity analysis was performed for CC threshold of 10-60% of household income.

Results: TB patients incurred substantial costs in accessing TB diagnosis and starting treatment. The prevalence of CC (20% threshold) was 44% (ACF) and 61% (PCF) (see figure).TB resulted in an average decrease in household income of 37% (ACF) and 38% (PCF). There was no difference in socioeconomic characteristics (education, occupation, sex and treatment status) between the groups. ACF patients presented significantly lower direct medical (USD14 vs. USD32; p=0.001), and non-medical (USD 3 vs. USD 10; p=0.004) costs during pre-treatment period. Costs incurred by ACF patients were also lower for non-medical costs during treatment period (USD 0 vs. USD 1.3; p=0.003) and total direct costs (medical and non-medical: USD 40 vs. USD 115; p=0.001) combining pre and treatment period.

Conclusions: ACF had a substantial impact on direct costs, both medical and non-medical. However, achieving the goal of zero catastrophic costs will require additional strategies such as socioeconomic support in synergy with intensified case finding.



[Prevalence of CC in TB patients diagnosed through ACF and PCF in pre-treatment and intensive phase]

EP-05-141-31 Prevalence of new pulmonary tuberculosis among health workers diagnosed in dedicated health worker clinics in Mozambique

M Polana,[1] P Mambo,[2] C Saeze,[3] T Ferreira,[4] R Frescas,[4] A Jaramillo,[5] H Muquingue,[2] [1]Jhpiego, TBIC/WPS, Maputo, Mozambique, [2]Jhpiego Mozambique, Monitoring and Evaluation, Maputo, Mozambique, [3]Jhpiego Mozambique, TBIC/WPS, Maputo, Mozambique, [4]Jhpiego Mozambique, Project Management, Maputo, Mozambique, [5]Jhpiego Mozambique, National Directorate, Maputo, Mozambique. e-mail: mico.polana@jhpiego.org

Background: Mozambique is among 22 countries most affected by TB(annual incidence: 551/100,000). The disease affects health care workers (HCW) but there is limited data about its magnitude, despite the risk of occupational exposure. Until recently, HCW underwent TB care with the general population. In 2016, the Ministry of Health established dedicated, exclusive clinics for HCW in major health facilities (HF). We report the characteristics of TB diagnosed among HCW assisted in these clinics, providing the first data on TB among HCW in Mozambique.

Methods: We reviewed clinic registers of 34,430 HCW from January 2016-December 2018, in 124 HF. The facilities represented 7.6% of all 1,630 health centers and hospitals and comprised 60% of the 57,502 HCW in Mozambique. The semiannual TB screening included clinical history, contact screening, sputum analysis and HIV testing. TB diagnosis included microscopy and GeneXpert, and identified drug resistant TB (MDR-TB). Facility HR departments confirmed the causes of HCW deaths.

Results: Of the 34,430 HCW assessed, 26,504 (63.8%) were screened for TB, with 493 (0.2%) new TB cases identified. No MDR-TB cases were reported. There were 60 TB related deaths (no HIV data). Among the 165 TB cases in 2018 (only year with category disaggregation), 60 (36.4%) were nurses, 10 (6.1%) physicians, 13 (7.8%) laboratory workers, and 82 (49.7%) support staff (clerks: 24). All TB cases were confirmed in care. TB diagnosis in HCW clinics contributed to 0.2% of TB detection rate for the general population in Mozambique.

Conclusions: Active surveillance for TB, enhanced infection control measures and semiannual screening for HCW in HFs is urgently needed to prevent HCW morbidity and mortality. Despite low TB prevalence among HCW, HCW clinics are a programmatic priority in countries with high TB burden and insufficient HCW: they find individuals who would not otherwise be identified, and would pass TB to clients and co-workers.

EP-05-142-31 Enhancing access to TB services through active case finding: results of targeted approach

S Pandurangan,[1] AK Pandey,[1] S Mohanty,[1] [1]International Union Against Tuberculosis and Lung Disease, TB Care and Control, New Delhi, India. e-mail: sripriya14@gmail.com

Background and challenges to implementation: India has approximately 27% of the total global burden of TB cases, and 33% of global deaths from TB. In order to move towards the target of TB elimination by 2025, we need to have multi-pronged strategies for TB detection and notification both in the public and private sector. To address the challenge of TB detection it is essential to ensure universal access to TB services for timely diagnosis and treatment. However, low awareness about TB, poor accessibility and affordability of health services result in delayed diagnosis, with resultant morbidity and mortality. This paper focuses on the effectiveness of multifaceted approach towards enhancing the access to TB services and early diagnosis of TB cases.

Intervention or response: Project Axshya is being implemented by The Union in 128 districts of 14 states of India with the objective of promoting early case detection through active case finding among key affected populations (KAP). The project conducts various interventions among the KAP which includes house to house visits in the KAP, organising health camps, active community surveillance and fast tracking of presumptive TB patients (PTBP) in the high loaded district hospitals. Through these interventions the project promotes awareness generation, active screening and identification of PTBPs, facilitate diagnosis and treatment initiation.

Results and lessons learnt: The results of various active case finding interventions in identifying presumptive TB patients and linking them with diagnostic and treatment services during the period Jan-Dec 2018 is shown below.

Indicator	House to house visits	Fast tracking intervention	Active community surveillance	Health camps	Total
No. of interventions conducted	1639994 HHs	125 hospitals	1731 surveillance units	725 camps	
Number of PTBPs identified	187229	50460	94137	19487	351313
Number of PTBPs examined	79510	41079	46774	9020	176383
Number of PTBPS diagnosed as TB and put on treatment	6800	9124	6685	633	23242
% positivity	9%	22%	14%	7%	13%

[Active case finding interventions Jan-Dec 2018]

Conclusions and key recommendations: The results of the intervention clearly show that multi pronged strategies among the key affected population areas have resulted in early detection of cases, thus contributing to identifying the missing TB cases.

EP-05-143-31 Finding the missing people with tuberculosis (TB): experience of engaging community health providers and volunteers in Tanzania

G Munuo,[1] A Maro,[1] L Ishengoma,[2] A Nyirenda,[1] J Lyimo,[3] F Ntogwisangu,[3] H Sasya,[1] [1]Amref Health Africa in Tanzania, Disease Control and Prevention, Dar es Salaam, Tanzania, United Rep., [2]Ministry of Health Community Development Gender Elderly and Children, National TB and Leprosy Tanzania, Dar es Salaam, Tanzania, United Rep., [3]Management and Development for Health, GF TB Project, Dar es Salaam, Tanzania, United Rep.. e-mail: gmunuo@gmail.com

Background and challenges to implementation: Tanzania is among the 30 high burden countries with Tuberculosis (TB) and among 13 countries accounting for 75% of missed TB cases globally.. According to 2018 Global TB report, Tanzania in 2017 missed 56% cases of TB from the estimated 154 000 cases, only 44% (68,500) were detected by the program, with treatment success of 90% percent.

Intervention or response: Amref Health Africa in collaboration with national TB program through Global fund HIV/TB grant is implementing community TB in 8 regions since June 2018. The program engaged Regional and district health management teams in introducing the and identifying community health care workers/volunteers (CHWs/Vs), traditional healers(THs), sputum fixers(SFs) and existing community based organizations' (CBOs). Then they were sensitized trained and continuous mentoring using the national quality improvement guideline. The modality of the engagement was through performance based incentive and enablers for weather and transport. Data were collected using community TB national tools and aggregated at the facility level where all referred cases and those found with TB were entered in the registers and then entered in electronic TB reporting system.

Results and lessons learnt: A total of 961 CHW/V, 275 THs, 128 SFs and 52 CSO were engaged. Collectively their actions contributed to tremendously increase to 1,952 cases in Quarter 4 (October-Dec, 2018) compared with 703 cases in January-March set as a baseline. There was variations in results in some regions with high level of engagement of community providers with tremendous increase in case detection.

Conclusions and key recommendations: Effective Engaging community providers is critical in finding missing people with TB. From this operational implementation in finding the missing TB cases, engaging and provision of proper incentive´s to CHWs/Vs, traditional healers, Sputum fixers and working with the Ex-TB groups will increase the contribution of community in TB case detection in countries with high TB burden.

Regions	January - March 2018	April - June 2018	July - September 2018	October - December 2018	Cumulative Results
Dodoma	244	149	135	780	760
Kagera	104	96	176	167	543
Mara	52	67	188	456	763
Mbeya	39	42	174	196	451
Ruvuma	39	36	222	226	523
Shinyanga	156	156	200	231	745
Simiyu	26	59	124	136	345
Tanga	41	91	213	288	633
Total	703	696	1432	1952	4783

[Table 1: Performance on Community confirmed TB cases by region 2018]

EP-05-144-31 Caring for tuberculosis in the homeless population of Delhi, India

A Khanna,[1] S Chandra,[2] KK Chopra,[3] N Sharma,[4] V Khanna,[5] S Sharma,[6] N Babbar,[1] TJ Padmini,[1]
[1]Government of NCT of Delhi, State TB Control Office, New Delhi, India, [2]Office of World Health Organization India, Tuberculosis Division, New Delhi, India, [3]New Delhi TB Centre, State TB Training and Demonstration Centre, New Delhi, India, [4]Maulana Azad Medical College, Department of Community Medicine, New Delhi, India, [5]Government of NCT of Delhi, District TB Office, New Delhi, India, [6]Municipal Corporation of Delhi, District TB Office, New Delhi, India. e-mail: stodl@rntcp.org

Background and challenges to implementation: With increasing urbanization and rapid growth of slums in cities, provision of quality health services in urban areas is becoming a global challenge especially for the homeless population. In order to address the complexities in disease dynamics of the homeless population and difficulties in their access to health care services, Revised National Tuberculosis (TB) Control Program Delhi has developed an innovative 'Night-Shelter' model to provide quality TB care in high burden compact cluster settings of night shelters.
Intervention or response: Between January 2019-March 2019, Central Delhi District in collaboration with outreach workers from Non- Government and Government partners screened 60 night shelters (shelter homes) in their area. Based on the 'Night-Shelter' model created, screening was done with structured questionnaire and samples were collected from presumptive TB patients. The indicators chosen for the assessment of feasibility of the model were (a) Yield of new TB cases (b) Duration between diagnosis and start of treatment (c) Adherence to treatment (d) Availability of cash benefit for nutritional support under programmatic conditions. Statistical analysis was performed using one sided Fisher's Exact test.
Results and lessons learnt: During the study period, 4200 people were screened in night shelters of Central Delhi. Among those screened, 29 TB patients were diagnosed giving a yield of 9% new TB cases. Out of those diagnosed, 25 (95%) were started on drug sensitive TB treatment and given the cash benefit for nutrition support under programmatic conditions. Adherence was a challenge with only 55% adhering to their therapy. There was no drug resistant TB case detected during the study.
Conclusions and key recommendations: Provision of quality TB care in high burden compact cluster settings of night shelters is beneficial to improve access to program services. The study shows that strong policy inducement promoting replication of the 'Night-Shelter' model is essential to improve health service access among homeless population in high burden settings.

EP-05-145-31 Comprehensive model of BRAC in missing tuberculosis case detection: intensifying interventions for enhancing accessibility

MA Islam,[1] G Raihan,[1] IA Rifat,[1] S Reza,[1] S Islam,[1]
[1]BRAC, Communicable Disease and WASH, Dhaka, Bangladesh. e-mail: akramul.mi@brac.net

Background and challenges to implementation: TB is a major public health concern in Bangladesh. BRAC, a development organization has been implementing TB control services since 1994 in collaboration with National Tuberculosis Control Program (NTP).Though the case detection rate is increasing over last few years, country is still missing 27% of cases. A comprehensive package involving all care providers is essential for universal access to TB care and prevention.
Intervention or response: BRAC expanded TB interventions through establishing 51 TB diagnostic centers at district level and in urban settings. All of these diagnostic centers are linked with different care providers from the community level to sub-district and sub-district to district/city level. A system has been developed and a number of public and private care providers have been engaged in referral of TB presumptive and in identifying the missing TB cases from different pockets of the community. The providers refer TB symptomatic for sputum examination at NTP designated laboratories in sub-district level and below. People with persistent TB symptoms and negative smear results are referred to the graduate doctors for further investigations.Doctors referred them to TB diagnostic centers at district or city level for x-ray and x-pert testing free of cost.
Results and lessons learnt: From January to December 2018, a total of 193,424 TB cases identified among which 117,308 were bacteriologically confirmed, 39,065 were clinically diagnosed, 29,856 were extra-pulmonary and 7204 relapse cases.In 2017, total case detected were 163,700. More than 29,000 additional cases identified in 2018 due to this comprehensive model.
Conclusions and key recommendations: Comprehensive model engaging different care providers enhanced the screening of more presumptive to identify different types of TB patients early. Networking with public and private graduate doctors both helped to increase more extra-pulmonary TB patients too.

EP-05-146-31 Tuberculosis case yield of risk group screening using optimised screening and diagnosis algorithms in Indonesian primary healthcare centres

B Alisjahbana,[1] G Parwati,[2] F Asnely Putri,[3] F Meyanti,[3] E Post,[3] M Noor Farid,[4] D Budi Wicaksono,[4] * Nurjana,[5] I Pambudi,[5] E Tiemersma,[6] [1]Padjadjaran University, Health Research Unit, Bandung, Indonesia, [2]World Health Organisation, Policy, Strategy and Innovation, Geneva, Switzerland, [3]KNCV Tuberculosis Foundation, Indonesia Branch Office, Jakarta, Indonesia, [4]University of Indonesia, Epidemiology, Jakarta, Indonesia, [5]Ministry of Health, National Tuberculosis Program, Jakarta, Indonesia, [6]KNCV Tuberculosis Foundation, Technical Division, Den Haag, Netherlands. e-mail: b.alisjahbana@gmail.com

Background: The National Tuberculosis Program (NTP) of Indonesia is seeking effective strategies to increase TB case finding, starting in primary health care centers (PHCs). We aimed to find the most optimal algorithms for enhanced case finding among PHC clients, based on combinations of client characteristics and symptoms of TB.

Methods: Between February and September 2018, we screened clients in 10 purposively selected PHCs in Bogor regency for TB-related symptoms, risk factors, and chest X-ray (CXR) abnormalities. All participants provided a spot sputum sample for Ziehl-Neelsen smear and Xpert MTB/RIF. A panel reviewed all clients with any positive laboratory result for final classification of TB cases.

Results: During the data collection period, 14,920 clients visited the PHCs and 10,038 (67%) were randomly selected for participation, of whom 6,087 (61%) participated. For 5,835 clients a sputum test result was available; 220 clients tested positive on Xpert and 210 were defined as TB cases. The following algorithms seemed most effective: 1) screening for cough for ≥2 weeks or hemoptysis and testing those screened positive with Xpert (n=943 Xpert tests yielding 139 cases (63.2% of all true TB cases found in the survey) 2a) additional screening of those who screened negative on step 1, testing those with BMI≤18, weight loss, history of TB or living with a TB contact with Xpert (n= 1764 tests yielding 56 additional cases i.e., 25.5% of all true TB cases), or 2b) additional screening on CXR and testing persons with suggestive CXR (n=255 yielding 40 additional cases; 18.2% of all true TB cases).

Conclusions: The scenarios sketched above seem effective as they use simple screening methods and test < 20% of PHC clients with Xpert while adding significantly more TB cases. Costing and feasibility data will be added to reach conclusions about the most cost-effective algorithms.

EP-05-147-31 Optimising opportunities to increase TB case finding: a case for private sector engagement in Ghana

NN Hanson-Nortey,[1] MN Mensah,[1] J Anaman,[1] R Osih,[2] S Charalambous,[2] G Churchyard,[3] [1]Aurum Institute Ghana, Ghana Operations, Accra, Ghana, [2]Aurum Institute, Aurum Global, Johannesburg, South Africa, [3]Aurum Institute, Head Office Management, Johannesburg, Ghana. e-mail: nnortey@auruminstitute.org

Background and challenges to implementation: The trend of TB case notification in Ghana has declined over the past 5 years. Opportunities for a systematic private sector engagement to contribute to national TB case detection have remained unutilized in spite of private sector seeing up to 40% of OPD attendants. Public-Private Partnership for TB control (PPM-DOTS) within the national TB strategic plan has not been adequately implemented and sustained. Optimising TB case finding activities within private facilities will increase case detection.

Intervention or response: Following a baseline assessment of TB notification within Accra and Kumasi Metros, Aurum Institute Ghana and partners engaged selected private facilities in high burden TB communities to conduct intensified case finding among OPD attendants and key and vulnerable populations within a TB REACH Wave 6 project. Presumed TB cases from OPD screening as well as from community TB screenings were tested and treated in the private facilities with support from community TB Detectors and cost reimbursement under national health insurance. We evaluated increased TB case notification using number diagnosed and enrolled on treatment.

Results and lessons learnt: Results from first quarter of implementation (Q4 2018) showed private sector contribution to TB case detection increased from 11.6% (22) to 15.4% (32) in Accra Metro and 0.9% (1) to 14.9% (14) in Kumasi Metro. This increased the overall notification by 8.6% in Accra and 2.7% in Kumasi Metro whilst notification in the control population decreased by 10.3%. More results are expected in the coming months.

Conclusions and key recommendations: Despite the late start and slow uptake of the project interventions, results immediately show there is potential to increase national case notification trend if the intervention is sustained in this first of four quarters of implementation. Therefore, when adequately engaged, private providers can contribute significantly to national TB case notification rates.

EP-05-148-31 Targeted community interventions to improve TB case finding in tea zones in Nyamira County, Kenya

BA Oketch,[1] GW Okoko,[2] FK Muma,[3] NJ Anastasia,[1]
[1]Our Lady of Perpetual Support (Kenya), GF Community TB Prevention and Control Program, Kisumu, Kenya, [2]Amref Health Africa in Kenya, Global Fund Tuberculosis Project, Nairobi, Kenya, [3]County Government of Nyamira, Department of Health, Nyamira, Kenya.
e-mail: brianawinyo@olpskenya.org

Background and challenges to implementation: Amref Health Africa in Kenya is working with sub-recipients to improveactive case finding among high risk populations at community level. Amref works through Our Lady of Perpetual Support(OLPS) to implement communityTB control activities. Nyamira is one of the Counties in Kenya where tea farming is the main livelihood. The tea-zone populations are mainly men whose socioeconomic disparity enhances their vulnerability, while living in remote locations, stigma, inadequate information on TB and inflexible working schedules worsen barriers to care. Government health facilities are usually located outside the tea-plantation territories further contributing to delayed diagnosis of TB.
Intervention or response: A 3 day Targeted Community Case Finding outreach was conducted in the villages with high concentration of tea pickers after realization of at least 5 bacteriologically confirmed cases among the tea picking villages over the period of January2018 to December2018. During the outreach, village elders mobilized the community for screening while the CHVs provided health education and screened the tea workers for TB using the symptomatic TB screening tool. Any symptomatic individual was diagnosed as presumptive TB case and was either referred or sputum sample collected and transported to an identified GeneXpert site by motorbike riders for TB evaluation.
Results and lessons learnt: A total of 2756 people from 809 households were screened for TB symptoms, Sputum was collected from 302 presumptive cases(11%)and evaluated for TB using GeneXpert. 12 cases(4%) were diagnosed with active TB. 3 of the 12 cases(25%) were diagnosed with Rifampicin resistant TB. All the 12 patients were tested for HIV and one child tested positive.
Conclusions and key recommendations: The identified presumptive TB and active TB cases could have been missed. Hence, the findings indicate that the targeted Community Active Case Finding intervention is vital to identify a significant number of TB cases within the tea zone populations and should be scaled up in other tea-growing areas in Kenya.

EP-05-149-31 Lessons learnt from the "TB in the mining sector" grant: a southern African response to high TB incidence among mineworkers and their contacts

R Pillay,[1] J Naidoo,[1] D Barnes,[1] A Chingandu,[1] S Pillay,[2]
[1]Wits Health Consortium, WDED, Johannesburg, South Africa, [2]Durban University of Technology, Enhancing Care Foundation, Durban, South Africa.
e-mail: rpillay@witshealth.co.za

Background and challenges to implementation: The incidence of tuberculosis (TB) among South African mineworkers is estimated at 3000-4000/100 000 people, ten times the WHO's emergency threshold. As a focused response to this high incidence, the Global Fund-supported "TB in the Mining Sector (TIMS)" grant established 11 Occupational Health Service Centres (OHSC) in 8 Southern African Development Community (SADC) countries.
Intervention or response: These OHSCs target mineworkers, ex-mineworkers, their families and communities, providing a comprehensive service including TB screening, diagnosis, follow up and application for compensation for those eligible. Several lessons on facility infrastructure, social mobilization, diagnostic processes and compensation submissions were learnt.
Results and lessons learnt: OHSCs were located based on geospatial mapping of key populations and consultations with National TB Programs. Each OHSC was run by a dedicated manager, whose qualification included occupational health. Each centre was equipped with a digital XRray, GeneXpert, audiometer, spirometer and other routine clinical equipment. All personnel were given trained in basic occupational health, audiometry and spirometry. Social mobilization was done by OHSC staff in surrounding districts that had a high key population density. A total of 26 953 clients were seen at the OHSCs, 19 256 of which comprised mine workers or ex-mineworkers. Of the total clients seen, 1 450 were diagnosed with TB, constituting 5,4% of the population. Of the mine worker and ex-mine worker subset, 7 543 were diagnosed with occupational lung disease (OLD), constituting 39,2% of that population. Of these, 1142 were assessed by the compensation panel in South Africa and 822 were found to be compensable.
Conclusions and key recommendations: A focused program targeting the mining key population produces a TB yield far higher than general community screening. Diagnostic equipment at the point of screening is vital to diagnose and initiate treatment. Lack of transport is a barrier to accessing care and must be addressed by TB programs.

POSTER DISCUSSION SESSION (PS)

PS-01-B6 Diabetes mellitus & tuberculosis: "nothing sweet about this comorbidity"

PS-01-501-31 Navigating health systems for TB-diabetes care: journey for diagnostic and treatment care for TB-diabetes comorbid patients in India

V Panibatla,[1] A Kudale,[2] M Phutane,[2] K Sayyad,[3]
[1]TB Alert India, Program, Hyderabad, India, [2]Savitribai Phule Pune University, Interdisciplinary School of Health Sciences, Pune, India, [3]TB Alert India, Programs, New Delhi, India. e-mail: vikass@tbalertindia.org

Background: Acknowledging the link between Diabetes Mellitus (DM) and Tuberculosis (TB), Indian Government recently developed National framework for joint TB-DM collaborative activities aiming to guide coordinated programmatic response to deal with this double burden of diseases. However, the way in which this programmatic push for integrated services is playing out in health systems has not been studied from patients' perspectives. Against this background, research study was undertaken to know patients' experiences while navigating health systems.
Methods: A qualitative study was conducted among 23 TB-DM co-morbid patients registered at 3 TB diagnostic centres in peri-urban areas of North Delhi. In-depth interviews of patients were carried out for elucidating their experiences of being co-morbid and challenges they came across while seeking care.
Results: Government tertiary care hospitals providing DM care are linked with TB centres to ensure bidirectional screening for TB-DM. However, feedback mechanism in prevalent referral system was poorly developed. Patients got firstly diagnosed for DM at either private or government laboratories.
In addition to these, random blood-sugar level testing by digital glucometers was purchased by patients at private pharmacies. Among comorbid patients' low awareness about DM, related complications, poor blood-sugar level monitoring and poor treatment adherence was observed. Patients shift on their own from government to private hospitals for seeking DM treatment dueto long waiting hours, unavailability of medicines and geographical distances. At same time due to financial constraints patients also reported to return from private to government hospitals to get DM medicines. Rarely, patients chose self-medication and then stopped taking treatment for DM.
Conclusions: On fragmented pathway of TB-DM care there is an emerging need to better coordinate TB-DM diagnostic and treatment services across public and private sectors to ensure continuum of care between two programmes as well as across public and private sector providers and facilities.

PS-01-502-31 Screening strategy for detection of pre-diabetes and diabetes among people affected by tuberculosis in slums of New Delhi

L P Gujral,[1] M Shivakumar,[2] C Bhan,[1]
N Ortuno-Gutierrez,[3] [1]Damien Foundation India Trust, New Delhi-Project, New Delhi, India, [2]Damien Foundation India Trust, DFIT Headquarters, Chennai, India, [3]Damien Foundation, Training, Research, Technical Assistance and Monitoring & Evaluation (TREAT-ME), Brussels, Belgium. e-mail: admindelhi@damienfoundation.in

Background and challenges to implementation: Diabetes-mellitus (DM) increases three-times the risk of developing tuberculosis (TB). India has highest TB-burden worldwide (1,9million cases notified in 2017), along with 11% prevalence of DM in the urban-area. The Revised National Tuberculosis Control Programme (RNTCP) recommends bidirectional screening. There are different DM-screening approaches among TB-cases that documented effectiveness. Damien Foundation INDIA Trust (DFIT) implemented a systematic DM-screening in Ten TB clinics of New-Delhi. Our aim was to determine effectiveness of DM-screening and risk-factors associated to Pre-Diabetes and Diabetes.
Intervention or response: In 2017, all TB-susceptible diagnosed patients above 14-years of age were offered to have fasting blood-sugar glucometer-test. In case of glycemia above 126 mg/dl, patients were referred to DM-clinic for diabetes-management. A questionnaire for data-collection included clinical-data, socio-demographics and DM risk-factors.
Results and lessons learnt: 2014 (90%) from a total of 2236 susceptible TB-Patients were enrolled. Among not enrolled: 196 were children below 14-years and 26 because of other reasons. Known-DM were found in 745(37%) of all patients screened. Pre-diabetes was detected in 220(11%) and 156 were known diabetic-patients (8%). Among pre-diabetes, diabetes was newly confirmed in 43 cases (19%) and they were treated according to the national guidelines. In newly-diagnosed diabetes cases, there were positive family history of DM in 18.6%, sedentary occupation in 51%; smoking in 26% and monthly income varies from < Rs5000 in 23%, Rs5000-10000 in 28% and >Rs 10000 in 49%
Conclusions and key recommendations: In all TB-cases enrolled, diabetes was confirmed in around 2% (New diabetic-patients), however total prevalence was 39%. Also, diabetes was more frequent in patients with a monthly-income above Rs10000. Acceptability of our

screening strategy was high (90%). We believe that this strategy could be useful for similar settings to increase coverage of screening of diabetes among people affected by tuberculosis.

PS-01-503-31 Screening of diabetes mellitus among tuberculosis cases in urban Bangladesh

S Biswas,[1] KK Paul,[1] YM Alkabab,[2] S Saba,[1] S Ahmed,[1] MKM Uddin,[1] MS Bashar,[3] RS Banu,[3] SK Heysell,[2] S Banu,[1] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh, [2]University of Virginia, Department of Medicine, Division of Infectious Diseases and International Health, Charlottesville, VA, United States of America, [3]Directorate General of Health Services, National Tuberculosis Control Programme, Dhaka, Bangladesh. e-mail: samanta.biswas@icddrb.org

Background: In Bangladesh, a high tuberculosis (TB) burden country, diabetes mellitus (DM) screening is not standard of care at public TB treatment centers. Thus, we assessed the utilization of a point-of-care test for glycosylated hemoglobin (HbA1c) for DM diagnosis among people treated for TB and the impact of HbA1c level on TB treatment response.
Methods: Diabetes mellitus screening by HbA1c was offered to all people initiating TB treatment enrolled in five icddr,b run TB treatment facilities in the capital city of Dhaka. Socio-demographic, programmatic and clinical data were collected. Patients with HbA1c≥6.5% were referred for concurrent DM management.
Results: From October'18 to March'19, 260 patients with median age 31 years (range: 12-81 years), were screened for DM. Of them, 160 (62%) were male, 194 (75%) had pulmonary TB, 169 (65%) were bacteriologically diagnosed (B+) and 249 (96%) were newly diagnosed TB patients. Eighty-six (33%) patients had HbA1c≥6.5% (including 49 previously diagnosed with DM), and 174 (67%) patients had HbA1c< 6.5% (3 previously diagnosed with DM). Both groups had comparable gender distribution. TB patients with HbA1c≥6.5% were significantly older (median age 46 vs. 28 years, p< 0.001) and had higher body mass index (median 22 vs. 20 kg/m^2, p=0.003). Smear microscopy results of 111 B+ patients were available after completion of the intensive treatment phase. Among patients with HbA1c≥6.5%, smear conversion occurred in 28 (78%) patients with 2 (6%) deaths, while in patients with HbA1c< 6.5%, 65 (87%) patients had smear conversion and 3 (4%) patients had died.
Conclusions: Screening for DM during TB treatment initiation identified a considerably high proportion with DM range HbA1c values that despite linkage to DM care was associated with a delayed smear conversion. Further study is necessary to determine the impact on later outcomes from integrated TB and DM management.

PS-01-504-31 Screening diabetes mellitus patients for tuberculosis in Southern Nigeria: a pilot study

E Aniwada,[1] N Ekeke,[2] J Chukwu,[2] C Nwafor,[2] A Meka,[2] C Alphonsus,[2] N Murphy-Okpala,[2] M Anyim,[2] J Ikebudu,[2] C Eze,[2] [1]University of Nigeria Teaching Hospital, Community Medicine, Enugu, Nigeria, [2]German Leprosy and Tuberculosis Relief Association, Medical, Enugu, Nigeria. e-mail: anthony.meka@dahw.org

Background: Diabetes mellitus (DM) and tuberculosis are of great public health importance globally and especially in Sub-Saharan Africa. Tuberculosis (TB) is the third cause of death among subjects with non-communicable diseases of which DM is one of the most important. DM weakens the immune system, and increases the risk of progressing from latent to active tuberculosis. This study was aimed to ascertain yield of TB cases and number needed to screen (NNS) among DM patients.
Methods: A cross-sectional study was conducted at 10 selected health facilities with high DM patient load and readily accessible DOTS centre in 6 states of Southern region of Nigeria over a period of 6 months under routine programme conditions. All patients visiting the Diabetes Clinics in the health facilities who gave consent were included in the study. Yield and NNS were calculated using appropriate formula.
Results: The total number screened was 3457 with a mean age (SD) of 59.9 (12.9) years. Majority were male, 2277 (65.9%). Of the number screened, the overall prevalence of TB was 0.8% (800 per 100,000). Sixteen (0.5%) were known TB cases (old cases). Presumptive cases were 221 (6.4%) out of which 184 (83.3%) were sent for Xpert MTB/Rif assay. Eleven (0.3%) new cases of TB were detected, giving additional yield of 40.7% and number needed to screen (NNS) of 315. All the 11 patients were placed on anti-TB treatment.
Conclusions: Prevalence of TB among DM patients was higher than general population. Yield was also good and comparable to findings outside Nigeria. This underscores the need to institute active screening for TB among DM patients. However, further studies are recommended to identify associated factors to guide policy makers in planning and development of TB-DM integrated services.

PS-01-505-31 Treatment outcomes among tuberculosis patients with diabetes mellitus in Jiangsu, China

Q Liu,[1,2] N You,[1] P Lu,[1] L Zhu,[1] W Lu,[1] [1]Center for Disease Control and Prevention of Jiangsu Province, Department of Chronic Communicable Disease, Nanjing, China, [2]Nanjing Medical University, Department of Epidemiology, Nanjing, China. e-mail: liuqiaonjmu@163.com

Background: There are 100 million diabetes patients in China however few clinical studies have fully evaluated treatment outcomes of tuberculosis patients with

diabetes mellitus in China. We investigated treatment outcomes and risk factors of tuberculosis patients with diabetes in Jiangsu Province, China.

Methods: In 2017, the National Basic Public Health Service Diabetes Patients Physical Examination Project was conducted in the cities of Danyang, Rugao, and Jiangyin. Data on treatment outcomes of tuberculosis-diabetes patients were obtained from the Tuberculosis Information Management System. Descriptive and logistic regression analysis were used to analyze the risk factors of the treatment outcomes for tuberculosis patients with diabetes.

Results: A total of 152 tuberculosis-diabetes patients were included in the analysis. Of these, 49 (32.2%) were cured and 88 (57.9%) completed treatment, a treatment success rate of 90.1%. Univariate logistic regression demonstrated that smear-positivity, retreatment, and pulmonary cavitation were risk factors for failing treatment. Multivariate logistic regression analysis results demonstrated that risk factors for treatment failure included sputum smear-positivity (Adjust Odds Ratio [OR], 7.91, 95% Confidence Intervals [CI], 2.13-29.44), retreated patients (Adjusted OR, 5.12, 95% CI, 1.70-15.43) and pulmonary cavitation (Adjusted OR, 5.03, 95% CI, 1.64-15.42).

Conclusions: We found that tuberculosis treatment success among diabetes patients was lower among sputum smear-positive, those previously treated for tuberculosis, or with pulmonary cavities. Strengthening early diagnosis and identifying tuberculosis patients with diabetes that are at high-risk of treatment failure is needed in areas with a high-burden of both diabetes and tuberculosis.

PS-01-506-31 Does diabetes mellitus affect the treatment outcomes of tuberculosis? Results of a 10-year cohort Israeli study

Z Mor,[1,2] I Tzanani,[3] A Yaffe,[3,4] D Ben Dayan,[3,5]
[1]Ministry of Health, Department of Health, Tel Aviv, Israel, [2]Ashkelon Academic College, School Health Sciences, Ashkelon, Israel, [3]Tel Aviv University, Medicine, Tel Aviv, Israel, [4]Hillel Yaffe Hospital, Endocrinology, Hadera, Israel, [5]Shmuel Harofeh Hospital, Lung, Beer Yaakov, Israel.
e-mail: zmor100@gmail.com

Background: Diabetes mellitus (DM) is a non-communicable disease which impairs host immunity and may increase susceptibility to tuberculosis. This study aims to assess patients′ characteristics and treatment outcomes of hospitalized tuberculosis patients with DM (TB&DM+) in Israel.

Methods: This cohort study included all patients who were hospitalized in the only referral tuberculosis hospital in Israel from 2005 to 2015. Demographic, clinical, and laboratory characteristics were compared between all 80 hospitalized TB&DM+ (known DM or newly diagnosed) during the study period with a random sample of 227 tuberculosis patients without DM (TB&DM-). DM was defined as two consecutive results of fasting blood sugar levels greater than 125md/dL or HbA1C≥6.5%.

Results: TB&DM+ patients were more commonly Israeli citizens, older and lived in lower socioeconomic areas than TB&DM-. No statistical significant differences were found in multi drug resistance rates between TB&DM+ and TB&DM- (1.6% vs. 9.2%, respectively, p=0.07), positive sputum sample (60.8% vs. 48.97%, respectively, p=0.1) and culture (83.8% vs. 77.9%, respectively, p=0.3). The adherence of TB&DM+ to treatment was better, but it took those patients longer time to convert their positive culture than TB&DM- (62±38 days vs. 49±16, p=0.04) and their mortality rate was higher (20.0% vs. 8.9%, respectively, p< 0.01). Treatment success was lower in TB&DM+ than TB&DM-, but did reach significant statistical differences (76.2% vs. 83.1%, respectively, p=0.2).

Conclusions: The presence of DM was not associated with unfavorable treatment outcomes among TB&DM+ in this study, although death rates among TB&DM+ were higher. It might be that close follow-up and efficient control of blood glucose levels among TB&DM+ improved their treatment outcomes.

Older tuberculosis patients and those from lower socioeconomic areas are vulnerable populations, suggesting that they should be prioritize for DM screening. The relatively slow response to treatment among TB&DM+ requires better longer isolation to prevent further infections.

PS-01-507-31 Impact of diabetes mellitus on treatment outcomes of patients with MDR-TB: a retrospective analysis in Bangladesh

N Arefin Saki,[1] PK Modak,[1] M-U Alam,[2] MS Bashar,[1] MS Islam,[1] [1]National Tuberculosis Control Program, DGHS, Dhaka, Bangladesh, [2]Interactive Research and Development, Health, Dhaka, Bangladesh.
e-mail: nazis.arefin@yahoo.com

Background: Multidrug-resistant Tuberculosis (MDR-TB) is a continuing threat to TB control especially in developing countries. Compared to first line therapy, MDR-TB treatment is less effective and outcome depends on many factors. There is growing evidence suggesting that diabetes mellitus (DM) affects treatment outcome in tuberculosis patients. This study aimed at investigating the role of DM on MDR-TB treatment outcomes.

Methods: This was a retrospective cohort study where MDR-TB patients' records were reviewed to evaluate the treatment outcomes of patients with and without DM. Data were collected from five MDR-TB hospitals in Bangladesh enrolled between January and December 2015. Information of DM was obtained by analyzing the baseline laboratory investigations and hospital records.

The SPSS v.23 software was used for data analysis. Outcome findings were compared between the patients with and without DM.
Results: Of 657 MDR-TB patients enrolled, 103(15.7%) had DM and among them 48(46.6%) were diagnosed during baseline investigations of MDR-TB treatment. Mean age of the patients were 35.24(±14.82) years and none was HIV positive. Among the MDR-TB patients with diabetes, 68.9% were treated successfully whereas 78.9% among non-diabetic. Patients with diabetes had 1.5 times higher risk of unfavorable treatment outcomes (95% CI 1.1-2.1, p=0.027) than the non-diabetics. Relative risk of death and treatment failure among the patients with DM was 2.1 (95% CI 1.5-3.6, p=0.01) and 3.3 (95% CI 2.4-5.5, p=0.002) respectively. Proportions of two-month culture conversion were lower in MDR-TB patients with diabetes than without diabetes (66% and 72%) but was not statistically significant.
Conclusions: The study revealed that DM had serious impact on MDR-TB treatment outcomes and were associated with increased death and failure. Culture conversion was also delayed in presence of DM. Routine screening for diabetes among MDR-TB patients is recommended for early detection. Further studies are required to identify better options to manage MDR-TB with DM more effectively.

PS-01-508-31 Outcomes of MDR-TB treatment in people with diabetes in Peru: an operational report from 2014-2015

E Herrera-Flores,[1] H Hernandez,[1] J Rios,[1] C Ugarte-Gil,[2,3,4] [1]Ministerio de Salud, Dirección de Prevención y Control de Tuberculosis, Lima, Peru, [2]Universidad Peruana Cayetano Heredia, Instituto de Medicina Tropical Alexander von Humboldt, Lima, Peru, [3]Universidad Peruana Cayetano Heredia, School of Medicine, Lima, Peru, [4]London School of Hygiene and Tropical Medicine, TB Centre, London, United Kingdom.
e-mail: edwher00@hotmail.com

Background: Peru has the highest multidrug-resistant tuberculosis (MDR TB) burden in the Americas, with more than 80% persons with MDR TB living in urban areas. Diabetes (DM) prevalence is increasing, particularly in urban areas and is associated with poor TB treatment outcomes. There is limited data on the characteristics of MDR TB in persons with DM (MDR TB-DM) in Peru, information that is needed to design effective control measures in this vulnerable population.
Methods: MDR TB electronic records from the Peruvian National TB Program (NTP) operational database and clinical records submitted to NTP were reviewed. Adult persons with MDR TB-DM who started treatment between 2014-2015 in Peru were included, excluding persons with extensively drug-resistant TB. We evaluated patient's characteristics, operational variables and treatment outcomes.
Results: We identified 2662 persons with MDR TB, 167 (6.27%) were MDR TB-DM and we reviewed the 126 (75.45%) available records. The median age in MDR TB-DM was 49.71 years (IQR:41.6-57.3); 89 (70.63%) were men, 97 (76.98%) from Lima, 14 (11.11%) malnourished, 48 (38.10%) overweight/obesity, mean Body Mass Index(BMI) was 23.47 (SD: ±4.44), time of DM was 5.77 years (SD:±5.35), basal fasting glucose was 200.5 (SD:±95.58), 63 (61.76%) used insulin, 48 (47.06%) non-adherence to DM treatment. Regarding TB treatment outcomes 62 (50.41%) had successful treatment, 9 (7.14%) died, 13 (10.32%) had treatment failure, 39 (30.95%) lost to follow-up. Unsuccessful outcome (defined as death, treatment failure and lost to follow-up) was associated with non-awareness about TB (OR:8.33, CI95%:3.68-18.86), non-adherence to DM treatment (OR:2.95, CI95%:1.30-6.67), non-culture conversion at 3rd month (OR:7.88, CI95%:2.18-28.54). There was no association with glycemic control, nutritional status or radiological characteristics.
Conclusions: DM was present in 6.27% of MDR TB, they were mostly older adults. Unsuccessful outcomes were associated with non-awareness about TB, non-adherence to DM treatment and non-culture conversion at 3° month.

PS-01-509-31 Prediabetes and the presentation of a moderate-extensive pulmonary tuberculosis in drug-susceptible cases

B Martel Chávez,[1] C Ugarte-Gil,[2] K Tintaya Miñán,[1] J Jimenez Guevara,[1] E Sánchez Garavito,[3] D Vargas Vasquez,[4] L Lecca García,[1] CD Mitnick,[5] [1]Socios En Salud Sucursal Peru, Tuberculosis Department, Lima, Peru, [2]Universidad Peruana Cayetana Heredia, Institute of Tropical Medicine Alexander Von Humboldt, Lima, Peru, [3]Hospital Nacional Sergio E. Bernales, Department of Research and Teaching, Lima, Peru, [4]Hospital Nacional Hipolito Unanue, Department of Pulmonology, Lima, Peru, [5]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America.
e-mail: bmartel_ses@pih.org

Background: Prediabetes is frequent in patients with pulmonary tuberculosis (PTB). It may occur due to an inflammatory response induced by tuberculosis infection. Hyperglycemia may, in turn, lead to a proinflammatory response and progression of TB disease. Unlike for diabetes mellitus (DM), limited research has explored the association between prediabetes and extent of disease. We estimate the association between baseline prediabetes and moderate-extensive pulmonary involvement in patients with newly diagnosed drug-susceptible PTB.
Methods: We included 180 consenting adults with newly diagnosed, previously untreated, smear positive (≥2+) PTB in Lima, Peru, between 2013 to 2015. All participant isolates were susceptible to isoniazid and rifampin by GenoType MTBDRplus 2.0 and met other eligibility

criteria for the parent study, a Phase II trial of high doses of rifampin. Patients with baseline normal (< 5.7%) HbA1c or prediabetes (5.7-6.4%) were included. Chest X-ray was interpreted by a pulmonologist to define limited, moderate and extensive tuberculosis; we dichotomized the outcome as limited vs moderate-extensive. Baseline covariates were included in the regression. We used Log-Poisson (robust) regression to determine prevalence ratio (PR).
Results: We excluded 4 patients from the analysis: one had HbA1c above the cutoff for pre-diabetes and three were missing HbA1c and/or X-ray data. 30 (17.1%) patients had prediabetes and 104 (59.1) had moderate-extensive PTB. Moderate-extensive PTB was more common in prediabetic than in normal glycemic patients (80.% vs. 54.8%; p=0.011). In multivariable analysis prediabetic patients were 1.32 times more likely to have moderate-extensive disease than normal glycemic patients (PR 1.32; 1.01-1.72, p=0.043).
Conclusions: Prediabetes is common in patients newly diagnosed with PTB. We found an association between prediabetes and moderate-extensive disease on chest X-ray in drug-susceptible cases. In this cross-sectional study, we can't ascertain the direction of the relationship. Hyperglycemia should be carefully followed as part of patient-centered care for TB.

PS-01-510-31 Diabetes mellitus as comorbidity in pulmonary tuberculosis associated with increased smear grade, extent of lung involvement and cavitation

S Prakash Babu,[1,2] A Narayanan,[1] PB Narasimhan,[1] S Knudsen,[3] NS Hochberg,[4] P Salgame,[5] RC Horsburgh Jr,[6] JJ Ellner,[5] G Roy,[1] S Sarkar,[1] [1]JIPMER, Preventive and Social Medicine, Puducherry, India, [2]JIPMER, Puducherry, India, [3]Boston Medical Center, Epidemiology, Boston, MA, United States of America, [4]Boston University School of Public Health, Boston Medical Centre, Boston, MA, United States of America, [5]Rutgers University, Department of Medicine, Newark, NJ, United States of America, [6]Boston University School of Public Health, Epidemiology, Boston, MA, United States of America.
e-mail: prco.indoustb@gmail.com

Background: Diabetes mellitus (DM) is a known co-morbid condition for tuberculosis (TB) and also a major risk factor in the development of active TB.
Methods: Aim: To study sputum positivity and lung involvement in active pulmonary TB patients with and without the co-existence of DM.
Methodology: The data is obtained from RePORT India cohort, JIPMER. The study population was comprised of 18 healthy community controls (HCC) and 214 active pulmonary TB patients, of which 129 (60.3%) were TB+DM+ and 72 (33.6%) had only TB+. Sputum smear positivity (1+, 2+, 3+), and chest X-ray (% of lung affected and cavitation) were the parameters analysed.
Results: The percentage of smear positivity was higher in the co-morbid group compared to TB alone group for each smear grade (1+ smear positivity: TB+DM+: 64%, TB+: 35.6%; 2+ smear positivity: TB+DM+: 69.4%, TB+: 30.6% and 3+ smear positivity: TB+DM+: 59.4%, TB+: 40.5%). Patients with diabetes as a co-morbidity had significantly greater extent of affected lung (85.2%) and greater likelihood of cavitation in the affected lung (25%). In the TB+ group 63.3% had affected lung was 18% with cavitation.
Conclusions: Comorbidity with DM increases the smear positivity grade and affects the lungs by increased involvement and cavitation. It is of concern that diabetes may be associated with increased lung damage and transmission of TB. This suggests further detrimental interactions, if not synergy, between the co-epidemics of diabetes and TB.

PS-01-511-31 The effects of statin vs. non-statin lipid-lowering agents on tuberculosis and other infections in type 2 diabetes patients

W-J Su,[1,2] S-W Pan,[1,2] Y-F Yen,[2,3] J-Y Feng,[1,2] [1]Taipei Veterans General Hospital, Department of Chest Medicine, Taipei, Taiwan, [2]National Yang-Ming University, School of Medicine, Taipei, Taiwan, [3]Taipei City Hospital, Division of Infectious Disease, Taipei, Taiwan.
e-mail: wjsu.mail@gmail.com

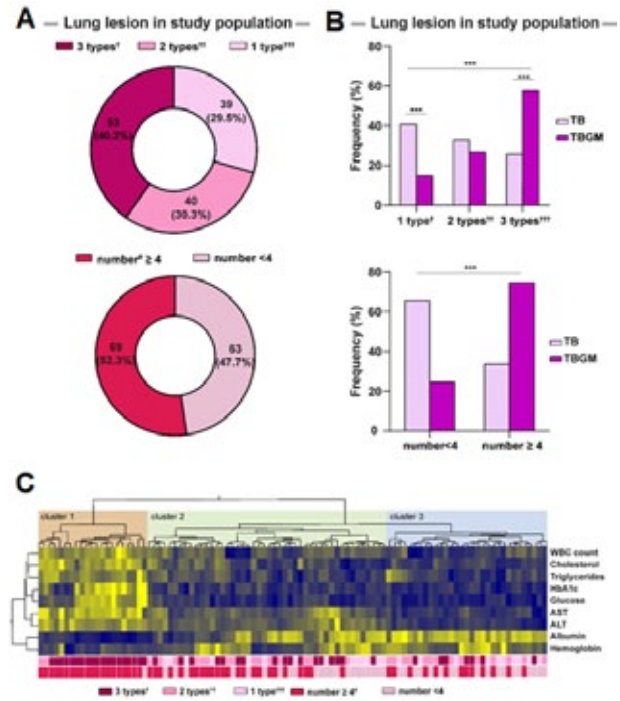
Background: Patients with type 2 diabetes mellitus (T2DM) are susceptible to tuberculosis (TB). Although statins have demonstrated anti-TB action in basic researches, the effects of statins versus non-statins lipid-lowering agents (NsLLA) on reducing TB and other infections in T2DM patients remain uncertain.
Methods: Newly diagnosed T2DM patients between 2001-2013, without prior lipid-lowering agent (LLA) treatment were enrolled in this study based on the Taiwan national health insurance research database. The patients were classified as statin-users, NsLLA-users, and LLA-free group. Patients were observed for incident TB, the primary outcome, from T2DM diagnosis until treatment crossover or December 2013; the secondary outcomes included herpes zoster and pyogenic liver abscess. Statin-user and NsLLA-user were the time-dependent variables in Cox regression analysis.
Results: Observation of 240782 person-years, TB incidences were 115, 182, and 279/10^5 person-years in statin-users (n=17696), NsLLA-users (n=5327), and LLA-free group (n=22316), respectively. TB risk was 34% lower in statin-users than NsLLA-users (HR: 0.66; 95% CI 0.44-0.99); and in a matched subcohort (HR: 0.50, 95% CI 0.28-0.89). The incidence of herpes zoster in statin-users, NsLLA-users, and LLA-free group was 957, 690, 812/10^5 person-yeaars, respectively. Statin-users had a 23% higher risk of herpes zoster than NsLLA-users (HR: 1.23, 1.01-1.50). No statistical difference on risk of

TB between NsLLA-users and LLA-free group.
Conclusions: Compared with NsLLA, statin use is associated with a decreased TB risk but an increased risk of herpes zoster among diabetic patients.

PS-01-512-31 Impact of altered glycaemia on radiographic manifestations in pulmonary tuberculosis patients from Lima, Peru

N Barreda Ponce,[1] M Arriaga,[2] OM Sanabria,[3] L Lecca,[1] R Calderon Espinoza,[4] [1]Socios En Salud Sucursal Peru, Lima, Lima, Peru, [2]Universidade Federal da Bahia, Bahia, Bahia, BA, Brazil, [3]Socios En Salud Sucursal Peru, Medical, Lima, Peru, [4]Universidade Federal do Rio de Janerio, Rio de Janeiro, RJ, Brazil. e-mail: nbarreda_ses@pih.org

Background: Radiographic manifestations in pulmonary tuberculosis (TB) patients with altered glycaemia have been documented but some references were not consistent. Some differences had related with number, location and extension of lung lesions and all this could be related with metabolic changes reveled by different biochemical and hematologic profiles. Some limitations were described but we have the hypothesis that improvements in glycaemia diagnosis will show different and better relations on radiographic profiles in TB patients with DM or preDM (GMD).
Methods: Between February and December 2017, chest radiographs (CXRs) in 132 TB patients were enrolled. Serum glucose, HbA1c and oral glucose tolerance test were performed to diagnose GMD. Biochemical and hematological tests were performed by health center TB program. Radiographic lesions include alveolar infiltrates, fibrous tracts and cavities. Potential effects of sociodemographic and clinical factors on detection of hyperglycemia were analyzed.
Results: 40.2% and 52.3% of TB patients showed 3 lesion types and ≥4 radiographic lesions. (See Fig A) Approximately, 60% TB-GMD patients have 3 lesion types and more than 75% of TB-GMD patients have ≥4 radiographic lesions.(See Fig B) Significant differences were found in the number and type of radiographic lesions in TB patients affected with DM or preDM. TB-GMD patients showed more alveolar infiltrates, fibrous tracts and cavities. Additionally, significantly high levels of WBC counts, Cholesterol, triglycerides and transaminases and low levels of albumin and hemoglobin were related with more type diverse and bigger number of lesions. (See Fig C)
Conclusions: Hyperglycemia significantly influenced the presentation of radiographic manifestations and the number of lesions in patients with pulmonary tuberculosis. This had a very good relation with metabolic changes reflected by a significantly alteration of biochemical profiles which could be associated with slow and poor evolution or worst treatment outcomes. Atypical radiographic profiles in TB-GMD patients show the need to improve the glycemic diagnosis to ensure the properly control of the comorbidity.



[Frequency of X-rays manifestations and clustering analysis with chemical and hematological profiles]

PS-02-C13 MPOWER lessons from Southeast Asia

PS-02-514-31 Cigarettes attract customers: views of cigarette retailers on the importance of providing cigarettes in their stores

NM Kurniati,[1] PA Swandewi Astuti,[1,2,3] NM Dian Kurniasari,[1,2] [1]Udayana Center for NCDs, Tobacco Control and Lung Health (Central), Research, Denpasar, Indonesia, [2]Udayana University, Biostatistics and Demography, Denpasar, Indonesia, [3]University of Sydney, Public Health, Sydney, NSW, Australia. e-mail: kurni.nimade@gmail.com

Background: Cigarette retailers are ubiquitous in Indonesia, a recent study in Denpasar mapped a high density of cigarette retailers with close distance to schools. The retailers were also admitting selling cigarette to young people. There is no regulation and there is no systematic documentation on the reliance of the retailers to cigarette selling. This study aims to explore the reliance of retailers around school to income from cigarette selling.
Methods: This was a qualitative exploration through in-depth interview with 40 cigarette retailers in four Indonesian cities: Denpasar, Semarapura, Depok and Jogjakarta in January-February 2019. We selected cigarette

retailers based on their presence around school, type of retailers and schools' level. Interview questions include direct profit from selling cigarettes, comparison of selling single sticks and packed cigarettes, and why they are selling cigarettes. The interviews were recorded, transcribed and analysed with Thematic Analysis.
Results: Most retailers admitted that the direct profit from selling cigarette is small, around IDR. 1,000. - to IDR 1,500. - per pack. There is difference from selling loose and packed cigarette, but it is still small. They also need relatively big amount of capital to be able to stock cigarettes which also depend on the size of the stores.
The main reason of selling cigarettes are due to high demands from customers and to attract customer to come to their stores which may also buy other products. The retailers raised their concern of potency to lose customers and loose potential bigger profit from selling other products if they do not provide cigarettes.
Conclusions: Cigarettes are complementary product to attract customers yet yield certain importance to the retailers. It will need a step by step process to try to regulate cigarette selling starting from prohibition of selling to young people, followed with other stronger regulation such as licensing.

PS-02-515-31 Utilisation of non-communicable disease clinics for tobacco cessation services: a plausible possibility

S Goel,[1] G Bhatt,[1] N Kaur,[2] GB Singh,[2] [1]Post Graduate Institute of Medical Education and Research, Community Medicine and School of Public Health, Chandigarh, India, [2]Government of Punjab, Health and Family Welfare, Chandigarh, India. e-mail: sonugoel@yahoo.co.in

Background and challenges to implementation: Non Communicable Diseases (NCDs) are responsible for 38 million (68%) of the world's 56 million deaths. Tobacco use is a major preventable and modifiable behavioural risk factor for NCDs. As per National Programme for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) there is a provision of screening of risk factors for NCDs (including tobacco) besides providing them treatment and behavioural advice for NCDs. However, NCD clinics are not being used optimally utilized for providing cessation services.
Intervention or response: A comprehensive tobacco cessation intervention package was designed to be delivered at NCD clinics for NCD patients who are tobacco users as well which was further validated after taking inputs from experts, academicians, tobacco users and program managers of tobacco control and NCD Control. The package comprises of a booklet for Health Care Providers (HCPs) at NCD clinic, Disease specific pamphlets (for patients), and stage of behaviour change specific short text messages (SMS) in vernacular language. The program managers were oriented for implementation of this package.
Results and lessons learnt: The knowledge and skills of HCPs at the NCD clinics, with regard to tobacco cessation services can be enhanced which will provide an opportunity to integrate two national programs for synergistic outcomes.
This approach could be cost-effective and operationally viable for long term sustainability as it will be a part of an existing service under the national programme. However, this approach of integration shall face challenges in terms of resistance of staff for perceived additional responsibility, poor compliance of patients for follow up, and sub-optimal coordination between program managers.
Conclusions and key recommendations: Delivery of effective patient centric, disease specific, culturally sensitive tobacco cessation services at NCD clinic, might prove to be an efficient measure in reducing complications of NCDs among patients using tobacco.

PS-02-516-31 Exploring the mapping analysis of tobacco licensing system to tobacco control in city corporations and municipalities of Bangladesh

A Islam,[1] A Islam,[1] KM Hasibul Huq,[1] [1]AID Foundation, Program, Mohammadpur, Bangladesh. e-mail: aminulislambakul@gmail.com

Background: AID Foundation implementing a 2-year project title "Introduce, implement and monitor national and sub national licensing policy for tobacco sales" in the 22-district, 5-City Corporation and 18-Municipality under Dhaka and Khulna Divisions. The aim of the project is to introduce stringent licensing system for tobacco sales in Bangladesh.
Methods: This research mainly explored the progress of project intervention and situation of introduce, implement and monitor national licensing policy for tobacco sales in project areas. The research used simple random samplings techniques for selecting sample the 119 respondents, e.g. City Corporation & Municipality Mayors, Commissioners, Secretary, licensing officers, revenue officers, health officers, sanitary inspector and BATA members. Questionnaire survey and informal discussion tools were mainly used for data collection from the respondents.
Results: Findings of the research revealed that 96.5% of respondents are known about the tobacco control law (TCL) and 54% of the respective organizations like City Corporation and Municipality have a licensing guideline.
The research also found that 27.8% of respective organizations have annual budget allocation (average, USD$ 2,024) for taking initiatives of the TCL at their working areas. Only 38.3% of respondents said that their organ-

ization has conducted mobile court to control openly selling tobacco product and follow-up the licensing.
However, a good percentage (53.5%) of respondents said that their organization is providing licensing for controlling tobacco sale at local level. From the informal discussion observed, the majority of the unregulated tobacco traders and sellers did not have any legal permission or license to sell the tobacco commodities. However, they wanted to license to continue their business and expected an alternative job opportunity for them at locally.
Conclusions: The survey suggests that special efforts like apply TCL, licensing, Mobile Court with follow-up and alternative employment opportunity would be required to control the selling of tobacco commodities at local level.

PS-02-517-31 Identifying and changing smoking places through health promotion approach in Karuwalagashinna village in Anuradhapura, Sri Lanka

A Wijerathne,[1] M Roushan,[1] H Gunarathna,[1] N Karunarathna,[1] S Gunasekara,[1] N Rathnayake,[1] HDSP Subhani,[1] S Kumara,[1] GND Guruge,[1] Children Society in Karuwalagashinna [1]Rajarata University of Sri Lanka, Health Promotion Department, Anuradhapura, Sri Lanka. e-mail: asinsalawijerathne@gmail.com

Background and challenges to implementation: Over 20,000 people die per a year from tobacco related illnesses in Sri Lanka. Therefore, actions should be taken to address this issue. Objective of this study was to identify the smoking places and to change those places in Karuwalagashinna village in Anuradhapura district using health promotion approach.
Intervention or response: At first, we discussed about location of the village with the children society. Then, Children drew their village map and unprotected places were marked on it. They identified some places where people used for smoking & drinking alcohol as gangs and some shops where people used to smoke mostly as unprotected places. After identifying unprotected places, they developed interventions to change these places. Then they discussed with their parents and key persons in the village about these places and how those places can be risky in particularly for children.
Video clips were used as evidence to discuss about how these places can be risky. Awareness about these places was improved using the community map. Posters campaign, hanging expenditure calendars mentioning how much of money is spent per year due to smoking, a box to put money saved as a result of reducing number of cigarettes and changing the way of responding to those places and smokers were some interventions that used to change these unprotected places.
Results and lessons learnt: Children's awareness was improved in order to identify smoking places as unprotected.
Awareness level of the villagers was improved about these places and risk of these places.
There were four places which used for smoking and drinking alcohol as gangs and three shops where people used to smoke. Number of cigarette buds were reduced near these three shops. Smoking & drinking alcohol were reduced at these unprotected places.
Conclusions and key recommendations: Health promotion approach is an effective way to empower people to take actions for reducing smoking behavior.

PS-02-520-31 Monitoring survey of display and tobacco advertising, promotion, and sponsorship ban at modern retailers in Depok City, 2018

B Priyono,[1] B Hafidhah,[2] Wihardini,[3] R Nuryunawati,[1] [1]No Tobacco Community, Bogor, Indonesia, [2]No Tobacco Community, South Tangerang, Indonesia, [3]No Tobacco Community, Depok, Indonesia. e-mail: bhanks.priez@gmail.com

Background: Depok City is a Child-Friendly City, which also pays attention to the health protection of its citizens from the effects of tobacco pruduct as evidenced by the Depok City Local Regulation No.3 of 2014 concerning Smoke-Free Area (SFA).
On the 13th article (2) it stated that Persons and / or institutions and / or agencies that sell cigarettes in Smoke Free Area are prohibited to clearly show the types and products of cigarettes but can be indicated with a sign"cigarette available".
The implementation of this article has not been maximized, a pre-survey and post-survey was carried out in order to see the extent to which display bans and tobacco advertising, promotion and sponsorship (TAPS) ban in modern retailers in Depok City 2018.
Methods: The pre-survey was conducted on 7-17 September 2018 (before Depok City Mayor's Letter No. 300/357-SatPol.PP circulated) and the post survey was conducted on 25 November-16 December 2018 with samples of 40 and 400 modern retailers respectively (including the mall). Both are descriptive observational surveys to see compliance and support and experience of modern retail managers in implementing SFA using the monitoring sheets.
Results: The results of the pre and post survey are as follows. Found cigarette displays from 95% to 19.5%, found cigarette advertisements as much as 87.5% to 21.75%, found cigarette promotions as much as 75% to 16.25%, there are writings available here cigarettes at 0% to 79.25% and found sponsors there was a decrease of 5% to 2.5%. And the regulatory support for cigarette display closure rose from 92.5% to 99.75%.
Conclusions: This shows that there was a decrease in large numbers of violations in the implementation of bans on displays and TAPS ban before and after the Mayor's letter.

PS-02-521-31 Smokeless tobacco use and dependence among slum dwellers in Bhubaneswar city, India

R Gadtia,[1] PK Jena,[1] N Satpathy,[1] [1]KIIT Deemed to be University, School of Public Health, Bhubaneswar, India.
e-mail: rasmirekha50@gmail.com

Background: Monitoring tobacco use and offering help to quit are two important interventions for tobacco control. Considering high burden of smokeless tobacco in Eastern India, this study was conducted to assess the burden of smokeless nicotine or tobacco dependence using tool i.e. FTND (Fagerstrom Test for Nicotine Dependence) and ICD-10 (International Classification of Disease, 10th edition) criteria.
Methods: About 251 individuals from Bhubaneswar city Odisha were included in this study. A interview schedule using GATS questionnaire, FTND tool for smokeless tobacco and ICD-10 criteria was developed and data collected using mobile based Epicollect 5.0 application and data was analyzed using R package.
Results: About 80.87% (63.35% male and 36.45% female) respondents were current smokeless tobacco users among them 53.38% were daily users. Mean FTND score among daily smokeless tobacco users was 3.91±1.87 respectively and 60% (95%CI: 52%-69%) daily smokeless tobacco user had medium or high dependence to nicotine. ICD-10 criteria identified 42% (95%CI: 38%-64%) of the smokeless tobacco users as dependent.
The factors that found to be significantly associated with Nicotine Dependence among smokeless tobacco users included age, gender, education and marital status. Concordance between FTND Scale and ICD-10 criteria was higher for the group with FTND score four or more.
Conclusions: As a high proportion of daily smokeless tobacco users are nicotine dependent, the government should focus on reaching these people with tobacco cessation services. Four out of ten smokeless tobacco users were clinically dependent. These findings reflect urgent need to fulfill the unmet need for offering assistance to tobacco user for quitting as per WHO MPOWER strategy. This study also found the usefulness of FTND in community settings to assess dependence.

PS-03-D1 Still far from zero TB deaths

PS-03-523-31 Tuberculosis and cardiovascular disease risk: a systematic review and meta-analysis

CA Basham,[1,2] S Smith,[3] K Romanowski,[2] J Johnston,[1,2,4] [1]University of British Columbia, School of Population and Public Health, Vancouver, BC, Canada, [2]British Columbia Centre for Disease Control, Provincial TB Services, Vancouver, BC, Canada, [3]University of Manitoba, Max Rady College of Medicine, Winnipeg, MB, Canada, [4]University of British Columbia, Division of Respiratory Medicine, Vancouver, BC, Canada.
e-mail: umbashac@myumanitoba.ca

Background: There is increasing epidemiological evidence of an association between tuberculosis (TB) and cardiovascular disease (CVD) risk. The primary objective of this study was to estimate a pooled risk ratio (RR) of CVD among persons diagnosed with TB compared to persons not diagnosed with TB.
Methods: We systematically searched EMBASE, MEDLINE, and Cochrane databases for terms related to TB, CVD, and epidemiological study designs. Two reviewers screened studies, applied ROBINS-I tool to assess risk of bias, and extracted data independently from included studies. Random effects meta-analysis was used to estimate a pooled RR of CVD for persons diagnosed with TB compared to those not diagnosed with TB.
Results: A total of 5,628 articles were identified, with full text assessment of 211. Fifteen studies were included in the review and subsets of estimates from non-overlapping populations with sufficient data were meta-analyzed.
We estimated a pooled RR of 2.06 (95%CI: 1.58 to 2.68) for CVD among those with TB. We determined a pooled risk of bias across studies of "serious" using the ROBINS-I tool.
Conclusions: We found significantly increased risk of CVD among persons diagnosed with TB in the reviewed literature. Prospective studies of TB and CVD are required to understand the relationship between TB and CVD.

PS-03-524-31 Case fatality and recurrent TB among privately treated TB patients in Patna, India

S Huddart,[1,2] M Singh,[3] N Jha,[3] M Pai,[1,2] [1]McGill International TB Centre, Epidemiology, Montreal, QC, Canada, [2]McGill University, Epidemiology, Montreal, QC, Canada, [3]World Health Partners, TB, Patna, India.
e-mail: sophie.huddart@mail.mcgill.ca

Background: A key component of the WHO End TB Strategy is quality of care, for which case fatality is a critical marker. India accounts for 29% of global TB deaths and half of India's TB patients are treated in the highly unregulated private sector. Our study estimated the case fatality ratio (CFR) and rate of recurrent TB among privately treated Indian TB patients.
Methods: Through the Private Provider Interface Agency (PPIA) project in Patna, World Health Partners has treated more than 65,000 patients since 2014. Of these, a random sample of 4,000 patients treated from 2014 to 2016 were surveyed for case fatality and recurrent TB via phone survey or home visit. CFR is defined as the proportion of patients who die during the period of interest. Treatment CFRs, post-treatment CFRs and rates of recurrent TB were calculated. Predictors for fatality and recurrence were identified using Cox proportional hazards modelling. Selection bias due to unreachable patients was adjusted for using inverse probability selection weighting.
Results: Of 4,000 patients, 2,151 (53.8%) were surveyed by April 2019, of whom 217 had died. The selection bias-adjusted treatment CFR was 7.19% (6.17%, 8.26%). The adjusted CFR was 1.28% (0.81%, 1.78%) at 12 months post-treatment and 2.98% (2.06%, 3.92%) at 24 months post-treatment. The adjusted rate of recurrent TB was 1.14% (0.69%, 1.63%) at 12 months post-treatment and 3.23% (2.26%, 4.22%) at 24 months post-treatment. Age was a significant predictor of post-treatment fatality (HR 1.06, CI: 1.04, 1.08).
Conclusions: PPIA-treated patients in Patna experienced a moderate treatment CFR but rates of recurrent TB and post-treatment CFRs were low.
Our data, however, might reflect the best-case scenario in the private sector, as providers engaged in the PPIA project have received training, incentives, free diagnostics and drug vouchers, and adherence support for their patients.

PS-03-525-31 Estimating the impact of pre-treatment loss to follow up on TB mortality estimates at public health facilities in Uganda

S Zawedde-Muyanja,[1] J Musaazi,[1] YC Manabe,[2] A Katamba,[3] B Castelnuovo,[1] A Cattamanchi,[4] [1]Infectious Diseases Institute - College of Health Sciences, Makerere University, Research, Kampala, Uganda, [2]Johns Hopkins University School of Medicine, Division of Infectious Diseases, Department of Medicine, Baltimore, MD, United States of America, [3]Makerere University Kampala, Department of Medicine, Kampala, Uganda, [4]University of California San Francisco, Medicine, San Francisco, CA, United States of America.
e-mail: szawedde@idi.co.ug

Background: Tuberculosis (TB)-associated mortality estimates derived only from cohorts of patients initiated on TB treatment may under-represent actual mortality as they exclude pre-treatment deaths. We sought to estimate the impact of deaths among patients with pre-treatment loss-to-follow-up (LFU) on TB mortality estimates in Uganda.
Methods: We retrospectively reviewed data on all patients with bacteriologically-confirmed pulmonary TB at 10 health facilities from January to June 2018, including 3 primary care facilities, 4 district hospitals and 3 tertiary referral hospitals. Pre-treatment LFU was defined as not starting TB treatment within two weeks of diagnosis. We traced all pre-treatment LFU patients to ascertain their vital status. We updated mortality outcomes of patients successfully traced. We then carried out sensitivity analyses to ascertain how the results would be modified if all patients who were not successfully traced were assumed to stay alive or die after diagnosis.
Results: Of 510 TB patients included, 100 (19.7%) experienced pre-treatment LFU. Of these, 42 were successfully traced. There were no differences in age, sex and HIV status between patients successfully traced or not. Of the 42 patients successfully traced, 10 (24%) had died (all prior to TB treatment initiation). After correcting for mortality among patients with pretreatment LFU, overall mortality estimates increased by 28.4% from 6.7% (95%CI 4.6%-9.6%) to 8.6% (95%CI 6.3%-11.7%). Stratified by level of care, updated mortality estimates were (5.6% (95%CI 2.6%-12.2%) at primary care facilities; 7.9% (95%CI 4.4% -14.3%) at district hospitals and 10.6% (95%CI 7.0%-15.7%) at tertiary referral hospitals. Sensitivity analyses treating all patients not successfully traced as alive or dead resulted in updated mortality estimates of 7.6% (95%CI 5.6% - 10.4%) and 19.8% (95%CI 16.5%-23.7%) respectively.
Conclusions: TB associated mortality estimates should be corrected using vital status of patients who experience pre-treatment LFU. Further tracing exercises are needed to define outcomes of these patients.

PS-03-526-31 Case fatality among Indian tuberculosis patients: a systematic review and meta-analysis

S Huddart,[1,2] A Svadzian,[1,2] V Nafade,[1,2] S Satyanarayana,[3] M Pai,[1,2] [1]McGill International TB Centre, Epidemiology, Montreal, Canada, [2]McGill University, Epidemiology, Montreal, Canada, [3]International Union Against Tuberculosis and Lung Disease, Center for Operational Research, New Delhi, India.
e-mail: sophie.huddart@mail.mcgill.ca

Background: More than a quarter of the global TB deaths occur in India. Patient mortality is an important marker of care quality as prompt diagnosis and appropriate treatment should prevent deaths both during and after treatment. This systematic review seeks to estimate the case fatality ratio (CFR) for Indian TB patients.
Methods: We searched Medline, Embase and Global Health for eligible papers published between 2006 and 2017. The treatment and post-treatment CFRs were extracted and, when sufficiently homogeneous, pooled using Normal-Binomial Generalized Linear Mixed Models. Pooling was also performed in key patient subgroups. Study quality was evaluated using a modification of the SIGN Cohort criteria.
Results: A total of 125 relevant studies were identified. The overall treatment CFR was 0.06 (95% CI: 0.04, 0.07). The CFR was higher for HIV+ [0.11 (0.08, 0.15)] and DR-TB patients [0.12 (0.08, 0.17)]. We found similar CFRs for adult [0.05 (0.03, 0.08)] and pediatric [0.04 (0.02, 0.09)] patients. The public sector CFR was 0.05 (0.04, 0.07) but only 4 of 125 (3.2%) papers described privately treated patients, precluding a pooled estimate for this strata. Only 11 (8.8%) papers described post-treatment fatality and these could not be pooled. Out of 125 studies, 78 (62.4%) had limited generalizability, 31 (24.8%) had selection bias, and 6 (4.8%) had short follow-up times. Quality concerns were present in 74.4% of papers.
Conclusions: Our study shows that overall, Indian TB patients experience a CFR equal to that called for in the WHO End TB strategy. However, the CFR is not well described or is unacceptably high for important vulnerable groups. This work highlights the need for more high quality patient follow-up, especially in India's large private healthcare sector.

PS-03-527-31 All-cause mortality after loss to follow-up among patients with drug-resistant tuberculosis, country of Georgia

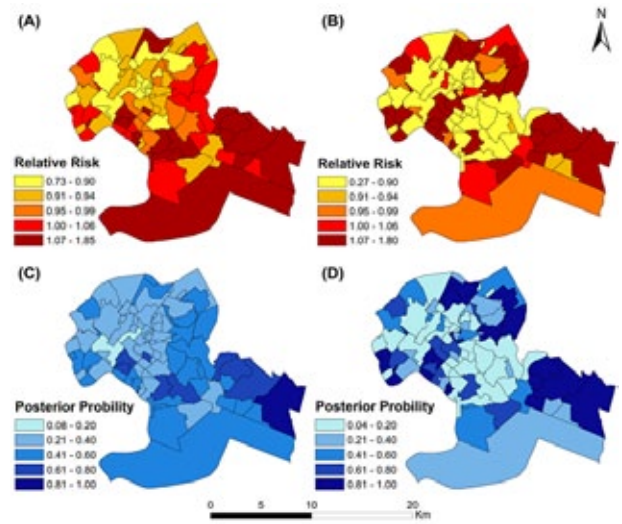
N Adamashvili,[1] D Baliashvili,[2] G Kuchukhidze,[3] H Blumberg,[4] R Kempker,[4] N Lomtadze,[5] Z Avaliani,[5] M Magee,[6] [1]National Center for Disease Control and Public Health, Global Fund Tuberculosis Program, Tbilisi, Georgia, [2]Rollins School of Public Health, Emory University, Epidemiology, Atlanta, GA, United States of America, [3]World Health Organization, Division of Health Emergencies and Communicable Diseases, Copenhagen, Denmark, [4]Emory University School of Medicine, Division of Infectious Diseases, Atlanta, GA, United States of America, [5]National Center for Tuberculosis and Lung Diseases, Surveillance and Strategic Planning Department, Tbilisi, Georgia, [6]Georgia State University School of Public Health, Division of Epidemiology and Biostatistics, Atlanta, GA, United States of America.
e-mail: dbalias@emory.edu

Background: Loss to follow-up (LFU) is common among patients with drug-resistant (DR-TB) receiving second-line TB treatment. However, little is known about mortality among DR-TB patients who were LFU. We aimed to determine all-cause mortality rates and identify factors associated with all-cause mortality after LFU among patients with DR-TB from the country of Georgia.
Methods: We conducted a retrospective cohort study using data from the Georgian National TB Program. Eligible participants included adult patients with DR-TB who initiated second-line TB treatment during 2011-2014 and were subsequently defined as LFU (treatment interruption for ≥2 consecutive months). Survival status and dates of death were determined by cross referencing patients with Georgia's National Death Registry. Clinical and laboratory data were abstracted from the National Center for Tuberculosis and Lung Diseases medical records. We used survival analyses to estimate all-cause mortality rates, age- and sex-adjusted hazard ratios (aHR), and 95% confidence intervals (95%CI).
Results: During 2011-2014, 2350 patients with DR-TB initiated second-line treatment and 30% (n=695) were LFU and included in analyses. Among LFU patients, 87% were male, median age was 35 years (range 18-85), 56% were previously treated for TB, and 30% resumed TB treatment after LFU. Among LFU patients there were 143 (21%) deaths during 2805 person-years (PY) post LFU (all-cause mortality rate 5.1 [95%CI 4.3-6.0] per 100 PY). In multivariable analysis, low weight at treatment initiation (BMI < 18.5 vs. 18.5-25; aHR=3.4, 95%CI 2.3-4.9), not returning to treatment after LFU (aHR=0.3, 95%CI 0.2-0.5), and past TB history (aHR=1.5, 95%CI 1.1-2.2) were associated with mortality.
Conclusions: High all-cause mortality occurred among patients with DR-TB who were LFU; more than one in five LFU patients died. Our data suggest additional efforts to assist patients with DR-TB who have low BMI and past TB history will enhance public health and may reduce mortality risk.

PS-03-528-31 Social determinants and tuberculosis deaths in the Brazilian midwest: evidence from the Bayesian approach

JD Alves,[1] JA Crispim,[2] LS Alves,[3] MAM Arcoverde,[4] IS Assis,[3] AMU Rodrigues,[5] CS Souza,[5] IC Pinto,[6] F Chiaravalloti-Neto,[7] RA Arcêncio,[6] [1]Federal Institute of Mato Grosso, Department of Education, Barra do Garças, MT, Brazil, [2]University of São Paulo at Ribeirão Preto College of Nursing, Nursing PhD Interunits Program, Ribeirão Preto, SP, Brazil, [3]University of São Paulo at Ribeirão Preto College of Nursing, Post-Graduation Program Public Health Nursing, Ribeirão Preto, SP, Brazil, [4]State University of Western Paraná, Campus of Foz do Iguaçu, Foz do Iguaçu, PR, Brazil, [5]University of São Paulo, Ribeirão Preto College of Nursing, Ribeirão Preto, SP, Brazil, [6]University of São Paulo at Ribeirão Preto College of Nursing, Maternal-Infant and Public Health Nursing Department, Ribeirão Preto, SP, Brazil, [7]University of São Paulo, Epidemiology Department, São Paulo, SP, Brazil.
e-mail: ricardo@eerp.usp.br

Background: The reduction of TB mortality by 95% in 2035, proposed by the End TB Strategy, is challenging for Brazil because the territorial extension, cultural variations and inequalities in the distribution of social protection and health resources. The objective of this study was to analyze the spatial and temporal-space relationship of social determinants (SD) and the risk of TB deaths.
Methods: An ecological study conducted in Cuiabá, capital of the state of Mato Grosso, Central West region of Brazil. The units of analysis were the Human Development Units (HDUs) and the population was constituted by cases of TB deaths (basic cause) recorded between 2006 and 2016. There were three Bayesian models using the Integrated Nested Laplace Approximation (INLA) in software R:
(1) temporal-space model,
(2) spatial model and
(3) spatial model adjusted for covariates representative of schooling, income, housing and occupation.
Results: Were recorded 225 deaths from TB. The temporal-space model indicated an average relative risk reduction between 2006 (RR = 1.03) and 2016 (RR = 0.98). The model with random spatial effects also showed a reduction of the risk in several HDUs between 2006 (mean 0.96; min: 0.71; max.: 1.96) and 2016 (mean 0.92; min: 0.68; max.: 1.88). In the third model, the representative covariates of SDs explained part of the risk of deaths from TB (Figure 1). Since the rate of a standard deviation of household income corresponded to a 31% decrease in mortality risk (mean. 0.691, 95% CI: 0.496-0.915).
Conclusions: The results suggest an association of social determinants with the risk of mortality from TB and the existence of risk areas that persist for more than a decade. The investment in public policies of improve in the income distribution; especially in regions at higher risk can contribute to reducing TB death.



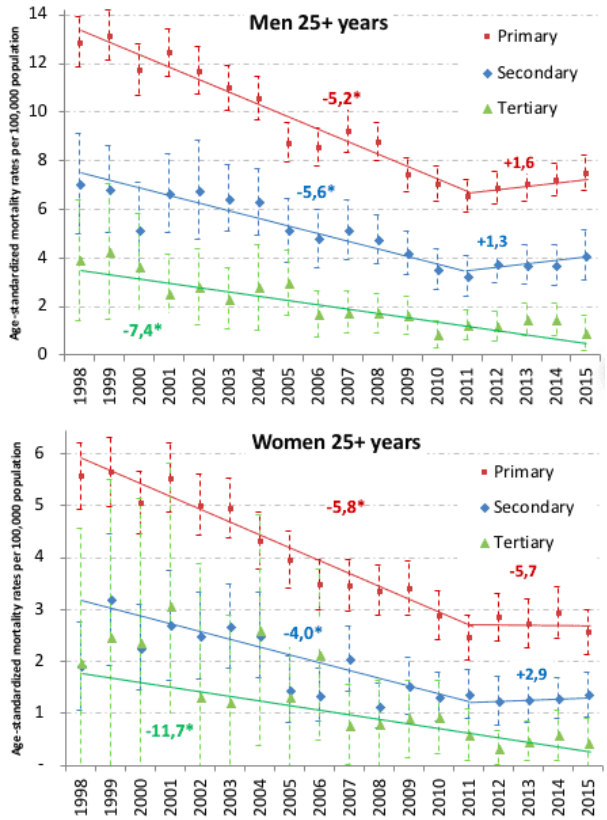
[Relative risks and posterior probability: (A-C) Spatial model; (B-D) Model adjusted for covariates]

PS-03-529-31 Trends of educational inequalities in tuberculosis mortality in Colombia: an unequal progress, 1998-2015

S Valencia-Aguirre,[1] ID Arroyave Zuluaga,[2] C Castañeda-Orjuela,[1] IA Ordóñez Monak,[3] [1]Instituto Nacional de Salud, Observatorio Nacional de Salud, Bogotá, Colombia, [2]Universidad de Antioquia, Salud Pública, Medellín, Colombia, [3]Universidad Nacional de Colombia, Salud Pública, Bogotá, Colombia.
e-mail: salomevalenciaaguirre@gmail.com

Background: Tuberculosis (TB) is a leading cause of morbidity and mortality, mainly in low- and middle-income countries. Educational status is a determinant of access to diagnosis and treatment.
The aim of this study is to describe trends of TB mortality according to the educational level in Colombia between 1998 and 2015.
Methods: First, Age-Standardized Mortality Rates (ASMR) per 100,000 inhabitants by educational level (primary, secondary and tertiary) and sex (>25 years) were calculated. To asses inequalities, relative measures such as Rate Ratios (RR) and the Relative Index of Inequality (RII) through Poisson regression models were implemented. Finally, to evaluate the changes over time, the Annual Percentage Change in mortality (APC) was estimated. A joinpoint regression was used to verify if the changes over time were statistically significant.
Results: ASMR per 100,000 deaths were: 6.8 for men and 2.7 for women. There is an increased risk of mortality in the group with primary education while comparing with tertiary level: RR-men 5.00 and RR-women 5.3, RII-men 6.7 and RII-women 8.0.
Trends in mortality among the most educated showed a decreased during the whole period (APC: men = -7%, women = -11%). The groups with primary education (APC: women = -5.8%, men = -5.2%) and secondary

(APC: men = -5.6%, women = -4.0) had a significant reduction in the first cut-off period of the joinpoint regression (1998-2010), and a non-significant increase in the second (2011-2015).



[Trends of Age-standardized TB mortality rates for men and women over 25 years, including Annual Perc]

Conclusions: Mortality due to TB was higher among the two groups with primary and secondary educational level and did not show significant changes since 2010. While mortality among the most educated had a significant decrease during the period of study. Education status influences TB mortality in Colombia. Therefore, policies to address the control and prevention of the disease must be approached from the perspective of the social determinants of health.

PS-03-530-31 Risk factors associated with mortality among TB-HIV co-infected patients in Paraguay

G Aguilar,[1,2] P Ovelar,[3] G Estigarribia,[1] T Samudio,[4] S Aguirre,[5] G Sequera,[6] C Rios,[7] [1]Universidad Nacional de Caaguazu, Instituto Regional de Investigación en Salud, Coronel Oviedo, Paraguay, [2]Ministerio de Salud Publica y Bienestar Social, HIV / AIDS Control Program / ITS-MSPyBS, Asunción, Paraguay, [3]Programa Nacional de Control de VIH ITS, Departamento de Atención Integral, Asunción, Paraguay, [4]Ministerio de Salud Pública y Bienestar Social del Paraguay, HIV / AIDS Control Program / ITS-MSPyBS, Asunción, Paraguay, [5]Ministerio de Salud Pública y Bienestar Social del Paraguay, National Tuberculosis Control Program-PNTB-MSPyBS, Asunción, Paraguay, [6]Ministerio de Salud Pública y Bienestar Social del Paraguay, General Directorate of Health Surveillance-MSPyBS, Asunción, Paraguay, [7]Universidad Nacional de Caaguazu, Facultad de Ciencias Medicas, Coronel Oviedo, Paraguay. e-mail: lalyestigarr@gmail.com

Background: The lethality of TB/HIV co-infection in Paraguay was 20, 29% in the period 2014-2018. Our aim was to determine the risk factors associated with mortality among TB/VIH co-infected patients in Paraguay.
Methods: We conducted a retrospective case-control study between January 2014 to December of 2018. Patients with TB/VIH reported as deceased to the TB and VIH Control Program were considered cases, and those patients with TB/VIH whose that were found to be alive at the end of 2018 were considered controls. The risk factors assessed were: age, sex, region of residence, type of population (indigenous, persons deprived of liberty, key population, general population), baseline cd4, cd4 count and viral load >100000 copies/ml the time of coinfection TB/VIH, ART initiation, TB location. The chi-squared test were used for the categorical variables. The strength of association was determined by calculating odds ratios (OR) and their 95% confidence intervals (CIs). Regressions analyses were used to determine the association of variables.
Results: 197 cases and 591 controls were included. The factors associated with mortality were: No initiation of ART [OR; 3.8 95% CI; 2.5-8 P = .000], baseline CD4 count less than 200 cells/ml^3[OR; 3.4, 95% CI; 2-0-6.1 P = .000],CD4 count less than 200 cells/ml^{3}at the time of coinfection: [OR; 2.6, 95% CI; 1.3-5.5 P = .002], viral load >100000 copies ml at time of coinfection TB/VIH[OR; 2.1, 95% CI; 1.2-3.6 P = .001], extrapulmonary location[OR; 2.3, 95% CI; 1.1-4.7.6 P = .011]. By multivariate analysis the two first associations were confirmed.
Conclusions: Implementing effective strategies for early diagnosis of HIV , TB / HIV co-infection and access to ART in Paraguay is of utmost importance for the reduction of TB/VIH mortality.

PS-03-531-31 Implementation of TB mortality reviews in countries with high TB case fatality rate: sharing experience from Eswatini

D Vambe,[1] F Chihaye,[2] N Dlamini,[1] S Masuku,[3] J Sibanda,[4] B Kerschberger,[5] A Kay,[6,7] S Haumba,[8]
[1]National TB Program, PMDT, Manzini, Eswatini, [2]University Research Co., LLC (URC), TB/HIV, Mbabane, Eswatini, [3]National TB Control Program, Monitoring and Evaluation, Manzini, Eswatini, [4]National Tuberculosis Program, Community TB, Manzini, Eswatini, [5]Médecins Sans Frontières (Operational Centre Geneva), Research, Mbabane, Eswatini, [6]Baylor Children's Foundation, Paediatrics TB/HIV Research, Mbabane, Eswatini, [7]Baylor College of Medicine, Paediatrics Research, Houston, TX, United States of America, [8]University Research Co., LLC (URC), TB/HIV Health Systems, Mbabane, Swaziland.
e-mail: dvambe@gmail.com

Background and challenges to implementation: In Eswatini, two-third of TB patients are co-infected with HIV. Despite high HIV treatment coverage in this group (98%) and 4-fold reduction in TB cases nationally, mortality remains high (12-14%) among drug susceptible TB (DS-TB) and (16-21%) among drug resistant TB (DR-TB).

Here we share the TB Mortality Review (TMR) outcomes and toolkit designed to identify risk factors for death and inform targeted strategies to reduce TB mortality.

Intervention or response: The Eswatini National TB Control Program (NTCP) and TB/HIV partners developed a structured mortality review process and toolkit. This toolkit included TB mortality register, standard operating procedure for conducting TMRs and case report forms (CRFs) for documenting TMR outcomes.

The toolkit was piloted, followed by refinement and full implementation. 146 Health Care Workers (HCWs) were trained to conduct TMRs using the toolkit; and 66 TB facilities successfully implemented TMRs.

Results and lessons learnt: Overall, 50% of TB deaths were clinically diagnosed vs. 40% in all TB cases. TB deaths were over represented (92%) in people living with HIV (PLHIV), while 69% of TB cases occur in PLHIV nationally. ART uptake was far lower (62.5%) in PLHIV who died with TB when compared all patients with HIV-associated TB (98%).

Notably the majority deaths (81%) occurred at home, limiting information on cause of death. Most deaths happened before smear conversion within 1-3 months of treatment initiation.

Conclusions and key recommendations:

- Engaging community health care workers to conduct home visits following TB diagnosis may be an effective strategy for reducing mortality and can improve data quality on cause of death for patients dying at home
- Early introduction of ART is key for PLHIV diagnosed with TB
- Diagnostics for other infections and malignancies are urgently needed as are non-sputum based diagnostics to support or refute TB diagnosis in severely-ill patients
- The TMR toolkit may have potential for use in other similar settings.

PS-03-532-31 Monitoring universal health coverage in high TB burden countries: TB mortality an important tracer of progress

M Reid,[1] G Roberts,[2] E Goosby,[1] P Wesson,[3] [1]University of California, Medicine, San Francisco, CA, United States of America, [2]N/A, N/A, New York, NY, United States of America, [3]University of California, Epidemiology & Biostats, San Francisco, CA, United States of America.
e-mail: michael.reid2@ucsf.edu

Background: Despite increasing recognition that achieving Universal Health Coverage (UHC) and ending the global TB epidemic are inter-dependent, there is a paucity of empiric data characterizing whether TB disease burden and/or TB service coverage are useful surrogates for UHC.

We hypothesized that indicators of TB burden and coverage are more useful tracers of UHC than other disease-specific indicators of service provision, regardless of country TB disease burden.

Methods: Multiple linear regression analyses was used to estimate the correlation between World Health Organization's UHC service coverage index (SCI) score and TB burden (incidence and mortality rates) for 183 countries. A dominance analysis (a regression-based approach) was used to determine the relative importance of TB treatment coverage in predicting UHC SCI scores, compared to 16 other disease-specific indicators of service provision, stratifying countries by TB burden.

Results: Both TB incidence rate and TB mortality rate were negatively correlated, with UHC SCI score, (r=-0.67 and r=-0.74, respectively) across the 183 countries included in this analysis. In linear regression models, TB incidence rates explained 45% of the variability in SCI scores; TB mortality rate explained 55% of the variability. Restricting models to the 30 highest TB burden countries, both incidence and mortality explained less of the variability in SCI score (16% and 36%, respectively). In dominance analysis, TB effective treatment coverage ranked ninth (out of 16). Stratifying countries by TB burden, the TB treatment coverage estimate ranked sixth in the 30 high burden countries and ninth in the 153 non-high burden countries (table 1).

Conclusions: TB treatment coverage and mortality are both useful trackers for progress to UHC. Though not as strong a predictor as hypothesized, TB treatment coverage is a more efficient tracker compared to other disease-specific indicators especially in high TB burden, low income countries.

	High burden TB countries (n=30)		Non-high burden TB countries (n=153)		All countries (n=183)	
	Standard Dominance Coefficient	Rank (out of 16 health indicators)	Standard Dominance Coefficient	Rank (out of 16 health indicators)	Standard Dominance Coefficient	Rank (out of 16 health indicators)
TB effective coverage	0.08	6	0.06	9	0.06	9
Family planning demand satisfied	0.10	3	0.10	3	0.094	4
Antenatal care, 4 or more visits (%)	0.07	7	0.09	4	0.09	3
Child immunization (DTP3) (%)	0.06	11	0.057	11	0.057	11
HIV antiretroviral treatment (%)	0.059	9	0.057	10	0.057	10M
Fasting glucose screening	0.007	13	0.004	13	0.0048	13
Health work force density	0.13	2	0.13	1	0.13	1

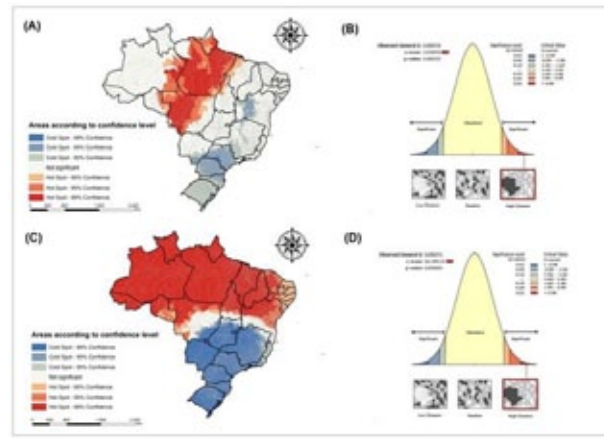
Table truncated: other WHO UHC service coverage indicators included in the full table are child pneumonia coverage, basic water sanitation provision, screening for hypertension, tobacco use screening, hospital beds/ population, medication compliance regulations [for full list see Hogan et al, Lancet Global Health, 2018]

[Table 1. Dominance analysis, ranking TB effective treatment coverage stratified by TB burden (n=183 countries)]

PS-03-533-31 Spatial analysis of the deaths by non-specified pneumonia and tuberculosis in children in Brazil, 2006-2016

TZ Berra,[1] ISd Assis,[1] LH Arroyo,[1] JDA Crispim,[1] LT Campoy,[1] MAM Arcoverde,[2] LS Alves,[1] YM Alves,[1] FLd Santos,[1] RA Arcêncio,[1] [1]University of São Paulo, Ribeirão Preto College of Nursing, Ribeirão Preto, SP, Brazil, [2]Parana West State University, Nursing Department, Foz do Iguaçu, SP, Brazil. e-mail: ricardo@eerp.usp.br

Background: There is evidence from clinical studies and autopsies that in regions with a high incidence of tuberculosis, many cases of childhood tuberculosis are misdiagnosed as Pneumonia, which worries health authorities around the world. The literature recognizes the great difficulty of establishing the diagnosis of tuberculosis in childhood due to the impossibility, in most cases, of bacteriologically confirming the disease. Therefore, the objective was to analyze the spatial distribution of deaths due to pneumonia and infant tuberculosis in Brazil.
Methods: An ecological study carried out in Brazil with a population composed of all cases of tuberculosis and pneumonia deaths in children under five years of age obtained in the DATA-SUS from 2006 to 2016. From the geocoding of the cases, the Getis-Ord Gi and Gi*.
Results: In all, 21,629 cases of child deaths were identified, of which 21,391 were caused by Pneumonia and 238 were cases of Tuberculosis in the period studied. It was possible to identify hotspots for death from tuberculosis in children under 5 years of age in the north, northeast and central-west regions of Brazil and coldspots in the northeast, central-west, southeast and all of the southern region of the country. As for mortality due to pneumonia, hotspots were identified in the north, northeast and center-west regions of Brazil and coldspots involving the northeast, center-west, southeast and throughout the southern region of the country.
Conclusions: It was possible to identify risk areas for deaths due to pneumonia and childhood tuberculosis in Brazil. Actions aimed at the elimination of tuberculosis also implies knowing the epidemiological reality of Pneumonias deaths. The findings lead to the hypothesis that among pneumonia, there may be many under-notifications of tuberculosis, which requires future studies to confirm this hypothesis.



[Hotspots and Coldspots for deaths by Tuberculosis and Unspecified Pneumonia]

PS-03-534-31 Revisiting the natural history of pulmonary tuberculosis: a Bayesian estimation of the disease recovery and mortality rates

R Ragonnet,[1] J Flegg,[2] S Brilleman,[1] N Nagelkerke,[3] E Tiemersma,[4] J Trauer,[1] E McBryde,[5] Australian Tuberculosis Modelling Network [1]Monash University, School of Public Health and Preventive Medicine, Melbourne, VIC, Australia, [2]University of Melbourne, School of Mathematics and Statistics, Melbourne, VIC, Australia, [3]United Arab Emirates University, Institute of Public Health, Al Ain, United Arab Emirates, [4]KNCV Tuberculosis Foundation, KNCV, The Hague, Netherlands, [5]James Cook University, Australian Institute of Tropical Health & Medicine, Townsville, QLD, Australia. e-mail: romain.ragonnet@monash.edu

Background: Tuberculosis (TB) natural history remains poorly characterised and new investigations are impossible as it would be unethical to follow up TB patients without treating them. Estimates of TB burden and mortality rely heavily on TB self-recovery and mortality rates, as around 40% of individuals with TB are never detected, making their prognosis entirely dependent on the disease natural history.
Methods: We considered the reports identified in a previous systematic review of studies from the prechemotherapy era, and extracted detailed data on mortality

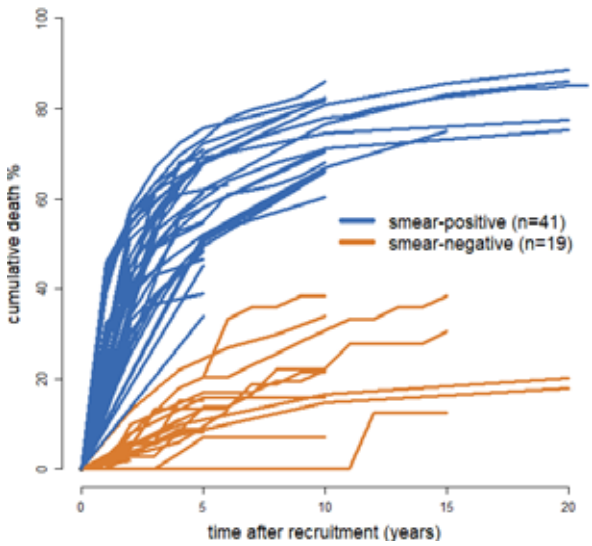
over time. We used a continuous-time Markov model in a Bayesian framework to estimate the rates of TB-induced mortality and self-cure. A hierarchical model was employed to allow estimates to vary by cohort. Inference was performed separately for smear-positive TB (SP-TB) and smear-negative TB (SN-TB).

Results: We included 41 cohorts of SP-TB patients and 19 cohorts of pulmonary SN-TB patients in the analysis. No data were available on extrapulmonary TB. The posterior median estimates of the TB-specific mortality rates were 0.390 year^{-1} (0.329-0.452, 95% credible interval) and 0.025 year^{-1} (0.016-0.036) for SP-TB and SN-TB patients, respectively.

The estimates for self-recovery rates were 0.233 year^{-1} (0.179-0.293) and 0.147 year^{-1} (0.087-0.248) for SP-TB and SN-TB patients, respectively. These rates correspond to average durations of untreated TB of 1.57 years (1.37-1.81) and 5.35 years (3.42-8.23) for SP-TB and SN-TB, respectively, when assuming a natural mortality rate of 0.014 year^{-1} (i.e. a 70-year life expectancy).

Conclusions: TB-specific mortality rates are around 15 times higher for SP-TB than for SN-TB patients. This difference was underestimated dramatically in previous TB modelling studies that parameterised models based on the ratio of 3.3 between the 10-year case fatality of SP-TB and SN-TB.

Our findings raise important concerns about the accuracy of past and current estimates of TB mortality and predicted impact of control interventions on TB mortality.



[Cumulative percentage of death observed in the 64 cohorts of TB patients]

PS-04-E1 Community involvement in finding missing cases

PS-04-535-31 Social interventions for improving coverage of tuberculosis contact investigation (CI)

W Imsanguan,[1] S Bupachat,[2] V Wanchaithanawong,[3] S Thawtheong,[4] S Nedsuwan,[5] A Wiriyaprasobchok,[5] K Kaewmamuang,[3] P Pungrassami,[6] S Mahasirimongkol,[7] J Ngamvithayapong-Yanai,[2]

[1]Chiangrai Prachanukroh Hospital, Internal Medicine Department, Chiang Rai, Thailand, [2]TB/HIV Research Foundation, Technical Management, Chiang Rai, Thailand, [3]Chiangrai Prachanukroh Hospital, Department of Pediatrics, Chiang Rai, Thailand, [4]TB/HIV Research Foundation, Statistics, Chiang Rai, Thailand, [5]Chiangrai Prachanukroh Hospital, Department of Social and Preventive Medicine, Chiang Rai, Thailand, [6]Ministry of Public Health, Department of Disease Control, Nonthaburi, Thailand, [7]Ministry of Public Health, Department of Medical Sciences, Nonthaburi, Thailand.

e-mail: minkworat@gmail.com

Background: Contact investigation (CI) is an important procedure to identify close contacts of people with tuberculosis (PWTB) and facilitate them for TB prevention and care. However, CI coverage is generally low due to poverty, TB stigma and misperception about TB. This study aimed to improve CI coverage by using invitation card and supporting transportation fee for contacts of PWTB.

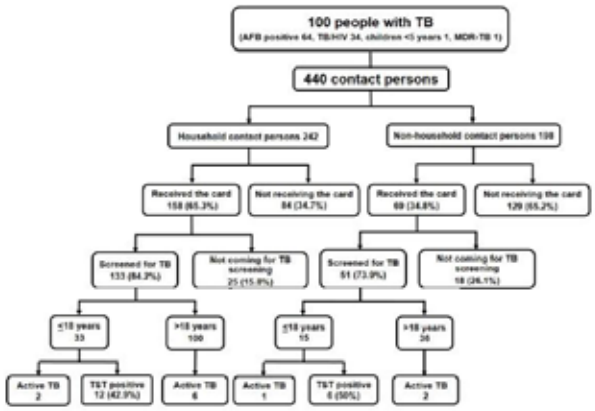
The card's contents included non-stigmatized information about the need of TB screening, curability and preventability of TB, free service with 250-baht (~ 8 USD) travel cost. The contacts presented the invitation card when they contacted the hospital.

Methods: A prospective cross-sectional study recruited 100 PWTB for the study. The PWTB who accepted the invitation cards but their contacts did not show up were followed up by telephone and home visit to know the reasons for not receiving TB screening. Data were analyzed using descriptive statistics. We measured CI coverage and detection rate of active TB and Latent TB infection (LTBI) by age group.

Results: Figure 1 summarizes the study outcomes. The 100 PWTB reported 242 household contacts (HC) and 198 non-household contacts (NHC). The acceptance for the invitation cards of HC and NHC were 65.3% and 34.8%. The CI coverage of the contacts under 5 years = 100%; 5-18 years = 79.1%; 19-60 years = 78.6% and aged over 60 years = 90.2%. Yield of active TB detection were 21.7%, 3%, 2.9% and 13.5% respectively.

Reasons for not receiving TB screening despite receiving invitation card were inability to travel due to aging and disability, no accompany persons, perceived no risk for TB. The coverage of tuberculin skin test (TST) in HC = 90.3% and NHC = 93.3%.

Conclusions: Contacts receiving invitation cards had high coverage of TB screening with high yield of active TB. Additional social interventions are needed for disabled and senior contacts.



[Figure 1: Outcomes of the social interventions on the coverage of contact investigation]

PS-04-536-31 Role of community linkage facilitators in sputum sample collection and transportation for TB diagnosis in contact tracing

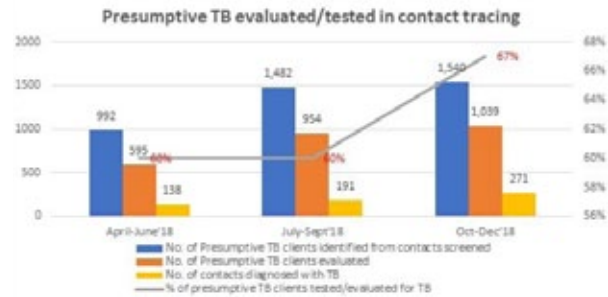
A Kazibwe,[1,2] D Lukanga,[1,2] H Ssentongo,[1,2] L Ruvwa,[3] S Turyahabwe,[3] A Nkolo,[1] [1]University Research Co., LLC (URC), USAID/Defeat TB, Kampala, Uganda, [2]The AIDS Support Organisation (U) Ltd, DPMCD, Kampala, Uganda, [3]Ministry of Health, National TB & Leprosy Division, Kampala, Uganda. e-mail: dlukanga@urc-chs.com

Background and challenges to implementation: Contact tracing is critical for diagnosing missing persons with TB, through targeting exposed persons in households and other dwelling places of persons with diagnosed TB. Contact tracing also defrays the transport cost for facility testing as sample collection can be done when the contact is located. However, the quality of sputum sample collection and the programmatic cost of transportation for investigation remains a significant challenge in completing the cascade for systematic contact tracing.

Intervention or response: The USAID Defeat TB project supported Civil Society Organizations (CSOs) to identify and train community linkage facilitators (CLFs) to conduct contact tracing in Kampala, Wakiso and Mukono; in July-December 2018. They were equipped with TB screening and sputum sample collection job aids; reporting tools, and sputum sample packaging equipment, to maintain quality of samples. They worked with health facility staff to line-list index clients; and proceeded to carry out screening of exposed household and close persons of the index patients. Contacts presumed to have TB were supported to collect sputum samples; which were then labelled, packed and transported by the CLFs for GeneXpert testing and later followed up on results. Performance was measured by number and percentage of presumptive TB contacts whose sputum samples were tested.

Results and lessons learnt: Compared to April-June 2018, the proportion and absolute number of presumptive TB contacts whose sputum samples were tested increased from 595 to 1,039. There was also an increase in the number of new TB patients identified from contact tracing. These findings suggest that CLFs can be empowered to support the sputum sample collection and referral process.

Conclusions and key recommendations: CSOs play a critical role to reach the unreached populations through the use of well-trained and equipped CLFs to collect and transport sputum samples for evaluation. In resource constrained settings CSO's can bridge the gap between the faciilty and community services .



[Presumptive TB evaluated from contact tracing April-December 2018]

PS-04-537-31 Community contribution to prevention, treatment and care of people with tuberculosis in Malawi

B Mtotha Nindi,[1] HS Kanyerere,[1] J Mpunga,[1] K Mshali,[1] P Chiwenkha,[1] B Girma,[1,2] [1]National Tuberculosis Programme, Ministry of Health and Population, Lilongwe, Malawi, [2]International Training and Education Centre for Health, I-TECH, Lilongwe, Malawi. e-mail: hkanyerere@gmail.com

Background and challenges to implementation: The implementation and scaling up of community-based tuberculosis (TB) activities in Malawi remained weak despite clear need and documented cost-effectiveness of these activities in other countries. Generally, there was lack of collaboration and absence of joint strategic planning, monitoring and evaluation of community-based TB activities in the country between Malawi National TB Programme (NTP) and non-governmental organizations (NGOs).

Intervention or response: In 2016, Malawi NTP, with support from Global Fund and World Bank, started strengthening community-based TB activities. World Health Organisation's guidelines for community engagement in TB activities were adapted to suit the local

context. A local NGO was identified as a sub-recipient for Global Fund money to revamp community-based TB activities. Activities included awareness-creation among community members, training of community-based volunteers and procurement of enablers, among others. Furthermore, monitoring and evaluation system was put in place. Community-based quarterly review meetings were also instituted. Data on community-based TB activities is submitted to NTP on quarterly basis. We therefore, analysed presumptive TB cases identified by community-based volunteers in Malawi and the yield for a three-year period (2016-2018).
Results and lessons learnt: The number of presumptive TB cases referred to health facilities by community-based volunteers increased from 372 in 1st quarter 2016 to 4,966 in 4th quarter 2018. The yield from community referrals decreased from 10.8% (40 persons with TB) in 1st quarter 2016 to 4.1% (208 persons with TB) in 4th-quarter 2018. The pick in terms of number of referrals was in 3rd quarter 2017 (5,733 presumptive TB cases), with the lowest yield in the same quarter at 2.7% (154 persons with TB).
Conclusions and key recommendations: Community-based TB activities have contributed to TB prevention, treatment and care in Malawi. The decrease in yield may be due to quality of sputum specimens collected by the volunteers. The NTP needs to put in place measures to make sure that community-based volunteers get good quality sputum specimens.

PS-04-538-31 Pharmacies engaged in presumptive TB case notification in Myanmar - an effective intervention model

YK Aung,[1] PP Swe,[2] MM Thet,[1] ZWY Bo,[3] ST Thein,[1] [1]Population Services International/Myanmar, Strategic Information, Yangon, Myanmar, [2]Population Services International/Myanmar, Program Management Department, Yangon, Myanmar, [3]Population Services International/Myanmar, Community Health Services Department, Yangon, Myanmar.
e-mail: ykaung@psimyanmar.org

Background and challenges to implementation: Myanmar is included in the 30 highest TB burden countries worldwide. Although Myanmar experienced a surge in case notification from 63/100,000 population in 1999 to 279/100,000 population in 2010, the national TB prevalence survey in 2010 showed case notification gaps. Aiming to increase TB case finding, Population Services International Myanmar (PSI) has established the accelerated TB case finding activity (ACF) through pharmacies in 15 townships of Bago Region since April 2017.
Intervention or response: Pharmacy staff were trained to refer, record and report presumptive TB cases. Such targeted pharmacy engagement in TB case finding was primarily initiated by PSI in the country. After one and half year of the project, the contribution of ACF to the National TB case notifications was examined using the township-level TB program data and PSI's routine data.
Results and lessons learnt: Total number of TB notified cases from April 2017 to September 2018 was 13,758 in 15 townships of Bago Region, where 1,238 (~9%) of TB cases were notified through pharmacies. At the start of the project (April-June 2017), pharmacies contributed only 3.8% to total notified cases. These contributions had increased steadily over the following quarters: 6.5% in July-September 2017, 8.2%, October-December 2017, 8.0%, January-March 2018, 10%, April-June 2018, and 12.4%, July-September 2018. Overall, the number of TB case notifications varied over these quarters, with the number fluctuating around 2,200 cases, but the trend showed an increase from 2,064 cases before the project (Q1 2017) to 2,351 in Q3 2018.
Conclusions and key recommendations: Trained pharmacy staff made successful referrals for TB case notifications via the current PSI's ACF model, as it contributed almost 9% to the National TB notification in this region over this reporting period. It showed that pharmacies could make an important contribution and possibly narrow the gap in TB case notification.

PS-04-539-31 Putting the "community" back into community tuberculosis management: engaging to strengthen capacities to act on TB symptoms in South Africa

PC Mugoni,[1] I Cillie,[2] Z Dlamini,[3] A Koch,[4] T Maphumulo,[5] NP Gumede,[5] K Madela,[6] P Dhliwayo,[7] [1]University Research Co., LLC - South Africa, Strategic Communication, Pretoria, South Africa, [2]University Research Co., LLC - South Africa, West Coast District, Pretoria, South Africa, [3]University Research Co., LLC - South Africa, uMkhanyakude District, Pretoria, South Africa, [4]Western Cape Government Health, West Coast District, Cederberg, South Africa, [5]KwaZulu-Natal Department of Health, uMkhanyakude District, Jozini, South Africa, [6]Mpilonhle, Grants, Mtubatuba, South Africa, [7]University Research Co., LLC - South Africa, Monitoring, Evaluation and Learning, Pretoria, South Africa.
e-mail: petronellam@urc-sa.com

Background and challenges to implementation: Enhancing community tuberculosis (TB) management contributes to improving low patient diagnosis, high loss to follow-up and low adherence rates. USAID Tuberculosis South Africa Project implemented a Community Dialogue Model in 2018/2019 in peri-urban districts of uMkhanyakude, KwaZulu-Natal province and West Coast, Western Cape province, South Africa.
Intervention or response: Community capacity building, dialogue and health education through TB champions, and partnerships with radio stations were utilised to incrementally increase public awareness about TB. Stakeholders included traditional, religious and political leaders, traditional health practitioners, educators,

community caregivers, healthcare workers, hospital management and media practitioners.

Results and lessons learnt: In West Coast, capacities of 105 stakeholders to provide TB education, identify symptoms and refer to healthcare facilities were enhanced through three workshops. Four dialogues in three communities reached 120 people. Door-to-door education and screening campaigns reached 937 people directly. 102 people with presumptive TB were identified, 71 were tested, eight tested positive and were initiated on treatment in collaboration with TB clinics.

In uMkhanyakude, 243 people were trained through four workshops. 1,451 people were reached through two campaigns, 763 with presumptive TB were tested on the spot in five communities, five were diagnosed, and two initiated on treatment. Traditional health practitioners referred two of those diagnosed. In all communities, people who declined to be screened or tested were referred to clinics.

Monthly community radio interviews to disseminate TB information reached 130,000 people via Mtuba Rise FM in uMkhanyakude and 74,000 via Namakwaland Radio in West Coast.

Conclusions and key recommendations: In uMkhanyakude, public healthcare facility headcounts increased. 17.4% increase recorded in TB screening over 12 months, suggesting contribution to more informed clients accessing services. In West Coast, while PHC headcounts decreased, presumptive clients tested increased by 8.7% and positivity rate by 8.2%, suggesting quality screening and that more people with TB accessed services. Educating communities about services supports identification of people with TB.

PS-04-540-31 TB patients hosted in traditional healers' premises in Mwanza region, Tanzania

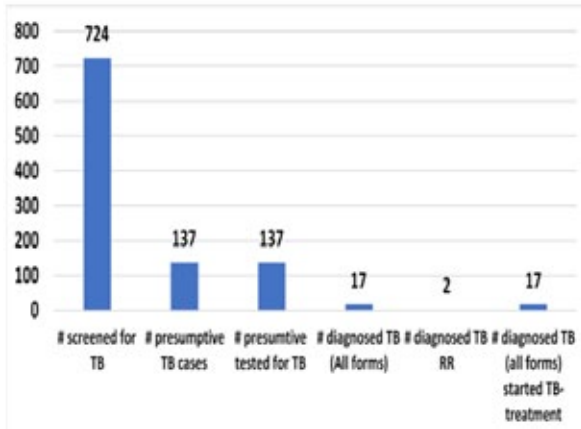
L Ishengoma,[1] R Olotu,[2] S Migeto,[3] B Mutayoba,[4] V Mahamba,[5] [1]National Tuberculosis and Leprosy Programme (NTLP), Preventive Services, Dar es Salaam, Tanzania, United Rep., [2]PATH, Community TB, Dar es Salaam, Tanzania, United Rep., [3]KNCV Challenge TB, Community TB, Mwanza, Tanzania, United Rep., [4]National Tuberculosis and Leprosy Programme (NTLP), Preventive Servces, Dodoma, Tanzania, United Rep., [5]KNCV Nigeria / Challenge TB, Programme Management, Dar es Salaam, Tanzania, United Rep.. e-mail: lilyishe2003@gmail.com

Background and challenges to implementation: Tanzania is among the 30 high burden countries with TB with the incidence of 269/100,000. (WHO, 2018) and only 44% treatment coverage. Recently, the county has realized several Traditional healers suffering from tuberculosis (TB). A quick assessment on TB disease among clients of Traditional healers was conducted in October 2018 to demonstrate TB situation among Traditional Healers and their clients and to document the effectiveness of this intervention.

Intervention or response: Four districts of Misungwi, Magu, Sengerema and Kwimba in Mwanza were involved. 25 Traditional healers' homes with high volume clients and admission services were visited. Health education on TB signs and symptoms was provided followed by TB screening, collection and transportation of sputum specimen to TB diagnostic centers for GeneXpert or Smear microscopy, referral for chest X-ray, provision of feedback laboratory results, and initiate TB treatment. The screening took four days to reach as many traditional healers' places as possible. Twenty-eight community health volunteers (CHVs) were involved. A standardized TB screening forms, community register and referral forms were used.

Results and lessons learnt: In one month of implementation, a total of 724 clients were screened for TB and 137 were identified as presumptive TB patients, all were tested for TB. Of those tested, 17 (12.4%) were confirmed susceptible TB and two were confirmed Drug Resistant TB patients, of which, one was a Traditional healer. Of 17 people with TB, 88.2% were confirmed via GeneXpert®, 11.8% via smear microscopy.

Conclusions and key recommendations: The results call for meaningful engagement of Traditional healers in finding missing people with TB to reach the End TB goal.



[TB screening at traditional healers' premises in three districts of Mwanza - October 2018]

PS-04-541-31 Active search for missing case identification in low case notification districts of Bangladesh

SM Ibna Mohsin,[1] MS Islam,[1] AKJ Maug,[2] DK Biswas,[2] AH Khan,[3] S Islam,[1] M Rifat,[1] MA Islam,[4] MS Islam,[3]
[1]BRAC, Communicable Disease Programme, Dhaka, Bangladesh, [2]Damien Foundation Bangladesh, TB Control Programme, Dhaka, Bangladesh, [3]Directorate General of Health Services, National Tuberculosis Control Program, Dhaka, Bangladesh, [4]BRAC, Communicable Diseases and Water, Sanitation & Hygiene, Dhaka, Bangladesh.
e-mail: sardar.munim@outlook.om

Background and challenges to implementation: BRAC, a development organization, is directly implementing in 45 out of 64 districts of Bangladesh (BRAC administered area) through funding from the Global Fund and the remaining districts are covered by sub-recipients (partner NGOs) of BRAC under the stewardship of NTP, where, 13 districts, case notification very low.

Intervention or response: Since 2017, special efforts, like micro planning to find out missing cases by active search, field staff and laboratory technician disseminate TB messages in the community during household visits, absentee visit (patients missed follow-up test date) and contact tracing.

Field staff sensitize and mobilize community before outreach sputum camp and organize two outreach camp every week. Laboratory technician organize one outreach sputum camp every week to improve access to diagnosis. In Bangladesh, rural settings, there are community clinics for every six thousand population run by government staff.

Our field staff also organize one sputum camp in that settings and government community health care providers also help during community mobilization before that camp. After sputum examination, presumptive with smear negative referred to the physician and provide further TB related investigation support and management.

Results and lessons learnt: In 2009 total TB cases were identified 24,453 and remain same 24,300 in 2016, after intervention number of cases increase 9% (25,633) in 2017 and 18% (26,912) in 2018 compare to 2016 baseline and reached high treatment success rate 92%. In 2017, in 19 upazilas of 11 districts, identified 11,50,665 people of 251499 households were symptom-screened and among 15,635 presumptive TB cases were tested by sputum smear microscopy and 188 (1.2%) Smear positive TB cases were diagnosed which were higher than national prevalence survey.

Conclusions and key recommendations: Active case finding approach and mobilize community people showed better result in TB case finding. This approach could increase early case detection and maintain high cure rate.

PS-04-542-31 Students are a potential force for TB awareness - an innovative approach

P Rebecca,[1] D Angamuthu,[1] B Thomas,[1] B Watson,[2] C Suresh,[1] [1]National Institute for Research in Tuberculosis, Department of Social and Behavioral Research, Chennai, India, [2]National Institute for Research in Tuberculosis, Department of Electronic Data Processing Unit, Chennai, India. e-mail: priscillamsw@gmail.com

Background: TB awareness in the communities remains to be a challenge in TB control. There is need for innovative strategies to create TB awareness for better reach into communities. School students could be potential ambassadors as was proved for HIV/AIDS control. It is against this background this study was conducted.

Methods: This is an intervention study conducted among students of classes 7 to 9 from 57 Chennai corporation schools. A baseline assessment of TB awareness was first conducted in after which students from these classes were sensitized on TB using student friendly intervention methods developed through this study (animated films, audio jingles, posters) along with their teachers.

Based on inputs from the teachers and the participation from students, we selected 200 students as ambassadors who were trained on innovative ways for TB sensitization which included folk theater, skits, and lively interactions. These ambassadors were responsible to further sensitize other students during the assemble hour. An end line assessment was done to understand the impact of the intervention.

Results: A total of 920 students were covered for the baseline assessment with a median age of 13 years (56% girls and 44% boys). For the end line assessment the coverage was 897. There was a significant ($p=0.003$) increase in TB awareness among the students with a 62% increase in awareness from pre to post intervention. Among the student ambassadors there was significant ($p<0.001$) retention of the initial TB information provided to them.

Conclusions: These findings highlight the increase in the level of awareness among school students. This increase could be attributed to the effect of the intervention. Also, the information retention was significant among the ambassadors.

PS-04-543-31 Redefining contact investigation: a closer look at NEPHAK's "Rafiki Yangu, Jukumu Langu initiative" in Western Kenya

V Okello,[1] [1]NEPHAK, Monitoring and Evaluation, Nairobi, Kenya. e-mail: vkizito@nephak.or.ke

Background and challenges to implementation: In Kenya, TB detection remains the biggest challenge and according to prevalence survey 2016, 67% of TB patients with symptoms are in the community but do not seek health care for various reasons and 80% of those who seek care with symptoms, do not get diagnosed at initial contact with the health facility and the gap between prevalence and notification rates is higher. While we acknowledging the milestones of active case finding strategy, there is still 40% of undetected cases in the community and there is need for open and honest on this topic.
Intervention or response: NEPHAK is beefing up Active Case Finding strategy with "Rafiki yangu,Jukumu langu" initiative a concept which upgrades contact investigation. The concepts involve counselling of the bacteriologically confirmed TB patients and requesting them to list and refer their close friends whom they spend most of their time with at work and during their free times. The patient's friends who do not turn up after a week to the hospital is being contact traced by the trained community health volunteer. This concept was motivated by the closed nature of the communities and the stigma which is still associated with TB in the region.
Results and lessons learnt: The strategy has created impact within six months of its implementation in the selected ten public facilities. There was an increased number of bacteriologically confirmed cases. Out of 225 cases reported within the period, 57(25.3%) were as a result of the initiative in the 10 selected facilities.
Conclusions and key recommendations: Results confirm that use of "Rafiki yangu,jukumu langu" initiative is a concept that can be relied upon in finding the missing cases in the community and should be adopted and used in complimenting active case finding strategy. NEPHAK will be ready to take the lead in coming up with its implementation guidelines and SOP if adopted.

PS-04-544-31 Impact of TB "hunters" in Imo State, Nigeria

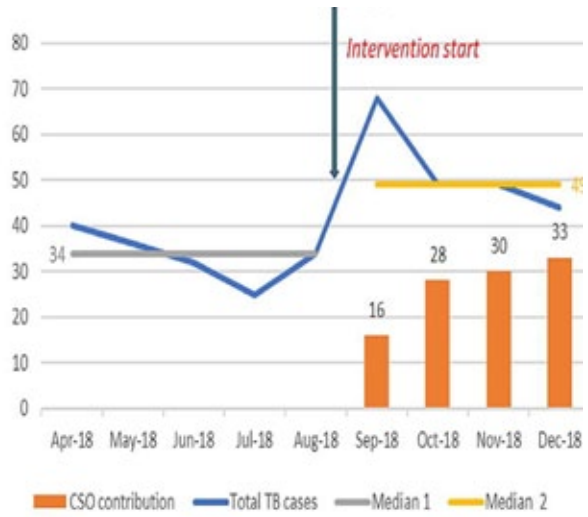
CA Okoro,[1] AO Awe,[2] AF Omoniyi,[2] MB Jose,[3] [1]World Health Organization, Communicable and Non-Communicable Diseases, Owerri, Nigeria, [2]World Health Organization, Communicable and Non-Communicable Diseases, Abuja, Nigeria, [3]World Health Organization, Communicable and Non-Communicable Diseases, Porthacourt, Nigeria. e-mail: drokoro2009@yahoo.com

Background and challenges to implementation: World Health Organization (WHO) estimated that 3.6 million tuberculosis cases were missed in 2017 with Nigeria contributing 324,000 (9%). Imo State contributes significantly to the missing cases in Nigeria with a case detection rate of 9.6% (1,165/12,189) in 2017.
WHO with the support of United States Agency for International Development, recruited a Tuberculosis Surveillance Officer (TUSO) in Imo to develop innovative approaches to increase TB case detection from the facilities providing no form of TB services and the community.
Intervention or response: The TUSO introduced the use of TB "Hunters" to find the missed TB cases. Thirty Community Informants (CIs), 30 Patent Medicine Vendors (PMVs) and 36 Directly Observed Treatment (DOT) staff from 6 prioritised LGAs were included, after sensitization on TB surveillance, as TB "Hunters" (TH) to search for TB in communities and link presumptive cases to National TB Program services for diagnosis, treatment and notification. Standard NTP community referral forms were used. An incentive of 1000 Naira (about 3 USD) was attached to every confirmed case. Confirmed cases were notified and collated data analysed using excel. The intervention was carried out over 10 months (March to December, 2018).
Results and lessons learnt: A total of 239 TB cases were notified through the overall activities of the TUSO (18% of total cases from the state in 2018). TH contributed 85 cases (35.6%): CI-49 (57.6%), PMVs- 33(38.8%), DOT facility staff- 3(3.6%). DOT staff contributed the least due to time constraints. The use of individuals with no health facility commitments proved to yield more cases. The lack of incentive for presumptive cases not confirmed as TB cases was a major discouraging factor for the TH.
Conclusions and key recommendations: This community-focused intervention is an added advantage to support TB programmes find the missed TB cases. The intervention can be improved on and replicated in similar settings.

PS-04-545-31 Civil society organisations play a crucial role in finding missed persons with TB disease among urban populations: experience from Central Uganda

H Kisamba,[1] T Nsubuga,[1] A Nkolo,[1] S Turyahabwe,[2]
[1]University Research Co., LLC (URC), Technical, Kampala, Uganda, [2]Ministry of Health, NTLD, Kampala, Uganda.
e-mail: jhkisamba@gmail.com

Background and challenges to implementation: In Uganda half of the estimated 89,000 TB cases expected are notified each year. Each undetected person with TB increases the risk of community spread. The WHO strategy to end the global TB epidemic by 2035 emphasizes coalition with civil society and communities to improve TB services. By December 2017, only about 20% of CSO operating in central Uganda were engaged in provision of community TB services. The Ministry of Health in Uganda is working with implementing partners to innovatively engage civil society organizations (CSO) in the provision of TB services.
Intervention or response: In July 2018, 10 CSOs were sub-granted to implement community-level TB interventions in 3 urban districts, with the objective of increasing TB case finding and improving TB treatment outcomes. USAID-Defeat TB and the district health teams built the capacity of CSOs through didactic training, supportive supervision and guidance on the use of standard operation procedures for community TB activities. By September 2018, the CSOs, in close collaboration with health facilities and community resources persons, were implementing community-level TB interventions to increase case finding such as TB sensitization and screening among close contacts of TB patients and high-risk populations.



[TB case Detection in 20 CSO supported sites]

Results and lessons learnt: By the fourth month of the CSO led community- level TB activities, 162 community volunteers were established in the CSO operation locations to support TB activities. The monthly median number of TB cases notified at 22 TB diagnostic units in Kampala, Wakiso and Mukono districts increased from 34 - pre-intervention to 49 in the intervention period.
Conclusions and key recommendations: Systematic engagement of CSOs in community TB interventions presents a key opportunity for finding missed persons with TB disease and establishes capacity of communities to end TB in urban and peri-urban settings in developing countries.

PS-05-E1 A bit of everything: stigma, community engagement, media & technology

PS-05-546-31 Tuberculosis stigma among household contacts and its association with participation in TB early diagnosis in Badung district, Bali province, Indonesia

IWG Artawan Eka Putra,[1,2] A Probandari,[3] HB Notobroto,[4] CU Wahyuni,[2] [1]School of Public Health, Faculty of Medicine, Universitas Udayana, Public Health and Preventive Medicine, Denpasar, Indonesia, [2]Faculty of Public Health, Universitas Airlangga, Epidemiology, Surabaya, Indonesia, [3]Faculty of Medicine, Universitas Sebelas Maret, Public Health, Surakarta, Indonesia, [4]Faculty of Public Health, Universitas Airlangga, Biostatistic, Surabaya, Indonesia. e-mail: gedeartawan@unud.ac.id

Background: Early detection among household contacts is an important strategy for TB cases finding. During the previous implementation, household contacts participation on TB examinations in Badung were very low (20.1%). This study aimed to measure TB stigma among household contacts and assess its association to their participation on early detection.
Methods: This was a cross-sectional study in Badung District, Bali, Indonesia from July-August 2018. Simple random sampling was performed to select samples among TB household contacts that registered in January until June 2018. Household contacts were people that living and sharing room with TB patients in 3 months before diagnosis. We measured the participation of house contact following TB examination in public health centers (PHCs). Measurement of TB stigma covered stereotypes, anticipated (perceived) stigma and experienced stigma. Data were collected using a structured questionnaire through face to face interview. Logistic regression was performed to assess the association.
Results: This study succeeded to interview 165 household contacts from 184 selected. The average of age was 38.3 years old and 57.6% were female. The participation of household contact following examination was 30.9%. TB stereotypes belief by household contacts were disease because of past sins (38.8%), disease for low in-

come people (30.3) and hereditary disease (14.6%). Perceived stigma was fear of exclusion (30.9%), discrimination (30.3%), devalued (26.1%), and being ridiculed (24.2%). Study found internalized and anticipated construct perceived stigma. Belief on the TB stereotypes hinder participation with adjusted odds ratio (AOR) = 0.297 (95% CI: 0.099-0.889) and perceived stigma hinder participation with AOR=0.228 (95%CI: 0.071-0.730).
Conclusions: Stigma is a major barrier to TB active case finding among household contacts. Psycho-education and psycho-social support is needed on the patient center approach and contact investigation.

PS-05-547-31 Experiences of HIV stigma among new and existing TB patients from six public health facilities in Buffalo City Metro Health District, East Cape Province, South Africa

D Bresenham,[1] C Bezuidenhout,[1] R Mawarire,[1] P Ngwepe,[1] A Kipp,[2] A Medina-Marino,[1] [1]Foundation for Professional Development, Research Unit, Pretoria, South Africa, [2]Vanderbilt University Medical Center, Department of Medicine (Epidemiology), Nashville, TN, United States of America. e-mail: danab@foundation.co.za

Background: The duel burden of HIV/AIDS and TB accounts for a significant proportion of illness and death, particularly in South Africa. HIV stigma has been identified as a significant psychosocial risk factor resulting in increased delay in case finding, treatment initiation and adherence. We aimed to describe the relationship of HIV stigma among new and existing TB index patients in South Africa using the validated Visser Attributable HIV stigma scale translated into IsiXhosa and Afrikaans.
Methods: A cross-sectional study was performed among TB patients utilizing interviewer-administered questionnaires. Participants were enrolled from six public health facilities in Duncan Village Informal Settlement, East London, South Africa. Collected data included: socio-demographics, clinical factors, and HIV stigma. Stigma scores ranged from zero (no stigma) to 36 (highest degree of stigma). Two-sample t-test and multivariable linear regression were performed to detect differences in HIV stigma scores amongst TB patients newly initiated on treatment and those currently on treatment.
Results: Among 225 participants, HIV stigma score of newly diagnosed TB patients was statistically higher compared to existing TB patients (19.2 vs. 17.1; p-value = 0.012). After adjusting for socio-demographics, TB contacts, HIV status, TB stigma, and depression, newly diagnosed TB patients reported higher HIV stigma compared to existing TB patients (β = 1.68, 95% CI: -0.21, 3.58).
Conclusions: High HIV stigma scores among newly diagnosed TB patients may adversely affect TB treatment outcome and consequently adversely affect the transition and retention onto HIV treatment, post-TB treatment. Understanding the unique impact of HIV stigma among new and existing TB patients offers an opportunity to better target interventions that decrease the impact of HIV stigma among TB patients. Stigma reduction efforts must be incorporated into TB and TB/HIV programmes to optimize patient outcomes.

PS-05-548-31 Emotional storytelling: a method for shifting behaviour norms related to stigma in the social and cultural context of TB

U Guha,[1] S Sen,[1] P Mathur,[1] C Barman,[1] O George,[2] K Chadha,[2] [1]Storytellers, Creatives, New Delhi NCR, India, [2]Abt Associates Inc., IDD, New Delhi, India. e-mail: urvashi@storytellers.org.in

Background: Reducing stigma and discrimination to enable early and universal diagnosis, and treatment success, is a priority of the TB program in India. In this first attempt, stigma against persons with TB, and their circle of close family and friends (′inner-circle′), is being addressed through mass media. The communication strategy focuses on the inner-circle as they are stigmatized by society, and in turn stigmatize the person with TB. This stigmatizing behavior is deep-rooted in the fear of getting the disease from the person with TB, and of being ostracized by society.
Methods: Communication to shift existing behaviors was built by mapping insights and laddering effects to develop the concept that there comes a moment of reckoning when you have to decide on whether you want to stand with your person with TB, or turn away. Public Service Announcement films were scripted and made into narramatics and pre-tested with the inner-circle and others in the community. A total of 12 Focus Group Discussions with 7 members each were carried out in two urban centers of Delhi and Hyderabad, with women and men, aged 18-29, and 30-55 years.
Results: The emotional messaging, ‘apno ka jodd, hai TB ka todd’ (‘the bond of loved ones, is the way to break TB’) expressed by positive deviance from family and friends, resonated with all the discussion groups. The bond of positive deviants was reassuring, motivating treatment completion. It communicated that there is no reason to fear spread of infection, once treatment is initiated.
Conclusions: Stigmatization is contingent upon social and economic situations emanating from fear and leading to otherization, separation, rejection, exclusion, and discrimination. The only way to level these dynamics is to tug at the heart, and make an emotional appeal in that moment of reckoning. Emotional storytelling through positive deviance is a potent way to mitigate stigma.

PS-05-550-31 Community engagement in research and development: STREAM experience in building CABs networking

O Rucsineanu,[1] ET Santos-Filho,[2] P Rucsineanu,[3] S Doltu,[4] G Munkhjargal,[5] D Jikia,[6] [1]Moldovan National Association of TB Patients, Health, Balti, Moldova, [2]REDE-TB, Brazilian TB Research Network, Rio de Janeiro, RJ, Brazil, [3]Moldovan National Association of TB Patients "SMIT", Health, Balti, Moldova, [4]Council for Preventing and Eliminating Discrimination and Ensuring Equality in the Republic of Moldova, Public Health, Chisinau, Moldova, [5]Mongolian TB Coalition, Health, Ulaanbaatar, Mongolia, [6]Georgia Patients Union, Health, Tbilisi, Georgia.
e-mail: oxana_rucs@yahoo.com

Background and challenges to implementation: The STREAM study is an international, multi-center, randomized, controlled trial in people with multi-drug resistant tuberculosis. A Community Engagement (CE) Plan was written in 2016 and as of April 2019, thirteen Community Advisory Boards (CABs) had been established in seven countries.The limited practice of CE in a multi-country TB trials and skepticism towards cross-site sharing value are challenges to improve performance of CABs by exchange of experiences in a multi-cultural scenario.

Intervention or response: CABs cross-site collaboration by means of annual joint CAB meetings, creation of a regional network, exchange meetings and collective calls/webinars have been settled. Agendas have ranged from TB and research awareness to advocacy for policy change. Besides evaluation of treatment regimens for MDR-TB, STREAM focuses on ethics and human rights approach when engaging communities in clinical trials. On each site, outreach events, trainings and policy meetings have been conducted quarterly to build treatment and research literacy among various stakeholders.

Results and lessons learnt: The increased understanding of different experiences and common challenges on the global level has strengthened collective community messages in the local, country level to affected people, service providers, local and national governments and to the general society. An improved interaction between communities and research teams has been noted within sites and across sites.

Conclusions and key recommendations: The diversity of the STREAM CABs is an asset. Interventions such as webinars reveal common challenges while results show that building cooperation across sites is useful to boost CABs' performance, by setting a network to increase sustainability. CE has proved to be essential in research and development for raising TB awareness, to turning research data into friendly information to affected people and their closed-ones, and finally to influencing policy change, according to country needs and considering cultural, gender and several other aspects.

PS-05-551-31 Evaluation of dissemination of preliminary results from STREAM stage 1

S Kozikott,[1] J Nan,[1] L Patel,[1] E Tavora Dos Santos Filho,[2] F Conradie,[3] G Bronson,[1] [1]Vital Strategies, Research Division, New York, NY, United States of America, [2]REDE-TB, Community Engagement, Rio de Janeiro, RJ, Brazil, [3]Wits Health Consortium, Clinical HIV Research Unit, Johannesburg, South Africa.
e-mail: skozikott@vitalstrategies.org

Background: Preliminary results from Stage 1 of the STREAM clinical trial were disseminated at Stage 1 and 2 sites. Dissemination activities were evaluated to assess: effectiveness of dissemination materials/presentations; effectiveness of dissemination events; participant/community stakeholders' comprehension of results; and strengths/weaknesses of the process.

Methods: Data from Principal Investigators (PIs) were collected using an online survey; trial participants/community members were interviewed via telephone. PIs rated materials for each target audience based on detail, technical complexity, and clarity.

Participants rated materials based on amount of information and clarity. Participants answered questions on effectiveness, safety, and cost of trial regimens to assess comprehension of results. Descriptive statistics were produced from quantitative data; qualitative data were analyzed using thematic analysis. Quantitative and qualitative findings were triangulated.

Results: Ten PIs completed the survey. Twenty-seven participants completed telephone interviews. More than 70% of PIs rated the technical complexity and detail of information in materials for PIs, study teams, and Community Advisory Boards (CABs) "just right".

More than 80% of PIs rated PI dissemination materials "clear" or "very clear"; only 50% of PIs rated dissemination materials for CABs "clear" or "very clear".

Questions on effectiveness, safety and cost of trial regimens were correctly answered by 15%, 19% and 56% of the participants, respectively (Table1).

	Shorter Better	Both regimens the same	Longer Better	Don´t Know
		Total respondents= 27		
Trial Results	n (%)	n (%)	n (%)	n (%)
Effectiveness	23 (85%)	4 (15%)	0 (0%)	0 (0%)
Safety	19 (70%)	5 (19%)	2 (7%)	1 (4%)
Cost	15 (56%)	3 (11%)	3 (11%)	6 (22%)

[Participant Comprehension : Results of Participant Interviews]

Strengths of dissemination included: participatory nature of dissemination events, presence of physician at dissemination events, and availability of materials in local languages. Weaknesses included inadequate use of visuals in participant materials.

Conclusions: Dissemination materials/events for PIs and study teams were very effective. Dissemination materials/events for participants required improvement, as a majority of participants did not understand the results. Future dissemination efforts should ensure prior review of participant materials by CABs to ensure appropriateness for the target audience. Despite these challenges, broad-based dissemination strengthened researcher-participant relationships and ownership of research results, and was important for empowering the community.

PS-05-552-31 Effect of "mHealth" interventions on adherence to treatment and outcomes in tuberculosis patients of district Shimla, Himachal Pradesh, India: a randomised controlled trial

H Singh,[1] AK Gupta,[2] AK Bhardwaj,[3] S Kumar,[3] R Gupta,[2] [1]Dr Rajendra Prasad Government Medical College, Community Medicine, Kangra, India, [2]Indira Gandhi Medical College, Community Medicine, Shimla, India, [3]Dr. Radhakrishnan Government Medical College, Community Medicine, Hamirpur, India.
e-mail: drhvsbajwa@gmail.com

Background: India bears the major burden of Tuberculosis patients worldwide. Application of Mobile technology can prove to be a boon in complementing patient centric approach in otherwise hard to reach areas. This study envisaged to study the effects of 'mHealth' interventions on adherence and outcomes of newly diagnosed TB patients in an area with a difficult terrain but excellent literacy rates and a very high tele-density.
Methods: A Randomized controlled trial design was adopted to study the effectiveness of 'mHealth' interventions in the form SMS reminders and voice calls under 'HEAL-TB' banner amongst newly diagnosed TB patients. The intervention arm received the messages in the national language 'Hindi' on their scheduled days of treatment and follow-up. Educational messages were also sent. Queries related to aspects of treatment were received by the investigators through an advertised mobile number. The patients were followed up till the end of their scheduled treatment. The groups were compared in terms of treatment outcomes and number of doses and follow ups missed.
Results: Out of the 312 patients enrolled for the study, risk of adverse outcomes was 43% statistically lower in intervention group as compared to control group (OR; 95% CI: 0.57 (0.35-0.96)). Also the risk of >10% of missed doses of treatment was 67% lower in intervention group (OR; 95% CI: 0.33 (0.12- 0.90)). Risk of missing more than two follow ups was 50% lower in intervention group.
Conclusions: The study helps to build further evidence about the effective use of mobile technology in strengthening patient centric approach in Tuberculosis case management particularly in areas with diffuclt access.System generated reminders incorporated into the existing NIKSHAY portal may improve adherence. A dedicated "Counselling service" using voice calls may be incorporated in the existing programme structure to address patients' queries which will help improve adherence ultimately contributing to favourable outcomes.

PS-05-553-31 To evaluate the inter- and intra-observer agreement in the initial diagnosis by digital chest radiograph sent via WhatsApp messenger

SG Kotalwar,[1] AK Prakash,[1] A Mangla,[1] R Jain,[1] B Datta,[1] A Jaiswal,[1] [1]Medanta - The Medicity, Respiratory and Sleep Medicine, Gurgaon, India.
e-mail: drsameerkotalwar@gmail.com

Background: The present study aims to determine if images of digital radiographs captured on smartphone and sent by WhatsApp messenger are of sufficient diagnostic quality compared to viewing the original radiographs in PACS.
Methods: This is a hospital based observational double blinded prospective study to evaluate digital chest radiograph sent via WhatsApp messenger, and comparing the accuracy of the same, taking consensus of two senior pulmonologists on PACS as the gold standard .The Pulmonologists (R1 and R2) reported from 2 different districts X and Y with a washout period of 2 weeks between WhatsApp and PACS images. The results were divided into 21 variables on WhatsApp messenger as well as PACS. These results were compared, and intra and inter-observer variation analyzed.
Results: Out of 400 X-rays, After standardization, This consensus was taken as gold standard. For normal X-rays, Sensitivity was 95.81% and specificity was 88.69% with accuracy of 92.36 ($p < 0.0001$). Strength of agreement was 0.84 (Very Good) between WhatsApp messenger and PACS. Strength of agreement of Reader-1 in detection of normal X-ray was 0.86 (very Good) and by Reader-2 was 0.83 (Very Good). Inter-observer agreement was 0.74 (Good) for WhatsApp image. Thus it was considered that WhatsApp messenger is as good as PACS in diagnosing normal X-rays.
Conclusions: In the era of telemedicine, WhatsApp messenger though not very specific, could be a modality for teleradiology. For diagnosis of normal chest X-ray, Active Koch's, Old Koch's, and Pneumonia WhatsApp messenger images are comparable to PACS images.

PS-05-554-31 E-RCTC: enabling the tobacco control landscape in India

R Kumar,[1,2] S Goel,[2] [1]Postgraduate Institute of Medical Education and Research (PGIMER), School of Public Health, Chandigarh, India, [2]PGIMER, School of Public Health & CM, Chandigarh, India.
e-mail: rajeevchoudharyhp@gmail.com

Background: National Tobacco Control Programme (NTCP) in India mandates imparting public awareness about tobacco control legislation and the detrimental effects of tobacco use. The prevailing information on tobacco control is lying scattered at different sources, due to absence of a common platform. To fill the current gap in the country, PGIMER Chandigarh, an institute of eminence in North India, has developed a virtual Resource Centre for Tobacco Control (RCTC) with objective to serve as one-point reference systemfor all tobacco control updates and technical resource materials in the country.
Methods: Delphi Technique was used to undertake need assessment. This was followed up with a roundtable consultation of decision makers to finalize the framework of RCTC. A national advisory board and state resource management team was constituted to collate the information from all stakeholders across the country.
Results: A virtual centre for tobacco control (www.rctcpgi.org) contains information pertaining to various tobacco control activities. Experts from various public health organizations formed the part of state resource management team. Within six months of its global launch at Asia Pacific Conference on Tobacco or Health at Bali, Indonesia, the portal of E-RCTC has clocked over 20000 visitors from nearly 60 countries like India, the US, France, China, Japan, UK, Germany, UAE, Malaysia etc.
Conclusions: E-RCTC is a unique platform which fulfil the current gap in tobacco control landscape by providing updated and authenticated information on tobacco control in the country. The platform is likely to provide momentum to national tobacco control programmes in India.

PS-06-A3 Molecular testing and resistance

PS-06-555-31 High level moxifloxacin resistance among gyrA/B mutated strains of multidrug-resistant Mycobacterium tuberculosis

A Jain,[1] PK Singh,[1] U Singh,[1] P Dixit,[1] VK Raikwar,[1] [1]King George's Medical University, Department of Microbiology, Lucknow, India.
e-mail: amita602002@yahoo.com

Background: Under programmatic setting of India, high dose moxifloxacin (Mfx) containing MDR-TB regimen is recommended if strains have mutations in gyrA/B genes and have MICs not above clinical breakpoint (CB) in phenotypic susceptibility testing. CB for Mfx-testing is revised recently by World Health Organization; and here we aim to assess its impact on possible change in proportion of eligible cases for high dose treatment in Uttar Pradesh, India. We also evaluated the possible association between level of Mfx resistance and genetic mutation of M. tuberculosis.
Methods: A total of 108 M. tuberculosis isolates recovered from confirmed MDR-TB cases were included consecutively during Feb-Mar, 2019. All isolates were subjected to MGIT media based susceptibility testing for Mfx at revised (CB1; 1.0μg/ml) as well as currently used concentration (CB2; 2.0μg/ml). gyrA/B mutation profiles, as generated by Genotype MTBDRsl line probe assay, were correlated with phenotypic susceptibility at revised CB.
Results: Of total 108 gyrA/B mutated strains, 39.8% were sensitive and 16.7% were resistant both at CB1 and CB2. There were 43.5% strains that were resistant at CB1 but were found sensitive at CB2. D94G (61.1%), A90V (17.6%) and D94A (8.3%) mutations in gyrA gene were most common. We found that isolates with D94G mutation were strongly associated ($P < 0.001$) with phenotypic resistance at CB1. In contrast, A90V mutation was displayed predominantly ($P < 0.001$) by susceptible isolates.
Conclusions: Implementation of revised CB for Mfx susceptibility testing can make about 40% cases as 'ineligible' for high dose Mfx containing MDR-TB regimen; thus operational framework for treatment management needs to be strengthened accordingly. Study also suggests that gyrA mutations are associated with level of moxifloxacin resistance and may be carefully utilized in selecting high dose treatment.

PS-06-556-31 Molecular characterisation of rifampicin and isoniazid resistant M. tuberculosis strains in Tunisia

I Bouzouita,[1] L Essalah,[1] H Draoui,[1] A Ghariani,[1,2] E Mehiri,[1,2] L Slim-Saidi,[1,2] [1]National Reference Laboratory for Mycobacteria, A. Mami Pneumology Hospital, Ariana, Tunisia, [2]University of Monastir, Faculty of Pharmacy, Monastir, Tunisia. e-mail: leilaslimsaidi@gmail.com

Background: The emergence of drug resistant (DR) tuberculosis (TB) is hampering the efforts to control TB. Understanding the molecular mechanisms involved in DR-TB is essential to develop a new molecular methods and enhance the sensitivities of the existing tools. The aim of our study is to determine the molecular mechanisms involved in rifampicin and isoniazid resistance in Tunisia using the GenoType MTBDRplus assay V2.0 (Hain lifescience, Germany).

Methods: Our study included 85 strains of M. tuberculosis isolated in Tunisia during 2017-2018.

The phenotypic drug susceptibility testing (DST) was performed at the national reference laboratory for mycobacteria in Tunisia using the Bactec MGIT 960: 6 strains were rifampicin monoresistant, 35 were monoresistant or polyresistant to isoniazid and 44 isolates were multidrug resistant (MDR).

All the strains were tested by the GenoType MTBDRplus assay (V2.0).

Results: All the rifampicin resistant strains (n=50) harboured a mutation in the hot spot region of rpoB gene. Mutation rpoB S531L (Mut3) was the most involved in rifampicin resistance (n=39, 78.0%).

As regards isoniazid resistant isolates (n=79), 74 strains presented a mutation conferring resistance to isoniazid (93.6%): katG S315T (n=69, 87.3%) and/or a polymorphism in inhA promoter (n=6, 7.6%).

Five isoniazid resistant strains (including 1 MDR) (6.4%) did not present any mutation conferring resistance to this drug. The GenoType MTBDRplus confirmed 43 of 44 MDR strains (97.7%)

One isoniazid monoresistant strain was found to be MDR by the assay. The DNA of this isolate did not show any hybridization with the probe rpoB WT2.

Conclusions: Mutations rpoB S531L and katG S315T were the most involved in rifampicin and isoniazid resistance respectively in Tunisia during 2017-2018.

In this study, 6.4% of isoniazid resistant strains were considered as susceptible to this drug by the GenoType MTBDRplus and could , therefore, present other polymorphisms not targeted by this assay.

PS-06-557-31 Pulmonary tuberculosis with epidemic Beijing genotype of Mycobacterium tuberculosis in northern part of Russia

M Vinokurova,[1] N Evdokimova,[1] N Pavlov,[1] G Alekseeva,[1] L Mordovskaya,[1] A Kravchenko,[1] S Zhdanova,[2] O Ogarkov,[2] E Savilov,[2] [1]Phthisiatry Research-Practice Center, Department for Science, Yakutsk, Russian Federation, [2]Research Center of Problems of Family Health and Human Reproduction, Infections Department, Irkutsk, Russian Federation. e-mail: mkvin61@mail.ru

Background: Russia has been reported (WHO, 2017) among 20 countries with high incidence of multidrug-resistant tuberculosis (MDR-TB). Siberia and Russian Far East show more aggravated situation. Sakha Republic (Yakutia), large northern region, had a rate of 57.9% for MDR-TB in 2016. Spread of MDR-TB and low treatment success rate were linked to Mycobacterium tuberculosis (MTB) genotype, namely W-Beijing.

We studied clinical bacteriological characteristics of TB caused by Beijing cluster MTB in new patients with pulmonary TB.

Methods: 150 patients with pulmonary TB and Beijing cluster MTB were observed. Detection and drug sensitivity testing were performed in solid and liquid media. MTB DNAs were subjected to express genotyping using pure cultures, based on RD105 and RD207 differentiation regions (Reed M. et al., 2009), to a degree of certainty defined as either 'Beijing' or 'Non-Beijing', and 24-locus MIRU-VNTR genotyping.

Results: Patients were mostly young and middle-aged, (under 50 years; 88.7%), and male (74.7%). High prevalence rates for Beijing cluster were shown in all geographical zones of Yakutia (proportions in Yakutsk, Central zone, and Arctic zone: 67.3%, 14.7%, and 6.0%, respectively). By ethnicity, patients were mostly Yakut (60.0%); minorities made 4.0%. TB was mainly infiltrative (68.0%) and disseminated (16.7%).

MTB were sensitive (64.0%), mono-resistant (2.0%), or MDR (28.7%). CC2/W148 subtype was identified in 34 (22.6%) patients within Beijing cluster: 27 (79.4%) MDR; 2 (5.9%) extensively drug-resistant (XDR); 4 (11.8%) poly-resistant; 1 (2.9%) mono-resistant. Proportion of MDR and XDR strains among CC2/W148 subtype (34) was 85.3%, which was reliably higher than 14.6% among other Beijing subtypes (116 strains) ($df= 1; \chi^2 =26.005; p< 0.0001$).

Conclusions: In the north of Russia, particularly high incidence of Beijing cluster MTB was observed in indigenous, and in male middle-aged population. Prevalence of CC2/W148 Beijing subtype was considerable and epidemiologically significant (with MDR and XDR detected in 85.3%).

PS-06-558-31 Genetic analysis of resistance to second-line injectable in Mycobacterium tuberculosis strains circulating in Peru

D Santos Lazaro,[1] Z Puyen,[1] [1]Instituto Nacional de Salud, Public Health, Lima, Peru. e-mail: zpuyeng@gmail.com

Background: Second-line injectable (SLI) drugs are used in the treatment of MDR and XDR tuberculosis (TB). In 2019, the Genotype MTBDRsl v2.0 has been implemented in Peru in order to be used as a screening test for XDR-TB detection. This study analyzed the genes associated with kanamycin (KAN) and capreomycin (CAP) M. tuberculosis (MTB) resistant-strains in Peru.
Methods: 170 MTB strains were selected, 90 resistant and 80 susceptible to KAN and/or CAP. Genomes were sequencing trough Illumina technology. Assembly was done with BWA v0.7.12. Duplicated reads were removed with Picard-tools v1.119. ´Variant calling´ was made with GATK v4.0.12, and a ´Hard filtering´ (DEPTH ≥ 30; QUAL ≥ 30; AF ≥ 0.75) was performed by VCFtools v0.1.15. Nucleotide mutations were analyzed in genes associated with KAN (rrs and eis) and CAP (rrs and tlyA) resistance.

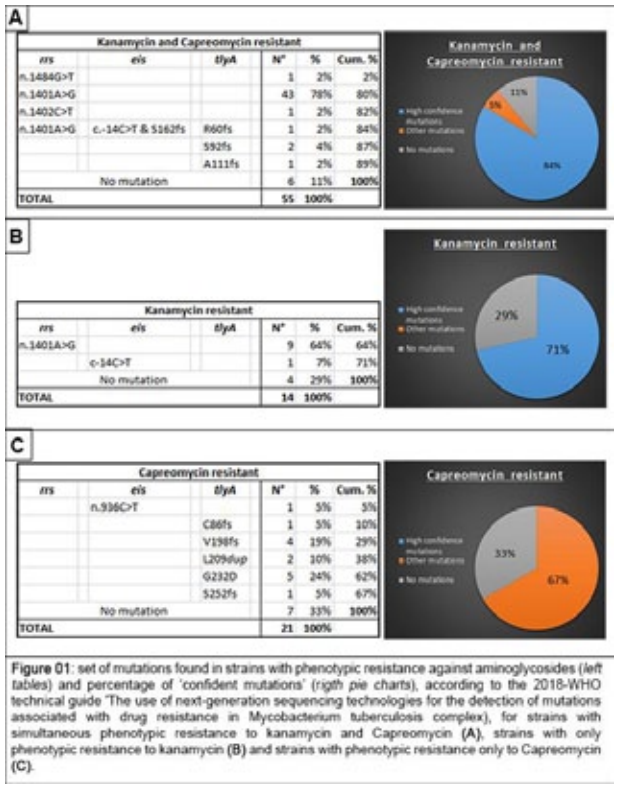


Figure 01: set of mutations found in strains with phenotypic resistance against aminoglycosides (*left tables*) and percentage of 'confident mutations' (*rigth pie charts*), according to the 2018-WHO technical guide 'The use of next-generation sequencing technologies for the detection of mutations associated with drug resistance in Mycobacterium tuberculosis complex), for strains with simultaneous phenotypic resistance to kanamycin and Capreomycin **(A)**, strains with only phenotypic resistance to kanamycin **(B)** and strains with phenotypic resistance only to Capreomycin **(C)**.

[Figure 1]

Results: Of the resistant strains, 55 showed simultaneous resistance to KAN and CAP (Group 1); 14 only to KAN (Group 2) and 21 only to CAP (Group 3). In group 1: 84%(46) developed mutations in the rrs (1484G>T, 1401A>G, 1402C>T) and eis (-14C>T) genes; 4%(3) showed only 'frame shift' changes (S92fs, A111fs) at tlyA gene, while 11%(6) showed no mutations (**Figure-01A**). In group 2: 71%(10) developed mutations in rrs (1401A>G) and eis (-14C>T) genes, while the remaining 29%(4) showed no mutations (**Figure-01B**). Finally, in group 3: only 5%(1) developed a mutation in the eis gene (936C>T), 62%(13) hosted mutations in the tlyA (C86fs, V198fs, L209dup, G232D, S252fs) gene, and 33%(7) showed no mutations (**Figure-01C**). No resistant-associated mutations were detected at susceptible strains.
Conclusions: 19% (17) of SLI-resistant MTB strains did not showed mutations in the rrs, eis (evaluated in the Genotype MTBDRsl v2.0) and tlyA genes. It is necessary a greater number of studies for determinate new genetic markers that complement the tools of molecular susceptibility diagnosis in Peru.

PS-06-559-31 Diagnostic accuracy of MTBDRplus and MTBDRs line probe assays for the direct detection of smear-negative drug-resistant tuberculosis in a programmatic setting

S Pillay,[1] B Derendinger,[1] G Theron,[1] M de Vos,[1] R Warren,[1] [1]Stellenbosch University, Division of Molecular Biology and Human Genetics, Cape Town, South Africa. e-mail: samantha18101985@gmail.com

Background: The detection of second-line drug-resistant tuberculosis (TB) in sputum is a key challenge. There is limited data on the only World Health Organization-endorsed rapid commercial assay (MTBDRsl) for second-line drug susceptibility testing (DST), especially when done on smear-negative specimens. We evaluated the accuracy of MTBDRplus and MTBDRsl on sputum.
Methods: 1001 Xpert rifampicin-resistant sputa were tested in a routine TB reference laboratory in Cape Town using MTBDRplus and MTBDRsl . Phenotypic culture-based DST served as reference standard.
Results: 85% (849/1001) sputa were culture-positive. Of these, 44% (373/849) were smear-positive and 56% (476/849) smear-negative. MTBDRplus and MTBDRsl detected TB-positivity in 82% (388/476) and 71% (307/431, p=0.003) in smear-negative sputa, respectively. Of these smear-negatives, 1% (4/388) and 12% (33/272) were indeterminate for at least one drug for MTBDRplus and MTBDRsl, respectively [therefore the proportion of non-actionable MTBDRsl results on smear-negatives is 36% (156/431)].
On smear-positive sputa the sensitivity for fluoroquinolone (FQ)-resistance, second-line injectable (SLID)-resistance and extensively drug-resistance (XDR) were 89% (75-96), 86% (65-97), 100% (71-100), and specificity was 93% (88-96), 97% (93-98), 97% (94-99), respectively.
On smear-negative sputa, the sensitivity was [84% (67-93), p=0.49 vs. smear-positives], [81% (54-95), p=0.01], [80% (44-97), p=0.11] and the specificity was [95% (89-98), p=0.51], [88% (81-93), p=0.02],

[98% (91-99), p=0.70], respectively. 60% (509/849) of Xpert rifampicin-resistant culture-positive sputa were multi-drug resistant by MTBDRplus and of these, 5% (27/509) were XDR on MTBDRsl. The median (IQR) time to result was 6 (5-7) days for both MTBDRplus and MTBDRsl.

Conclusions: When done directly on smear-negatives, MTBDRsl gives an actionable result in 7/10 patients. In those with an actionable result, MTBDRsl detects resistance in 8/10 FQ and 7/10 SLID-resistant cases. Similarly, 9/10 FQ and 9/10 SLID-susceptible cases will be correctly classified by MTBDRsl. These data support the roll-out of MTBDRsl as rule-out test on smear-negative sputa.

PS-06-560-31 Isoniazid and rifampicin resistance and patient treatment response in a tuberculosis and HIV-1 co-endemic population in Western Kenya

J Khayumbi,[1] PC Ouma,[2] C Likhovole,[2] [1]Kenya Medical Research Institute, Tuberculosis Research Laboratory, Kisumu, Kenya, [2]Maseno University, Biomedical Sciences, Kisumu, Kenya. e-mail: clementshiluli@yahoo.com

Background: The association of drug resistant mutations with HIV and the treatment response of HIV infected and uninfected patients with TB are not known. Patients with resistant TB require admission which increases transmission. In western Kenya the association of drug resistant mutations with HIV and the treatment response of HIV infected and uninfected patients with TB are not known.

Methods: The objectives of the current study were to determine the proportion of drug resistant Mycobacterium tuberculosis in sputum isolates and investigate the association of RIF and INH gene mutations with HIV status and monitor treatment response.

The study was longitudinal and patients with confirmed resistant TB were followed up for one year to establish the TB treatment response. A total of 1381 new and 18 previously treated TB patients were enrolled. Sputum samples were cultured on Mycobacteria growth indicator tubes, Drug susceptibility testing (DST) and Line probe assay (LPA) performed to detect gene mutations. Discordant samples were sequenced. Conversion rate was calculated by finding the percentage of smear negative and positive patients at follow-up and initial visit, respectively. Regression analysis was used to determine the association between HIV status and drug resistance and Mann-Whitney tests for mean comparison.

Results: Mutations as estimated by LPA and DST were as follows: MDR-TB, 0.95%, 1.53%; RIF mono-resistant TB, 0.88%, 0.66%; INH mono-resistant TB, 1.83%, 1.97%, respectively. RIF resistance was associated with HIV status (P = 0.025). Conversion time of HIV infected and uninfected patients with TB drug mutations was comparable (P = 0.180).

Conclusions: Patients with INH-mono resistant TB were high as compared to patients with RMR-TB. Sputum smear conversion time of 6.5 and 3 months in HIV infected and uninfected patients with gene mutation profiles were comparable. Tuberculosis contact investigation studies should be adopted for patients with drug resistant TB to enhance early identification.

PS-06-561-31 Molecular characterisation of pre-extensively drug-resistant Mycobacterium tuberculosis isolated from TB patients in Nepal

A Poudel,[1] B Maharjan,[2] Y Shah,[3] Y Suzuki,[4] [1]Chitwan Medical College Teaching Hospital (CMCTH), Microbiology, Bharatpur, Nepal, [2]German Nepal TB Project (GENETUP), Mycobacteriology, Kathmandu, Nepal, [3]National Zoonoses and Food Hygiene Research Centre, Microbiology, Kathmandu, Nepal, [4]Hokkaido University Research Center for Zoonosis Control, Bioresources, Sapporo, Japan. e-mail: ajy_25@yahoo.com

Background: Drug-resistant tuberculosis (TB) including pre-extensively drug-resistant TB (pre-XDR-TB) has become a major obstacle for TB control programs in Nepal. Pre-XDR-TB is defined as MDR-TB associated with resistance to fluoroquinolone (FQ) or a second-line injectable drug, but not both. This study was carried out to investigate drug-resistant associated and prevalent genotypes of pre-XDR Mycobacterium tuberculosis (MTB) isolated in Nepal.

Methods: A total of 57 phonotypically confirmed pre-XDR-MTB including 53 OFX-resistant and 7 CAP and/or KAN-resistant, collected over a 4-years period (2008 to 2012), were randomly selected from isolates bank at German Nepal TB Project, National Reference Laboratory, Nepal.

Mutations responsible for resistance to RIF, INH, ofloxacin (OFX), kanamycin (KAN) and capreomycin (CAP) were analyzed by sequencing of rpoB, katG and inhA, gyrA and gyrB, and rrs genes, and genotypes were identified by spoligotyping at Hokkaido University Research Center for Zoonosis Control, Japan.

Results: The predominant mutations conferring resistance to RIF and INH were rpoB Ser531Leu (63.2%) and kat Ser315Thr (84.2%), respectively. Among 53 OFX-resistant pre-XDR-MTB, the most common gyrA mutation was Asp94Gly (41.5%), followed by Ala90Val (17.0%) and Asp94Tyr and Asp94Asn (7.5%; each) and Asp94Ala (3.7%).

Mutations detected in gyrB were Asn538Ser and Asp500Asn (1.9% each), while 14 (26.4%) isolates had no mutations in both genes. A1400G substitution in rrs gene was found in 3 of 7 (42.9%) CAP and/or KAN-resistant pre-XDR-MTB isolates.

Furthermore, spoligotyping revealed that 63.2% and 21.1% isolates belonged to Beijing and Central Asian Strain (CAS) lineages, respectively.

Conclusions: The predominance of pre-XDR-MTB of Beijing lineage in Nepal highlights their epidemiological role for emergence of drug-resistant TB in Nepal. Hence, early detection of such isolates is important to prevent further progression into XDR-TB.

PS-06-562-31 An automated sample preparation method compatible with mucoid sputum samples for MTB

N Hirani,[1] A Joshi,[1] M Chugh,[2] S Panda,[2] L Tisi,[3] C Pereira,[3] D Rowland,[3] A Walsham,[3] [1]Grant Medical College, Microbiology, Mumbai, India, [2]Transasia, R&D, Mumbai, India, [3]Erba Molecular, R&D, Ely, United Kingdom. e-mail: l.tisi@erbamannheim.com

Background: Sample preparation remains the key technical challenge to providing low-cost molecular tests for MTB. A critical problem is the high levels of nucleic acids found in mucoid sputum samples which overloads and inhibits molecular assays. Whilst this issue can be circumvented by diluting the sample sufficiently, this reduces test sensitivity. Consequently, methods have evolved which use either filtration or centrifugation (or both) to first concentrate MTB but this introduces additional steps which add cost and complexity.
This study investigates the use of magnetic beads conjugated with specific oligonucleotide probes specific for MTB, to directly extract MTB rRNA from mucoid clinical samples without the use of centrifugation or filtration.
Methods: 32 culture positive and 18 culture negative highly mucoid sputum samples were extracted using the Erba Molecular reagents. Specifically, 0.5ml of sputum was liquefied with Erba Molecular lysis buffer and heat treated at 90˚C for 10 minutes. Magnetic beads where then added which allowed the specific binding of MTB specific rRNA to the beads. A KingFisher Duo™ was then employed which automates washing of the beads and then placing them in 100µl of an elution buffer compatible with an rRNA specific amplification assay which was subsequently run.
Results: All 32 mucoid culture positive clinical samples tested positive for rRNA following extraction. Of the 18 mucoid, culture negative samples, 15 also tested negative for MTB rRNA and 3 tested positive. Of the 3 which tested positive, one was also positive by GeneExpert.
Conclusions: MTB specific rRNA can be extracted from up to 0.5ml of mucoid sputum samples without the need for filtration of the sample or centrifugation using magnetic beads carrying oligonucleotides specific for MTB. The method therefore tolerates the high levels of DNA/RNA found in mucoid sputum samples allowing the facile automation of the extraction process.

PS-06-563-31 Insertion sequence IS6110 deficient Mycobacterium tuberculosis strains from Myanmar

MM Htwe,[1] PW Ei,[1] WW Aung,[1] AS Mon,[1] SM Win,[1] WW Nyunt,[2] JS Lee,[3] CL Chang,[4] [1]Ministry of Health and Sports, Department of Medical Research, Yangon, Myanmar, [2]National TB Reference Laboratory, National TB Program, Yangon, Myanmar, [3]Microbiology Section, International TB Research Center, Masan, Korea, Republic of, [4]Pusan National University, Department of Laboratory Medicine, Busan, Korea, Republic of.
e-mail: drwahwahaung@gmail.com

Background: Insertion sequence (IS) 6110 is a widely used target gene for detection of Mycobacterium tuberculosis (MTB). Molecular diagnosis of tuberculosis (TB) especially extra-pulmonary TB in Myanmar is based on detection of IS6110 from clinical samples. However, 8-11% of MTB stains in South-East Asia do not contain this target and this can lead to false negative results.
Methods: We performed IS6110 PCR assay to detect IS6110 deficient strains among 232 MTB isolates collected during 2015-2017 from adult TB patients in different regions of Myanmar. These isolates included 125 rifampicin-resistant and 107 rifampicin-sensitive strains detected by Xpert MTB/RIF. We also performed the first line phenotypic anti-TB drug susceptibility testing and 24-loci Mycobacterial Intersperses Repetitive Unit-Variable Number Tandem Repeat (MIRU-VNTR) typing on IS6110 deficient strains.
Results: Of 232 TB patient isolates, three isolates (1.3%) had absence of IS6110 gene element. All of three IS6110 deficient MTB isolates were sensitive to rifampicin, isoniazid and ethambutol but two isolates were resistant to streptomycin. Two isolates belong to Beijing genotype and one belongs to East African-Indian (EAI) genotype.
Conclusions: Myanmar MTB strains have low percentage of IS6110 deficient strain and these strains were found more in drug susceptible isolates. Although IS6110 based molecular diagnosis for TB in clinical samples is a useful method but there can be chance of false negative results. Further study with larger sample size should be conducted to discover the clinical significance of IS6110 deficient Myanmar MTB strains.

PS-06-564-31 Relative decrease in rifampicin-resistant tuberculosis in Benin

CN Sanoussi,[1,2,3] L Rigouts,[2,4] M Ali Ligali,[1,5] O Bodi,[1] K Arekpa,[1] M Odoun,[1,6] S Houeto,[1] F Massou,[1] BC de Jong,[2] D Affolabi,[1,7] [1]Laboratoire de Référence des Mycobactéries, PNT, Cotonou, Benin, [2]Institute of Tropical Medicine, Unit of Mycobacteriology, Antwerp, Belgium, [3]University of Antwerp, Department of Biomedical Sciences, Antwerp, Belgium, [4]University of Antwerp, Biomedical Sciences, Antwerp, Belgium, [5]Université d'Abomey-Calavi, Faculté des Sciences et Techniques, Génétique et Biotechnologies, Abomey-Calavi, Benin, [6]University d'Abomey-Calavi, Ecole Polytechnique d'Abomey-Calavi, Génie de Biologie Humaine, Abomey-Calavi, Benin, [7]Université d'Abomey-Calavi, Faculté des Sciences de la Santé, Cotonou, Benin.
e-mail: ndirasanoussi@gmail.com

Background: We aimed to evaluate the nationwide trend of anti-tuberculosis (TB) drug resistance in pulmonary TB patients in Benin, using for the first time GeneXpert MTB/RIF (Xpert) for a periodic drug-resistance survey.
Methods: Smear-positive patients were prospectively selected between April 2016 and August 2017 from 24 TB clinics representing 75% of pulmonary TB diagnosed in Benin. For each previously-treated patient included, the next four new patients diagnosed were also included. Xpert and culture (Löwenstein-Jensen) were performed, followed by phenotypic drug-susceptibility testing (pDST) for 1st line (all cases) and 2ndline drugs (for rifampicin (RIF)-resistant cases).
Results: In total 1125 TB patients including 896 new and 229 previously treated patients were included. HIV positivity was 15.9% (33/207) among previously-treated versus 11.1% (87/780) in new patients.
In new patients, RIF-resistance was 0.8% (7/880) using Xpert, and (0.8%, 4/521) using pDST, including 2 MDR (0.4%), similar to the 0.74% found by the 2010 survey (p=0.918, difference=0.06% (-1.4 to 1.4)). For two patients Xpert was RIF-sensitive whereas pDST was RIF-resistant, and opposite for another patient. Excluding migrants, RIF-resistance was significantly lower: 0.65% (5/769) by Xpert and 0.2% by pDST (1/450 different to 4.2% (4/71) in migrants, p=0.0003).
Regarding previously treated patients RIF-resistance was 4.1% (9/220) by Xpert and 6.7% (8/120) by pDST including 3 MDR (2.5%), which is not significantly different from 2010 (13.33%, p=0.175) and 2014 (14%, p=0.073) studies. Two Xpert RIF-sensitive patients were RIF-resistant in pDST. Excluding migrants, RIF-resistance remained similar 4.1% (8/197) by Xpert and 5.8% (6/104) by pDST.
All RIF-resistant isolates were sensitive to 2nd line drugs.
Conclusions: Overall, RIF-resistance appears to decline in Benin, but not significantly. In new patients, the RIF-resistance level is affected by the higher prevalence in migrants. Early testing for RIF-resistance, with efforts for risk groups, may further decrease its ongoing spread as patients receive appropriate treatment sooner.

PS-06-565-31 Evaluation of detection of inhA mutation by MeltPro TB assay in predicting ethionamide resistance in Mycobacterium tuberculosis clinical isolates

Y Song,[1] M Gao,[1] Q Li,[1] [1]Beijing Chest Hospital, Capital Medical University, Tuberculosis, Beijing, China.
e-mail: songyanhua2007@163.com

Background: Ethionamide (ETH) is still a drug selected for the treatment of multidrug-resistant tuberculosis (MDR-TB). The gene inhA mutation is a molecular mechanism of ETH resistance. The purpose of this study was to analyze the correlation between inhA mutation and ETH phenotype by MeltPro TB assay, and to evaluate whether inhA mutation can be used as a molecular marker for predicting ETH resistance.
Methods: A total of 382 tuberculosis patients with MeltPro TB assay positive results (with or without katG or inhA mutations) were enrolled in the study. The phenotypic susceptibility results of Isoniazid (INH) and ETH were compared to mutation patterns on the MeltPro TB assay.
Results: Among 382 MTB isolates, 118 (30.9%), 28 (7.3%),27 (7.1%) were resistant to INH, ETH and both drugs , respectively. Among 118 INH-resistant isolates, 62(52.5%),24(20.3%), 5(4.2%) had katG, inhA, and both gene mutations. Of 28 ETH phenotypically resistant isolates, inhA mutation accounted for 42.9% (12/28). Of 34 inhA mutants, 11 (32.4%), 18 (52.9%) and 12 (42.9%) were phenotypically resistant to low-level INH, high-level INH, and ETH, respectively. The sensitivity, specificity, positive predictive value and negative predictive value of inhA gene detection in the diagnosis of ETH resistance were 42.9%, 93.8%, 35.3% and 95.4%, respectively. Eight inhA mutants without katG or rpoB mutation were sensitive to ETH.
Conclusions: In China, inhA gene mutation may not be an ideal predictor of ETH resistance, especially inhA single mutant strains (no katG or rpoB mutation) may be effective for ETH treatment. Further detection of other drug resistance genes and phenotypic susceptibility tests are needed to guide the clinical use of ETH.

PS-06-566-31 Diagnosis of pulmonary tuberculosis by oral swab analysis (OSA): optimisation and development of non-sputum, point-of-care methods

C Ortega,[1] R Wood,[2] H Murton,[3] A Andama,[4] A Cattamanchi,[5] R Dixon,[3] G Morgan,[3] D Madan,[1] A Somoskovi,[1] G Cangelosi,[2] [1]Intellectual Ventures Lab, Global Good, Bellevue, WA, United States of America, [2]University of Washington, Environmental and Occupational Health Sciences, Seattle, WA, United States of America, [3]QuantuMDx, LTD, Clinical Assay, Newcastle-upon-Tyne, United Kingdom, [4]Makerere University College of Health Sciences, Medical Microbiology, Kampala, Uganda, [5]University of California (UCSF), School of Medicine, San Francisco, CA, United States of America.
e-mail: gcang@uw.edu

Background: Diagnostic tests for tuberculosis (TB) are usually conducted on sputum. A viscous material that is difficult to collect from many patients, sputum is also challenging to process at point of care (POC). Tongue swabs have been proposed as alternative samples that are non-invasive and easy to collect. We reported recently that the diagnostic yield of tongue swab qPCR approached that of sputum GeneXpert relative to confirmed TB within a South African cohort. The current study sought to 1) improve the sensitivity of OSA by increasing sample biomass; and 2) test the potential of a new POC molecular testing platform, the QuantuMDx Q-POC™, for OSA.
Methods: A PCR-based bacterial biomass proxy was used to quantify the material collected from tongue dorsa by various swab brands. The brand that performed best was then evaluated in a study conducted on suspected and confirmed TB patients in Uganda. Swab samples were tested by our previous manual qPCR methods and simultaneously by using automated Q-POC™ amplification technology to evaluate suitability for POC testing.
Results: An alternative swab brand, Copan FLOQswab, collected 2-fold more biomass than did our previous methods. When applied to TB suspects, FLOQswab samples exhibited 95% (21/22) sensitivity relative to sputum GeneXpert, using 1 swab/subject (our previous methods required 2 swabs/subject to achieve 93% sensitivity). No loss of sensitivity was noted when using Q-POC™ compared to manual qPCR. Specificity was 90% (9/10) and 100% (10/10) by using manual qPCR and Q-POC™, respectively.
Conclusions: Increasing sample biomass appeared to improve the sensitivity of OSA, although additional evaluations with larger numbers are needed. Tongue swab sampling is extremely fast and easy to perform. When combined with the Q-POC™ platform, OSA could enable non-invasive, highly sensitive, and automated testing for TB at POC without requiring sputum collection or productive cough.

PS-07-B1 Quality and efficacy for TB diagnostics

PS-07-567-31 Is tuberculosis a priority? An assessment of healthcare workers' workloads in peripheral health centres in Uganda

D Oyuku,[1,2] A Tucker,[3] T Nalugwa,[1,2] M Nantale,[1,2] K Farr,[4,5] A Katamba,[1,6] P Shete,[4,5,7] A Cattamanchi,[5,8,9] D Dowdy,[3] H Sohn,[3] [1]Uganda Tuberculosis Implementation Research Consortium, Makerere University, Department of Medicine, Kampala, Uganda, [2]Clinical Epidemiology and Biostatistics Unit, Department of Medicine, Makerere University, Department of Medicine, Kampala, Uganda, [3]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [4]Uganda Tuberculosis Implementation Research Consortium, Makerere University, Department of Medicine, Oakland, CA, United States of America, [5]University of California and Zuckerberg San Francisco General Hospital 5K1, Division of Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [6]Clinical Epidemiology and Biostatistics Unit Makerere University, Department of Medicine, Kampala, Uganda, [7]University of California San Francisco, Curry International Tuberculosis Center, Oakland, CA, United States of America, [8]Uganda Tuberculosis Implementation Research Consortium, Makerere University, Department of Medicine, San Francisco, CA, United States of America, [9]University of California, Curry International Tuberculosis Center, San Francisco, CA, United States of America.
e-mail: oyukudenis1@gmail.com

Background: Given the competing priorities of health interventions in Uganda, healthcare worker time for tuberculosis (TB)-related activities is an important constrained resource to consider in the implementation of TB prevention and care strategies. We sought to understand the current human resources dedicated to tuberculosis activities at peripheral health centers in Uganda.
Methods: We recruited health care workers (HCW) involved in TB-related activities at 5 peripheral health centers in rural and urban Uganda and implemented a self-reported time-and-motion (TAM) study between February and March of 2018. Participants were provided with TAM forms with which each participant reported start and end times for each discrete continuous activity. Activities were categorized based on clinical and laboratory activities, further grouped as either TB-specific or non-TB-specific. We calculated total and weighted mean daily person-minutes for each activity for each type of HCWs (clinical officers, TB focal personnel, laboratory staff, and nurses) participating in the study.
Results: 131 TAM forms were collected from 29 HCWs, representing 1,112 discrete activities. For all activities, Nurses reported the highest mean daily total person-time with 559 minutes, clinical officers (460 minutes), laboratory staff (430 minutes), and TB focal persons

(357 minutes). Across all personnel, observed person-time dedicated for TB was less than 20% of the total observed time at the clinic. Clinical officers spent the least amount of time on TB-related activities at 3.3%, nurses (10%), laboratory staff (17.3%), and TB focal person (19.0%). HCWs majorly spent their time on clinical visits (clinical officers 81%; nurses 64%; and TB focal person 34%) or non-TB laboratory procedures (laboratory staff 37%), followed by administrative or other non-patient related activities.

Conclusions: Given supply-side constraints in routine care in low-resourced peripheral settings, implementing interventions that allow more efficient use of allotted HCW time for TB is critical in prioritizing and improving the quality of routine TB services.

PS-07-568-31 Enhancing the role of the private sector in tuberculosis care and support: a model of private sector engagement in Bihar

R Pathak,[1] BK Mishra,[2] KN Sahai,[2] K Gaurav,[1] B Vadhera,[3] S Mase,[3] K Rade,[3] M Parmar,[3] R Ramchandran,[3] R Rao,[4] [1]WHO Country Office, Tuberculosis, Patna, India, [2]TBDC Patna, Health and Family Welfare, Govt of Bihar, Patna, India, [3]WHO Country Office, Tuberculosis, New Delhi, India, [4]Central TB Division, Ministry of Health & Family Welfare, Govt of India, New Delhi, India. e-mail: pathakr@rntcp.org

Background: Early diagnosis and appropriate care and management of tuberculosis (TB) in India is important to end the global TB epidemic. However, Revised National TB Control Programme (RNTCP) faces a unique challenge due to the health seeking patterns of patients. Nearly half of TB patients seek initial care in the private sector. Therefore, a priority focus of RNTCP is the substantial engagement and extension of its services to the private sector. India has recently implemented a successful model of systematic involvement of the private sector by engaging a third party agency; Public Private Support Agency (PPSA).

Methods: PPSA is an agency to manage end-to-end private-sector engagement and augment RNTCP's capacity to monitor and manage the needs of private-sector patients. We evaluated the extent of this PPSA model in three districts Patna, Darbhanga and Gaya of Bihar, the eastern state of India in from Jan-Dec 2018. Digitalised data on health establishment registered was extracted from the program portal 'NIKSHAY', data cleansed and analysed to evaluate the extent of TB notification and their public health action (PHA).

Results: During the study period, 823/2217 (37%) of registered private health facilities notified 23,322/33,570 (69%) of all notified TB cases. Among private sector notifications 1,940 (10%) were found positive in X-pert and 96% initiated on treatment. Of all the notified TB cases from private sector 8184 (24%) were Extra-pulmonary TB (EPTB) and 4216 (13%) were below 15 years of age.

Conclusions: The systematic involvement of the private sector has improved TB notification and utilization of RNTCP services. Engaging the private sector also provides the opportunity for improved case detection of EPTB and paediatric TB cases. The study highlights the need for scaling up this model in the areas with large private sector presence to reach the national goal to end TB by 2025.

Total TB cases notified (a)	Age Groups (in years)	No. notified Public Sector (b)	No. notified Private Sector (c)	% Notified by Public Sector (b/a)	% Notified by Private Sector (c/a)
33,570		10248	23322	31%	69%
Age * Group (in years) in RNTCP	0-14	685	4216	2%	13%
Age * Group (in years) in RNTCP	>14	10933	27538	33%	82%
Type of TB	Pulmonary	6840	13998	20%	42%
Type of TB	EP TB	1244	8184	4%	24%

[Age and Type of TB specific frequency of TB notification by Private and Public Health facilities from Jan to Dec 2018 in districts of Bihar, India]

PS-07-569-31 Nigeria Wellness on Wheels Mobile TB Diagnostic Units: differences in CAD4TB and GeneXpert results by time of day screened, day of week, gender and region

JN Scholten,[1] R Eneogu,[2] J Levy,[1] C Ogbudebe,[2] B Nsa,[3] [1]KNCV Tuberculosis Foundation, Technical Division, The Hague, Netherlands, [2]KNCV Tuberculosis Foundation Nigeria, Technical Division, Abuja, Nigeria, [3]KNCV TB Foundation Nigeria, Management, Abuja, Nigeria. e-mail: 10301010198@fudan.edu.cn

Background: Nigeria detects only one quarter of its estimated TB cases. Intensive efforts are needed to find and treat missing TB cases. KNCV, under the Challenge TB project, established two mobile diagnostic units in Nigeria focused in northern and southern regions of the country in 2018.

Methods: We analyzed CAD4TB screening with subsequent GeneXpert testing (based on cough and/or CAD4TB score). We evaluated screening by time of day , weekday versus Saturday screening, region and gender.

Results: We evaluated 61,821 client screenings with CAD4TB between April 2018 and March 2019. Overall, coming earlier for TB screening was more likely to result in a CAD4TB score ≥ 60 and to result in a GeneXpert MTB positive test. No significant difference in diagnostic results was observed by weekday vs. weekend screening for CAD4TB. For GeneXpert, the result was more likely positive on a weekday.

In the north, clients screened were more likely to have CAD4TB ≥ 60 scores and MTB positivity in the earlier screening period whereas there was not a significant dif-

ference in the south. In both the north and south, clients were more likely to have CAD4TB ≥ 60 scores on weekdays but not significant differences were observed for MTB positivity. In the north, no differences were observed between men and women in screening times and days whereas in the south men were more likely to be screened in the earlier times and on weekdays.

Conclusions: We observed clients at higher TB risk tended to present for earlier morning hours and weekdays. This may suggest that they found such services urgent but results varied by region and gender. Future screening endeavors should consider such patterns.

CAD4TB screening	CAD4TB ≥ 60	P-value	GeneXpert MTB+	P-value
Time				
8:18 AM-12:39 PM	2662 (8.7%)		589 (18.6%)	
12:40-18:30PM	2272 (7.3%)	< .001	329 (12.8%)	< .001
Day				
Monday - Friday	2655 (8.0%)		891 (16.4%)	
Saturday	279 (7.6%)	NOT SIGNIFICANT	27 (8.6%)	< .001

[Screening results CAD4TB and GeneXpert MTB+]

PS-07-570-31 Optimising GeneXpert output to maximise efficiency in Lagos State, Nigeria: is the for-profit private sector better positioned than the public sector?

E Baruwa,[1] E Ekanem,[1] B Olusola-Faleye,[2] A Iroko,[3] C Obanubi,[4] T Odusote,[4] I Okekearu,[5] E Adibo,[6] M Sorum,[1] F Nwagagbo,[2] [1]Abt Associates, International Development Division, Rockville, United States of America, [2]Abt Associates/ SHOPS Plus, International Development Division, Lagos, Nigeria, [3]Abt Associates, International Development Division, Lagos, Nigeria, [4]United States Agency for International Development, Office of HIV/AIDS and Tuberculosis, Abuja, Nigeria, [5]Abt Associates/ SHOPS Plus, International Development Division, Abuja, Nigeria, [6]El-lab Limited, Laboratory Services, Lagos, Nigeria.
e-mail: bolanle_olusolafaleye@shopsproject.com

Background and challenges to implementation: The Federal Ministry of Health (FMOH) and the National TB and Leprosy and Control Program (NTBLCP) chose their first for-profit private sector facility partner, EL-Lab, to receive a Cepheid GeneXpert IV machine for the diagnosis of drug-susceptible and drug-resistant tuberculosis (DS and DR-TB).

El-Lab based in Lagos State is one of only three laboratories in Nigeria with ISO 15189:2012 accreditation and is one of the state's 31 labs with GeneXpert machines. USAID's SHOPS Plus conducted this optimization analysis to identify criteria for optimizing GeneXpert use.

Intervention or response: An ingredient-based cost analysis of El Lab's inputs/operations was conducted and linear programming used to determine optimal test volumes and unit costs. Additional cost data on maintenance and cartridge costs covered by the Nigeria National TB Program were also collected. These data were compared with test volumes for all Lagos GeneXpert machines.

Results and lessons learnt: Given its constant power supply and number of laboratory scientists which accounted for over half its costs, El Lab has the capacity to run 924 samples a month which implies a unit cost of $2.30. This is 13% of the total unit cost of $16.57 per test which includes maintenance and cartridge costs that are covered by the National TB Program. Over October to December 2018, El Lab ran 1,836 tests so actual average unit costs were higher than $2.30; up to $4.70 in October. The average number of tests run over the quarter by other machines was 419 (lowest 80, highest 1,638). Module failure, cartridge stock outs and inadequate power supply were the most commonly reported issues.

Conclusions and key recommendations: Due to logistical issues, GeneXpert machines in Lagos state are functioning far below optimal capacity. Partnering with the for-profit private sector is an approach that can potentially increase the efficiency of GeneXpert machines in Lagos State.

PS-07-572-31 Assessment of screening strategies for tuberculosis diagnosis with GeneXpert MTB/Rif®, under programmatic conditions

D Affolabi,[1] F Massou,[1] M Fandohan,[1] AP Wachinou,[1] G Agodokpessi,[1] S Anagonou,[1] [1]National Tuberculosis Program, NTP, Cotonou, Benin.
e-mail: affolabi_dissou@yahoo.fr

Background: For decades in tuberculosis (TB) endemic countries, TB diagnosis has been based on microscopy in two sputa: one spot and one early morning sputa; but recently World Health Organization (WHO) has recommended to replace whenever possible, microscopy with GeneXpert MTB/Rif® (Xpert) performed on a spot sample. However, as it is known that bacterial load in early morning samples is higher than that in spot samples, one could expect lower sensitivity of Xpert performed only on spot samples.

In this study, we compared results of Xpert in spot samples versus early morning samples, under programmatic conditions in Cotonou, Benin.

Methods: From June to September 2018, all presumptive TB cases received at the Supranational Reference Laboratory for Tuberculosis of Cotonou were included in the study. From each patient, two samples were collected (one spot and one early morning) and Xpert was performed on both samples.

Results: In total, 886 participants were included in the study; among them, 737 provided both sputa and 149 gave only the spot sample. For the 737 participants who provided both sputa, Xpert was positive for both sam-

ples in 152 participants; for three participants Xpert was positive on spot sample but negative on morning samples while for another three, the test was positive on morning samples but negative on spot samples. The concordance between both strategies was excellent with Kappa = 99.18%.

Conclusions: For TB diagnosis under programmatic conditions in Cotonou, Xpert in spot samples gave similar results with the test in morning samples. Performing Xpert in both samples did not significantly increase the number of cases detected.

PS-07-573-31 Improving the quality of data on MDR-TB: the role of onsite mentorship at MDR sites in Uganda

H Namwanje Kaweesi,[1] T Kiyemba,[1] [1]USAID Defeat TB, University Research Co., LLC, Monitoring, Evaluation and Learning Department, Kampala, Uganda.
e-mail: hnamwanje@urc-chs.com

Background: In July 2015, Uganda MoH rolled out HMIS including DR-TB Quarterly reporting format which health workers in 17 DR-TB treatment units were expected to compile and electronically submit into the MoH DHIS2. Following DQAs conducted by the USAID/Defeat TB project in January 2018, for data reported for quarter Oct - Dec 2017, 50% discrepancy was between the figures reported in the MoH DHIS2 and those verified on site. Only 4 of 17 DR-TB treatment sites were found to have reported accurate DR-TB data with median discrepancy within the margin of +/-10%. The main reason cited by assessors was minimal understanding of data elements in the DR-TB report.

Methods: Defeat TB constituted a team of DR-TB mentors at national level who were oriented in DR-TB forms and data elements. These were dispatched to all 17 DR-TB sites to provide mentorship to health workers in compilation of the HMIS report. These activities were performed in April and July 2018. Teams were oriented on data elements in the DR-TB report as well as submission processes in MoH DHIS2. Orientation sessions included records staff who submit into MoH DHIS2 at the sites.

Results: DQA data collected in July 2018 showed a reduction in the median deviation between the number of DR-TB patients reported in DHIS2 and those verified from 50% to 0% between quarter of October-December 2017 to quarter of April-June 2018. Proportion of sites reporting within acceptable data quality margin (+/-10%) increased from 4 to 11 out of 17 treatment initiation sites.

Conclusions: Orienting both unit TB staff together with records persons in charge of entering MOH DHIS2 reports into the DHIS2 system led to enhanced understanding indicator compilation, improvement in the quality of reports. This has greatly enhanced planning, program management, decision making at facility and national levels.

PS-07-574-31 Bacteriologically-confirmed pulmonary tuberculosis patients: loss to follow-up, death and delay before treatment initiation in Bulawayo, Zimbabwe, 2012-2016

H Mugauri,[1] H Shewade,[2] R Dlodlo,[3] E Sibanda,[4] S Hove,[4] [1]Min of Health, AIDS and TB Unit, Bulawayo, Zimbabwe, [2]Research, International Union Against Tuberculosis and Lung Disease (The Union), South-East Asia Office, Operational Research, New Delhi, India, [3]International Union Against Tuberculosis and Lung Disease (The Union), Tuberculosis and HIV, Paris, France, [4]Bulawayo City Council, Health, Bulawayo, Zimbabwe.
e-mail: dumiwaboka@gmail.com

Background: Rapid identification and diagnosis of people with TB and their prompt initiation of appropriate treatment are essential to ending TB, particularly in Sub-Saharan Africa, which bears a disproportionate burden of the disease. TB Patients may be 'lost' after diagnosis and before treatment initiation. We sort to quantify and assess trends and risk factors for loss to follow-up (LTFU) and delays before treatment initiation among bacteriologically-confirmed pulmonary tuberculosis (TB) patients (laboratory-diagnosed) in Bulawayo, Zimbabwe, 2012-16.

Methods: We conducted a cohort study using secondary programme data. Presumptive TB patients' sputum samples were sent to the laboratory from the 19 primary health care clinics. Laboratory-diagnosed patients (microscopy or Xpert MTB/RIF) were tracked for treatment registration at the clinics.

Results: Of 2,443 laboratory-diagnosed patients, the mean (standard deviation, SD) delay from sputum receipt at the laboratory to testing was 2.7(1.6) days and from testing to result dispatch was 8.8(5.8) days. A total of 508(20.8%) were LTFU which included 252(10.3%) deaths. While the number of laboratory-diagnosed patients reduced over years, there was a significant increase in pre-treatment LTFU and death. Independent predictors of pre-treatment LTFU were age above 65 years, male gender and HIV positive/unknown. In addition, delay (≥3 days) between sputum receipt and testing was significantly associated with pre-treatment death. Among registered patients (n=1,935), the mean (SD) delay to initiate treatment was 29.1 (21.6) days which significantly declined over the years. Patients registered as new TB had significantly long treatment delay.

Conclusions: Interventions to mitigate the risk factors for high loss to follow-up, deaths and delays before TB treatment are urgently required.

PS-07-575-31 Introduction of GeneXpert MTB/RIF improves the diagnosis of TB in people living with HIV in Nigeria

E Agogo,[1] J Levy,[2] J Maltha,[2] D Egbule,[3] R Aguolu,[4] J Scholten,[2] A Ikpeazu,[5] [1]Nigeria Centre for Disease Control, Depute Director, Abuja, Nigeria, [2]KNCV TB Foundation, Technical Division, The Hague, Netherlands, [3]KNCV Tuberculosis Foundation, Nasarawa State Regional Office, Lafia, Nasarawa State, Nigeria, [4]National Agency for the Control of AIDS, Research and Publications Unit, Abuja, Nigeria, [5]National Agency for the Control of AIDS, Performance Management & Resource Mobilization, Abuja, Nigeria. e-mail: jens.levy@kncvtbc.org

Background: Tuberculosis (TB) remains the major cause of morbidity and mortality in people living with HIV (PLHIV) in Nigeria. GeneXpert (Xpert) has high sensitivity for the detection of TB among PLHIV due to low bacillary load. This study evaluates the impact of the introduction of GeneXpert on the diagnosis of TB in PLHIV in Nigeria.

Methods: This was a retrospective observational study, including 18 public health facilities providing HIV care. Data were obtained 12 months before Xpert installation until March 2016 (10-15 months after Xpert installation). All PLHIV with a positive TB symptom screen were included. Data were collected from the HIV and TB registers and care cards at the facilities. Positivity rate and time to diagnosis were compared for the period before and after introduction of Xpert (independent of the test performed) and between actual test performed (microscopy (AFB) and Xpert).

Results: 2733 individuals were included, 1314 (48.1%) and 1419 (51.9%) before and after installation of Xpert respectively. Test results were available for 1148 (42.0%) individuals, including 556 Xpert and 592 AFB results, of which 157 AFB were performed after installation of Xpert. Positivity rate was slightly higher in the post- vs pre-Xpert period (11.7% vs 9.7%, p = 0.35) and for Xpert vs AFB (10.7% vs 10.3%, p = 0.90). When using a conditional logistic regression to account for the clustering related to facility, we found that Xpert was 1.69 times more likely to have a positive test result (OR= 1.69; 95% CI: 1.05-2.72) relative to AFB. Time to diagnosis (median 1 vs 4 days) was significantly shorter for Xpert vs AFB, also after controlling for clustering effects of health facilities.

Conclusions: The utilization of Xpert improved the timely diagnosis of pulmonary TB among PLHIV in Nigerian public HIV treatment centers.

PS-07-576-31 Comparison of GeneXpert Cycle threshold values with smear microscopy and culture in five regional referral hospitals of Uganda

I Najjingo,[1] W Muttamba,[1] BJ Kirenga,[1] J Nalunjogi,[1] R Bakesiima,[2] F Olweny,[2] P Lusiba,[3] A Katamba,[2] W Ssengooba,[4] [1]Makerere University Lung Institute, Research, Kampala, Uganda, [2]Makerere University, Clinical Epidemiology, Kampala, Uganda, [3]Makerere University, College of Health Sciences, Kampala, Uganda, [4]Makerere University, Department of Medical Microbiology, Kampala, Uganda. e-mail: irenenajjingo@gmail.com

Background: GeneXpert gives cycle threshold (Ct) values as a potential measure for mycobacterial burden. For physicians to clearly interpret Ct values as measures of mycobacterial burden, this study compared the Xpert quantification capabilities with those of smear microscopy and culture. The study also determined the relationship between Xpert Ct values and MGIT culture time to positivity and a cut off Ct value which best predicts smear positivity

Methods: This was a cross-sectional study. It obtained data from the East African Public Health Laboratory Networking project which recruited 1,783 TB suspects. 495 were diagnosed with TB by genexpert and were considered for the study. Spearman correlation of genexpert Ct values with smear microscopy and culture positivity was determined. Receiver Operator Curve was used to determine the Ct values that predicts smear positivity. Linear regression was done to assess the association between MGIT culture time to positivity and Xpert Ct values.

Results: Excluding missing results and rifampicin resistant TB cases, a moderately strong correlation of 0.55 between Xpert Ct value and smear grade was obtained. A weak correlation of 0.37 was obtained between Xpert Ct values and MGIT time to positivity while that between Xpert Ct values and LJ culture was 0.34. The Xpert Ct values were found to increase by 2.57 for every unit increase in days to positive and HIV status was significantly associated with this relationship. A cut off Ct value of 23.62 was found to best predict smear positivity regardless of HIV status.

Conclusions: Our study findings show that GeneXpert Ct values are comparable to smear microscopy as a measure of M. tuberculosis burden and can be used to replace smear microscopy. However, given the low correlation between Xpert Ct value and culture positivity, Xpert Ct values cannot replace culture as a measure of M. tuberculosis burden among TB patients.

PS-07-577-31 TB-one stop services (TOSS) - can private tuberculosis management units improve patient care practices in the private sector?

K Arun Kumar,[1] P Vikas,[1] R Vijay Kumar,[1] A Shanta,[2] C Joseph,[3] [1]TB Alert India, Program, Hyderabad, India, [2]WHO Country Office, Program, Vishakhapatnam, India, [3]Stop TB Partnership, Program, Vishakhapatnam, India. e-mail: arunkmph8@gmail.com

Background and challenges to implementation: Better TB diagnosis and care Private Sector (PS) is key to achieving India's goal of eliminating tuberculosis (TB) by 2025. However, there exists a scope for improving standards of TB-care in the PS. TB One-Stop-Services-(TOSS), TB-Reach Wave-5 Project introduced TB Diagnostic-Hubs, modelled similar to National TB Programmes's TB Management Units (NTP-TU) within PS facilities. This revised abstract is submitted after 5 Quarters (Oct 2017 - Dec 2019) of TOSS Project of Implementation

Intervention or response: Five Diagnostic-Hubs were set-up in private Laboratories in two Districts of Andhra-Pradesh. Hubs followed NTP Diagnostic algorithm offering free Sputum Smear Microscopy(SSM), X-ray at subsidized rates and GeneXpert test at rates of 'Initiative for Providing Affordable Quality TB Test' (IPAQT). All sputum samples were tested by SSM and if negative, patients were screened on X-ray. Sputum of those with abnormal X-ray, extra-pulmonary and pediatric samples was tested on GeneXpert. Project staff sensitized doctors on standards of TB diagnosis and management, assisted referrals of TB-symptomatics from private doctors to Diagnostic-Hubs, notified TB-cases to NTP and followed-up with patients regularly from treatment initiation till treatment outcome.

[TOSS Project]

Results and lessons learnt: From October 2017-Dec 2018, 12041 TB-symptomatics were tested and 5765 TB-cases diagnosed; 45%(n) by SSM, 9%(n) by GeneXpert and 46%(n) clinically. Proportion of microbiologically confirmed cases was 54%(n=3140). Total TOSS Project facilitated cases (5765) accounts for 60% of total TB-cases (n=9631) notified by NTP(5 Quarters). There has been TWO-FOLDS increase in TB Case notifications from PS in 2018 (7560) , when compared to 2017(3717) with additional case yield of 3843 (n) TB-cases. Of the 5765 TB Cases put on treatment, 52% (n) reported successful outcomes till end of project period and balance cases are on treatment.

Conclusions and key recommendations: NTP-TU Models can be successful in PS to improve TB management standards. Policy makers must focus on such initiatives to effectively involve PS in Ending TB.

PS-07-578-31 Is chest X-ray an essential screening tool for contact investigation?

S Myat,[1] M Myat Aung,[2] Z Lin Tun,[2] K Mar Aung,[1] S Htut Aung,[1] T Naing Maung,[2] Z Myint,[3] [1]FHI 360 Myanmar, Challenge TB Project, Yangon, Myanmar, [2]Myanmar Medical Association, TB, Yangon, Myanmar, [3]National TB Programme, NTP Central (Yangon Branch), Yangon, Myanmar. e-mail: dr.sumyat13@gmail.com

Background and challenges to implementation: Myanmar has an estimated TB incidence of 358 per 100,000 population.[1] Approximately 53% of all registered multidrug resistant/rifampicin resistant (MDR/RR)-TB cases are found in Yangon. People living with MDR/RR-TB patients are at high risk of infection due to prolonged exposure during the infectious period. Systematic contact investigation is essential for identifying TB early among those contacts.

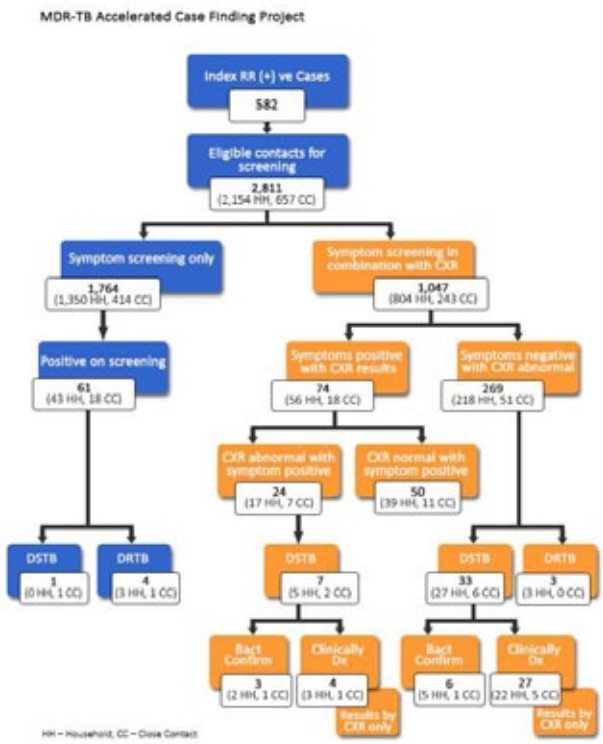
[1] WHO global TB Report, 2018

Intervention or response: The USAID Challenge TB (CTB) project collaborates with Myanmar Medical Association (MMA) to conduct "MDR-TB Accelerated Case Finding" in Yangon. CTB conducts systematic contact investigation in 13 Yangon townships with the highest MDR-TB burden, targeting household and other close contacts of MDR/RR-TB index patients. Contacts are screened by using a standardized symptom checklist and chest X-ray (CXR). Sputum samples from presumptive TB patients are tested by GeneXpert and patients are referred for further evaluation as necessary.

Results and lessons learnt: 2,811 contacts from 582 MDR/RR-TB index patients were screened for TB. 1,764 underwent symptom screening only, and 1,047 received both symptom screening and CXR. The yield of TB from symptom screening only was **0.3% compared to 4.1%** using combination screening. From combination screening, 74 out of 1,047 contacts were symptomatic and **7 of these 74** contacts were identified as having drug sensitive (DS) TB, of whom 4 were diagnosed by CXR alone; 269 of 1,047 contacts had abnormal CXR findings without symptoms, resulting in an **additional 33 DS-TB** and **3 MDR/RR-TB** cases.

Conclusions and key recommendations: In contacts of MDR/RR TB patients, using CXR in combination with symptom screening yields more TB cases than symptom screening alone. All MDR-TB household contacts should be screened with CXR in addition to regular symptom screening. The National TB Program should

adopt CXR as a first-line screening tool for MDR/RR-TB contact investigation and should include close contact screening in addition to household contacts.



[MDR-TB Accelerated Case Finding Project]

PS-08-D9 Money matters: analyses of societal and household TB expenditures

PS-08-579-31 Innovative financial social support model for TB patients: India

P Jha,[1] [1]The Union South East Asia, Tuberculosis, New Delhi, India. e-mail: prabhash.jha@theunion.org

Background and challenges to implementation: Evidences suggest catastrophe expenditure on household for availing treatment services, this has resulted in increased lost to follow-up of patients completing treatment. The Government of India envisaged processes to support notified TB patients under the programme by innovative financial social support mechanism. In order to ensure that beneficiaries receive the financial social support, a governance structure - Public Finance Management System (PFMS) was established to facilitate the process. The study here elaborates the process and results of the same.
Intervention or response: PFMS receives the information of eligible beneficiaries through a common web-portal from the programme staff at district level. The information contains details of bank-account, address, mobile number etc. A multi-stakeholder level validation process is in-built wherein - Programme, public finance and beneficiaries bank authenticate. Following the authentication process, the payment is now ready to be made to beneficiaries. Beneficiaries informed about the payment through SMS alerts - both from PMFS and bank.
Results and lessons learnt: Over a period of one year up to March, 2019, 2.6 million total eligible beneficiaries were enrolled for the Financial Social Support, out of which 1.6 million i.e., 61% of eligible beneficiaries received the support. The initial turnaround time for disbursement of support following notification is reduced to 7 working days from 4 weeks. PMS systems is in process to ensure all registered eventually receive support.
Conclusions and key recommendations: The innovative financial mechanism has ensured that every eligible beneficiary is provided social financial support to ensure successful TB treatment completion.

PS-08-580-31 Cost of diagnosing a TB patient in an active case finding programme using CHWs: experience from rural India

T Garg,[1] M Bhardwaj,[2] S Deo,[3,4] [1]Innovators in Health, Research, Patna, India, [2]Innovators in Health, Operations, Patna, India, [3]Indian School of Business, Operations Management, Hyderabad, India, [4]Indian School of Business, Max Institute of Healthcare Management, Mohali, India. e-mail: tgarg@innovatorsinhealth.org

Background: Active case finding (ACF) holds significant potential in winning the global fight against TB. Some previously employed ACF approaches such as blanket household surveys can incur significant costs. In contrast, rural community health workers (CHWs) become aware of the health status of their constituents as part of their routine work, e.g., home visits for post-natal care, immunization drives, etc. Leveraging this pre-existing information can streamline identification of suspected cases, eliminating the need for exhaustive door-to-door screening. However, the cost-effectiveness of this strategy has not been adequately studied.
Methods: We implemented an active-case-finding (ACF) program in three blocks in the Samastipur district in Bihar, India (1.02M pop.). CHWs (known locally as "ASHA") were engaged to generate referrals based on their knowledge of the community. Presumptive TB patients were then identified through symptom-based screening. The notification rates were compared with a control population (CP) in the district with similar demographics, epidemiology, and health systems. Program expenses were used to calculate the cost per TB case diagnosed and notified.
Results: Between June 2017 and June 2018, CHWs in the catchment generated and screened 11843 referrals, of which 10245 were identified as presumptive TB patients. Of these, 6185 patients were tested (the rest were tested

beyond the reporting period) and 1326 were diagnosed with TB. Notifications increased sharply in the catchment, from 52/100,000 pop. to 115/100,000 (NTP data). Notification in the control stayed at about 51/100,000. There was statistically insignificant impact on other output indicators involving CHWs, e.g. registration for antenatal visits (-3%), institutional deliveries (+1.2%), and immunization sessions (+3.6%). The overall cost per diagnosed case was USD 137. The cost drivers were human resources (38.2%) and drugs and diagnostics (30.4%).

Conclusions: ACF programs that utilizes existing CHW resources in the public health system is feasible, cost-effective and does not adversely affect other health programs involving CHWs.

PS-08-581-31 Cost of contact investigation for tuberculosis in rural South Africa

A Tucker,[1] L Mmolawa,[2] R Tampi,[1] C Hanrahan,[1] B Nonyane,[3] N Stracker,[1] N West,[1] L Lebina,[2] N Martinson,[2] D Dowdy,[1] [1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [2]Perinatal HIV Research Unit, HIV and Tuberculosis Co-Infection, Soweto, South Africa, [3]Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, MD, United States of America. e-mail: atucke20@jhmi.edu

Background: Contact investigation for TB is an important global health priority. There is limited evidence on the costs of contact investigation as feasibly implemented in rural Sub-Saharan Africa - a key underserved setting.

Methods: As part of a cluster randomized trial in Limpopo, South Africa, we conducted an empirical costing study of TB contact investigation from the health system perspective. Twenty-eight primary health clinics in two districts were randomized to perform contact investigation: 14 clinics (seven per district) used a household-based strategy, and 14 used conditional cash transfer incentives. In each district, two mobile teams traveled to all clinics on a twice-monthly basis over an 18-month period. For the household intervention, patients diagnosed with TB were offered home-based screening of all contacts, while for the incentive-based intervention, patients received coupons for a cash incentive ($3.75 to contacts and $1.50 to index patients per contact referred) if contacts returned to the referring clinic for screening. All screening was performed using Xpert MTB/RIF. We used a "bottom-up" approach to collect program and health system costs. We allocated the time cost of field staff via self-reported time-and-motion surveys. All costs are reported in 2017 USD.

Results: The total cost of the active case finding program over 18 months was $62,336 ($123 per clinic-month of screening). Household-based screening accounted for $29,587 (47%, $117 per clinic-month), while incentive-based screening cost $32,749 (52%, $130 per clinic-month). The largest proportion of program cost comprised vehicles/petrol (29%) and staff (23%) costs, with incentives accounting for 4% of costs in incentive-based clinics (Table). Contact investigation identified 12 additional TB diagnoses ($5195 per diagnosis made).

Conclusions: Implementing contact investigation in rural South Africa is resource intensive, largely reflecting the need for extensive travel between clinics. Given the importance of TB contact investigation, it is critical to identify innovative solutions for reducing this economic burden.

Cost Category	Household		Incentive	
Annual Costs	2017 ZAR	2017 USD	2017 ZAR	2017 USD
Staff	ZAR 93,963.41	$7,050.54	ZAR 94,422.49	$7,084.99
Vehicle	ZAR 116,517.46	$8742.89	ZAR 84,892.65	$6,369.92
Petrol	ZAR 22,475.82	$1,686.47	ZAR 16,375.50	$1,228.74
Building	ZAR 8,495.49	$637.46	ZAR 8,495.49	$637.46
Overhead	ZAR 6,638.71	$498.14	ZAR 6,638.71	$498.14
Operational	ZAR 10,521.87	$789.51	ZAR 10,521.87	$789.51
Incentive			ZAR 35,083.18	$2,632.47
Total Cost		$29,587.04		$32,749.38

[Itemized costs of delivering contact investigation to 28 rural South African clinics over 18 months]

PS-08-582-31 A cost comparison of homebased point-of-care TB testing vs. homebased screening with referral for testing, Buffalo City Metro Health District, South Africa

D Bresenham,[1] C Bezuidenhout,[1] R Mawarire,[1] P Ngwepe,[1] N Ngcelwane,[2] A Medina-Marino,[1] [1]Foundation for Professional Development, Research Unit, Pretoria, South Africa, [2]Buffalo City Metro Department of Health, District Department of Health, East London, South Africa. e-mail: danab@foundation.co.za

Background: Household contact investigations (HHCI) are integral for early detection and active case finding geared towards achieving the End TB strategy. Advancements in point-of-care technology now allows for the integration of homebased testing during HHCIs. We sought to compare the additional time and labour cost incurred when offering homebased testing using a portable, diagnostic TB testing platform, compared to home-based screening with referral for clinic-based testing.

Methods: A pilot study was implemented in the catchment area of six public health clinics serving the Duncan Village Informal Settlement, East London, South Africa. Community health workers obtained household contact lists from consenting TB index patients. HHCIs were conducted, and homes with at least one TB symptomatic person were randomized (1:1) to either:
(1) point-of-care testing (intervention), or
(2) referral for clinic-based testing (control).

Time-and-motion data were collected using a real time electronic platform to compare time and implementation costs.
Results: Among 281 TB index patients, 1010 contacts were listed of which 894 agreed to screening. Ninety-five individuals were consented and randomized; 46 were referred for clinic-based TB testing (control) and 49 were offered home-based testing (intervention). The average time spent screening each household contact was 2 minutes (IQR: 1 min) with an associated labour cost of R63.07 (~$1.47). The average time spent at a household offered and accepting a home-based TB test was 94 minutes (IQR: 28 min) with an associated labour cost of R161.88 (~$11.52).
Conclusions: Our data demonstrate the benefit of using time and motion indicators to inform operational models critical to the implementation of point-of-care testing. Our findings suggest a modicum increase in time and labour cost for a reduction in time to diagnosis. Additional cost modeling could provide further insight into the cost averted with early time to treatment initiation.

PS-08-583-31 The importance of collecting cost-benefit data to inform cost-effective point-of-care TB testing in informal settings: Buffalo City Metro Health District, South Africa

C Bezuidenhout,[1] D Bresenham,[1] R Mawarire,[1] A Medina-Marino,[1] N Ngcelwane,[2] [1]Foundation for Professional Development, Research, East London, South Africa, [2]Department of Health, TB Services, East London, South Africa. e-mail: charlb@foundation.co.za

Background: Active case finding (ACF) strategies for tuberculosis (TB) are geared towards early detection, diagnosis and linkage-to-care. Household contact investigations (HHCI) albeit effective, are resource intensive. We aimed to assess the use of cost-benefit data to inform implementation of HHCI strategies.
Methods: HHCIs were leveraged to assess the feasibility of point-of-care TB testing using portable GeneXpert devices. Up to 3 HHCIs were done for households in the catchment area of six public health clinics serving the Duncan Village informal settlement. An Electronic Data System was used to schedule HHCIs, capture outcomes and resources used. Using this data the overall cost incurred was used to estimate the marginal cost incurred for each marginal gain.
Results: Across 271 households, 440 HHCIs were conducted; 271 HHCIs were performed on a 1st attempt, 126 on 2nd attempt, and 43 on 3rd attempt. A total of 893 household contacts were screened of which 170 (19%) screened positive. Our data revealed that 691/893 (77.4%) contacts were screened during the first attempt and 146/170 (86.0%) of all positives were found. At the 2nd attempt 148/893 (16.6%) were screened and 16/170 (9.4%) positives were found while at the 3rd attempt 54/893 (6.0%) were screened and 8/170 (4.7%) positives were identified. The average cost of conducting a HHCI was estimated at R79 (~$5.60). The cost per case screened at first attempt was R30.89 (~$2.20), R67.26 (~$4.80) at 2nd attempt, and R62.90 (~$4.50) at 3rd attempt. The cost to identify a symptomatic individual at first attempt was R146.64 (~$10.47) compared to R622.13 (~$44.44) and R424.63 (~$30.33) at attempts 2 and 3, respectively.
Conclusions: Our work provides data on the cost and cost-effectiveness of implementing HHCIs in South Africa's informal settlement areas. Though beneficial, multiple visits showed diminishing returns. Cost/benefit data will be used to further inform the implementation of home-based TB diagnostic testing.

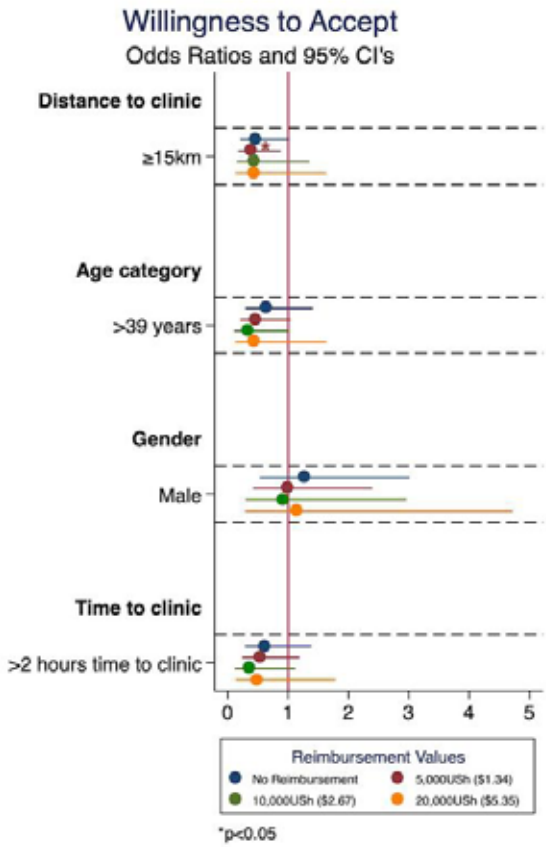
PS-08-584-31 Willingness to accept financial reimbursement for tuberculosis preventive therapy among people living with HIV in Kampala, Uganda

J Kadota,[1,2] A Musinguzi,[3] F Welishe,[3] J Nabunje,[3] JL Ssemata,[3] A Katamba,[2,4] FC Semitala,[3,4,5] A Cattamanchi,[1,2] DW Dowdy,[2,6] [1]University of California, Division of Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [2]Uganda Tuberculosis Implementation Research Consortium, Research Core, Kampala, Uganda, [3]Infectious Diseases Research Collaboration, Research Core, Kampala, Uganda, [4]Makerere University College of Health Sciences, Department of Medicine, Kampala, Uganda, [5]Makerere University Joint AIDS Program (MJAP), TB Care and Treatment, Kampala, Uganda, [6]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America. e-mail: jillian.kadota@ucsf.edu

Background: High costs faced by patients in completing clinic visits is one reason reported for low uptake of tuberculosis (TB) preventive therapy among people living with HIV (PLHIV). We assessed willingness to accept various reimbursement levels for clinic visits to facilitate short-course, weekly preventive therapy among PLHIV.
Methods: We conducted a willingness-to-accept survey experiment among 100 PLHIV accessing care at the Mulago AIDS Clinic, an urban facility in Kampala, Uganda. Participants were asked in a double-bounded contingent valuation format if they would return to clinic for 12 weeks to receive TB preventive therapy in exchange for 5,000 Ugandan Shillings (USh), 10,000 USh, or 20,000 USh (~$1.34-5.34 USD) per week. We compared associations between willingness-to-accept and patient characteristics using unadjusted logistic regression.
Results: The median participant age was 39 (interquartile range (IQR): 32-47), 70% were women, and median personal income was 44,500 USh (~$11.87 USD) per week (IQR: 15,000-95,650). On average, participants lived 15 km (IQR: 8-30) from the clinic and reported 5,000USh (IQR:3,000-7,000) in one-way transport costs.

The self-reported fair reimbursement amount for each clinic visit was 15,000USh (IQR:10,000-20,000). When prompted, 56 participants (56%) reported that they would accept treatment without any reimbursement offer, 20% would accept 5,000-10,000Ush per visit, 17% would accept ≥10,000Ush per visit, and 7% would not complete treatment regardless of financial reimbursement level. Older participants (>39 years) and those living ≥15 km from clinic were less likely to accept reimbursement (odds ratio for accepting 5,000USh 0.46 (95% confidence interval (CI): 0.20-1.04), for older participants and 0.39 (95%CI: 0.17-0.88) for distant residents, (**Figure 1**).

Conclusions: Financial reimbursements as low as 10,000USh ($2.68USD) are likely sufficient to enhance uptake of short-course TB preventive therapy among PLHIV in urban Uganda. Older participants and those living further from clinic may require greater financial support.



[Willingness to accept financial reimbursement for clinic visits by patient characteristics (n=100)]

PS-08-585-31 Coping mechanisms of individuals and families facing TB-related catastrophic costs: findings from National TB Catastrophic survey in Nigeria

O Kusimo,[1] A Awe,[2] A Hassan,[3] R Olukolade,[3] Q Ogbuji,[3] A Osho,[3] [1]World Health Organisation, TUB, Ogba, Nigeria, [2]World Health Organization, TUB, FCT, Nigeria, [3]Association for Reproductive and Family Health, TB, FCT, Nigeria. e-mail: awea@who.int

Background: WHO's End TB Strategy aims to achieve zero suffering in relation to TB by ensuring that no family experiences catastrophic cost due to TB by 2020. Nigeria, among other countries with high TB burden are far from achieving this goal. Poverty remains a structural driver of the TB epidemics hence low and middle income countries are those hardest hit by the disease and are also disproportionately affected by TB catastrophic costs. Most of the financial burden borne by TB patients is incurred before diagnosis. Hidden costs related to TB treatment have been associated with poor treatment adherence. This study seeks to explore the coping mechanisms employed by patients to mitigate the negative impact of TB catastrophic costs.

Methods: The study design adopted was a cross-sectional survey as part of the national Tuberculosis Catastrophic Cost survey guided by the World Health Organization study protocol. A multi-stage sampling technique was used to select 1,200 study respondents from forty clusters located in twenty states.

Results: Coping mechanisms described by respondents included selling of household items as well as capital goods such as cows, goats, among others. Borrowing from relatives, friends and neighbors was also identified as a key coping mechanism. Food insecurity, loss of jobs, divorce/separation, school interruption and social exclusion were identified as negative coping measures or consequences of the disease. Among the patients investigated, food insecurity and borrowing of money ranked highest among the list at 45% each, compared to loss of job (3%), divorce/separated from spouse/partner (5%), interrupted schooling (12%) and social exclusion (28%).

Conclusions: Interventions designed to control the TB epidemic should consider the socio-economic effect of the disease on patients' quality of life. Hence, social support systems should be integrated into TB care in ways that reduce the patients' vulnerabilities to TB-related catastrophic costs.

PS-08-586-31 Costs of seeking care for tuberculosis diagnosis after the implementation of universal health coverage in Indonesia

A Fuady,[1,2] [1]Erasmus MC University Medical Centre Rotterdam, Public Health, Rotterdam, Netherlands, [2]Universitas Indonesia, Community Medicine, Jakarta, Indonesia. e-mail: a.fuady@erasmusmc.nl

Background: Tuberculosis (TB) diagnostic delays and higher costs are associated with seeking care in multiple private providers. This study aimed to assess TB patients' seeking care behavior, costs incurred for diagnosis and their determinants after the implementation of universal health coverage (UHC) in Indonesia.
Methods: In July-September 2016, we interviewed adult TB patients in Indonesia who had been treated for at least one month to assess their seeking care behavior. We also asked direct and indirect costs incurred during pre-diagnostic phase, and calculate the costs in absolute terms (in US Dollars) and relative terms as a share to annual household income (in %). To identify determinants of costs incurred in absolute and relative terms, we applied general linear mixed model to adjust for our cluster sampling design.
Results: We included 282 patients in analysis. TB patients in rural district prefer to seek care firstly to private clinic than those living in urban district (OR=2.3, 95%CI=1.08-4.96, P=0.031). Patients with private clinic as the first contact appeared to have more visits significantly than patients who came firstly to PHCs (P< 0.05). Visiting private clinic as the first contact also led to a higher costs than visiting PHCs both in terms of facility costs (B=16.72, 95%CI=10.55-22.89, P< 0.001) and total costs (B=22.40, 95%CI=7.72-37.07, P< 0.001). In relative terms, the higher proportions of total costs to annual household income were related to private clinic as the first contact (B=2.21, 95%CI=1.13-3.29, P< 0.001), rural district (B=1.99, 95%CI=0.81-3.18, P=0.001), and poor household (B=1.82, 95%CI=0.80-2.83, P=0.001).
Conclusions: Despite the implementation of UHC in Indonesia, the preference to seek care to private providers was still high and led to high number of diagnostic shopping and higher costs. Along with health financing reform, a strategy to strengthen public-private mix is required to improve quality of diagnostic, reduce diagnostic delays, and minimize patients' costs.

PS-08-587-31 Mixed-methods study to estimate the social return on investment of a tuberculosis case finding and patient support intervention in Ho Chi Minh City, Viet Nam

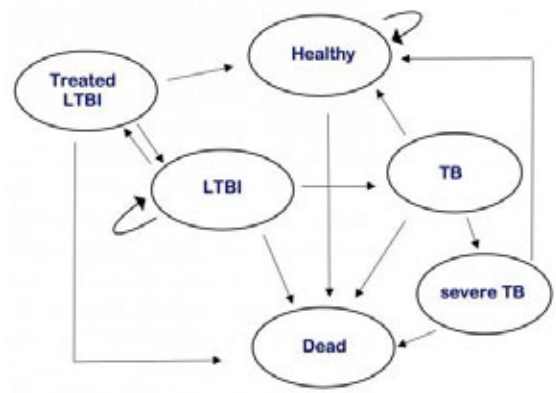
LNQ Vo,[1,2] RJ Forse,[3] VV Truong,[4] TN Vu,[5] GT Le,[5] GC Do,[6] LH Nguyen,[7] AJ Codlin,[8] M Caws,[9,10] [1]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [2]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [3]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [4]Pham Ngoc Thach Lung Hospital, Provincial TB Steering Department, Ho Chi Minh City, Viet Nam, [5]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam, [6]Pham Ngoc Thach Lung Hospital, Quality Assurance, Ho Chi Minh City, Viet Nam, [7]Pham Ngoc Thach Lung Hospital, Provincial TB Program, Ho Chi Minh City, Viet Nam, [8]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [9]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom, [10]Birat Nepal Medical Trust, Operations, Kathmandu, Nepal. e-mail: luan.vo@tbhelp.org

Background: Tuberculosis (TB) remains a main cause of avoidable death, and a heavy economic burden for patients and society. There is extensive evidence on the cost effectiveness of TB care and prevention, but few studies have assessed the social return on investment (SROI) of incremental case finding and patient support beyond the standard of care.
Methods: This mixed-method study estimated the societal benefit of a community-based TB case finding and patient support intervention. We conducted a literature review, two focus group discussions and 14 in-depth interviews to identify stakeholders and value drivers of the intervention. Qualitative data were analyzed using thematic framework analysis. Quantitative data sources included the National TB Program routine surveillance system, public ecological databases, published studies, project accounts and 11 beneficiary surveys.
From these data, we constructed a SROI model according to the methodology of Social Value UK, which entails mapping and monetizing value drivers, adjusting crude impact for four counterfactuals, and calculating the SROI based on the present values of benefits and costs in a 5-year discounted cash flow model.
Results: Our literature review initially identified 8 beneficiaries and 25 value drivers, which qualitative findings reduced to 5 and 14, respectively. Crude monetization of the value drivers over a 5-year time horizon yielded a cumulative benefit of USD64,168,005, which was reduced by 89% to USD7,072,408 after adjusting for the counterfactuals. Using a 3.5% discount rate, the present value of the cumulative benefits was USD6,601,494. Accounting for USD154,657 in total intervention costs, the net present value was USD6,446,836, and the SROI was 4,268% indicating that for every USD1.00 invested, the social value created was USD42.68.

Conclusions: The SROI model showed that comprehensive interventions for TB can generate additional societal benefits. However, estimates must include a thorough analysis of the counterfactuals to avoid overestimating the impact of these interventions.

[Adjusted total and net present value of investment and social returns]

research is needed to determine which risk groups, based on country of origin, age and risk factors for progression, should be targeted for more cost-effective strategies in the future.



[Diagrammatic representation of the Markov model used for cost effectiveness analysis]

PS-08-588-31 Cost effectiveness of latent tuberculosis screening among migrants in Stockholm

J Shedrawy,[1] A Siroka,[2] K Lönnroth,[1] C Deogan,[3]
[1]Karolinska Institutet, Public Health, Stockholm, Sweden, [2]World Health Organisation, Headquarters, Geneva, Switzerland, [3]Public Health Agency of Sweden, Public Health, Stockholm, Sweden. e-mail: jad.shedrawy@ki.se

Background: The majority of Tuberculosis (TB) cases in Sweden result from activation of latent Tuberculosis infection (LTBI) in migrants from endemic countries. LTBI screening is recommended for all asylum seekers from countries with an incidence of >100/100 000. Preventive treatment should be offered to young persons (in Stockholm < 18 years is the threshold) and older persons who have risk factors. This study aimed to assess the cost effectiveness of the current LTBI screening strategy in Stockholm.
Methods: A Markov model with six health states (figure 1) was built to predict the future costs and effects of the current screening strategy compared to no screening for different age groups over a period of 20 years. A societal perspective was used. Costs and epidemiological parameters were obtained from local data. Sensitivity analysis and probabilistic approaches were conducted. The soft threshold for cost effectiveness in Sweden is around 500 000 SEK/QALY, which was used as reference.
Results: Results differed according to age which reflect the probability of being treated. The incremental cost effectiveness ratios (ICER) were 720 000, 2 200 000, 2 300 000 SEK/QALY for cohort of 16, 30, 50 years old respectively.
Conclusions: LTBI screening was not cost-effective in any of the age groups, but it was borderline for young migrants. This is largely explained by not offering treatment to the majority of those screened positive. Further

PS-09-B1 GeneXpert

PS-09-589-31 GeneXpert: a hope for extra-pulmonary tuberculosis patients of Bhubaneswar, Odisha, India

HB Bal,[1] D Das,[1] S Pati,[1] [1]Regional Medical Research Centre, National Reference Laboratory-TB, Bhubaneswar, India. e-mail: drhbbal@gmail.com

Background and challenges to implementation: Extrapulmonary Tuberculosis (EP-TB) contributes approximately 10 to 15% of TB cases in India. Due to paucibacillary nature and lack of diagnostic means, they often remain untreated with greater proportion in pediatric and HIV patients. WHO recommended GeneXpert for EP-TB diagnostic and RNTCP established 1135 GeneXpert laboratories in India and developed guidelines for EPTB testing. So, the aim of this study was to evaluate EPTB referral enhancement for GeneXpert test and notification.
Intervention or response: GeneXpert machine was installed in Feb 2016. Both EP-TB and pulmonary samples from RNTCP, both public and private health facilities were received and processed before test as per the WHO guidelines.
Results and lessons learnt: Out of total 1858 tests done between Feb 2016 to Feb 2017, 38.1% were EP sample among which 65.3% & 34.5% referral from public and private respectively and there was no referral from RNTCP. 16.1% of EP-TB patient were TB positive and prevalence of rifampicin resistant was 1.7% among all the presumptive EP-TB cases. 19.8% of EP-TB samples were received from under 14-year children out of which 5% were TB positive. Out of total sample, 29.1%

of samples are BAL followed by CSF (22.1%) and pus (12.4%). TB positive is highest in Lympnode aspirate (50%) followed by pus (43.2%) and tissue (26.1%). All the TB positive cases has been notified to RNTCP program.

Conclusions and key recommendations: Despite the availability of culture support since 2014, there were very few EPTB referral in comparison to 38% increase in EPTB cases after GeneXpert facility. The underdiagnosed EP-TB cases has to be detected and treated properly to achieve the goal of end TB by 2025 and private health sectors equipped with advanced technologies will play a major role for EPTP treatment.

PS-09-590-31 Diagnostic paradox of childhood TB: can Xpert MTB/RIF Ultra on stool specimen help?

S Kabir,[1] S Ahmed,[1] KK Paul,[1] SMM Rahman,[1] MKM Uddin,[1] S Choudhury,[1] R Nasrin,[1] F Ather,[1] S Sultana,[1] S Banu,[1] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh. e-mail: senjuti.kabir@icddrb.org

Background: Paucibacillary nature of tuberculosis (TB), children's inability to expectorate sputum and non-specific clinical features hinder childhood TB (ChTB) diagnosis. In Bangladesh, proportion of ChTB is around 4% among the reported cases, far less than estimated. Improved diagnostic tool and alternative specimen are warranted for better ChTB diagnosis. We evaluated the performance of Xpert MTB/RIF Ultra using stool for ChTB detection.

Methods: Presumptive ChTB cases from four tertiary care hospitals in Dhaka were enrolled between January'18 and January'19. Induced sputum (IS) and stool were collected from participants and subjected to microscopy, Xpert Ultra and culture in solid media.

Children were diagnosed bacteriologically when positive in any of these tests and, also clinically by the treating physicians.

Proportion of positivity was compared by two sample test of proportions by STATA/SE (version 13.0). Accuracy of Stool Xpert Ultra was measured among all ChTB cases, considering final TB diagnosis (either bacteriological or clinical) as gold standard.

Results: We enrolled 339 presumptive ChTB cases with median age of 2.1 years (IQR: 0.74-6.5) and 55% were male. Ninety (27%) children were diagnosed with TB. Among them, 52 (58%) were bacteriologically confirmed (B+ve) and 38 (42%) were diagnosed clinically. Forty two (81%) of B+ve TB cases were identified by stool while 22 (42%) were identified by IS using Xpert Ultra (95% CI, $p< 0.001$). By Xpert Ultra, 12 (23%) B+ve cases were positive in both specimens, 10 (19%) were positive in only IS and, 30 (58%) were positive in only stool. Accuracy of Xpert Ultra was 86% among all TB cases (n=90). No additional case was detected by microscopy/culture.

Conclusions: Stool was found to be a significantly superior specimen to IS in ChTB diagnosis by Xpert Ultra. Being an easy to collect specimen, stool presents a great opportunity to improve ChTB detection.

PS-09-591-31 Evaluation of diagnostic tools in paediatric tuberculosis using latent class analysis

K Thiruvengadam,[1] NS Gomathi,[2] V Banurekha,[3] K Sanathya,[1] S Balaji,[4] S Balaji,[2] D Nair,[3] S Vijayalakshmi,[4] S Hissar,[3] S Swaminathan,[5] [1]National Institute for Research in Tuberculosis, Dept of Statistics, Chennai, India, [2]National Institute for Research in Tuberculosis, ICMR, Bacteriology, Chennai, India, [3]National Institute for Research in Tuberculosis, ICMR, Dept of Clinical Research, Chennai, India, [4]Institute of Child Health and Hospital for Children, Clinic, Chennai, India, [5]World Health Organisation, Research, Geneva, Switzerland. e-mail: syed.hissar@nirt.res.in

Background: Diagnosis of tuberculosis (TB) in children is a challenge due to lack of gold standard. Performance of diagnostic tests for the diagnosis of pediatric TB was evaluated using Latent class analysis (LCA) random effects model and the classical 2x2 table calculation.

Methods: Children aged <15 years with symptoms suggestive of intra-thoracic TB were prospectively enrolled in Chennai, Vellore and Madurai sites from 2013 to 2019. Two sputum/gastric aspirate were subjected to smear microscopy, Xpert MTB/RIF, solid culture [Lowenstein-Jensen (LJ)] medium and Bactec MGIT960. Tuberculin skin test (TST) with 2 TU -RT23 and chest radiograph were performed. All these tests were considered as an independent of each others in LCA. Children were classified as having confirmed and unconfirmed and/or unlikely TB. This classification was used as the gold standard to determine the sensitivity, specificity, and prevalence with a 95% confidence interval (CI) for the diagnostic tests in the classical calculation.

Results: Data from 1581 children and 2645 samples were analysed. The sensitivity of TST, Chest radiography, smear microscopy, Xpert MTB/RIF, LJ culture, and MGIT 960 was 61% (52-70), 60% (50-69), 33% (25-43), 85% (75-91), 82% (72-89) and 88% (79-93) respectively by LCA. MGIT 960 had maximum sensitivity and specificity followed by Xpert MTB/RIF and LJ culture. (Figure) The findings were similar for stratified analysis by age, gender and specimen type. The classical calculation of the sensitivity also revealed a similar scenario. The probability of being TB based on any of these tests individually was around 85%. But when a combination of any of these two tests was positive, the probability of TB was confirmed 100%

Conclusions: In pediatric, more than one bacteriological diagnostic test was required to confirm TB diagnosis and there is a need for better diagnostic tool for TB diagnosis.

PS-09-592-31 Diagnostic value of GeneXPert MTB/RIF from bronchoalveolar lavage fluid in sputum-scarce or smear-negative suspected pulmonary tuberculosis patients

PR Mohapatra,[1] S Rath,[2] S Firdaus,[2] G Purohit,[2] B Mishra,[2] - Mujeeb Rahman K K,[1] S Sahoo,[1] SK Bal,[1] MK Panigrahi,[1] S Bhuniya,[1] [1]All India Institute of Medical Sciences, Pulmonary Medicine & Critical Care, Bhubaneswar, India, [2]All India Institute of Medical Sciences, Microbiology, Bhubaneswar, India.
e-mail: prmohapatra@hotmail.com

Background: Although the cartridge-based nucleic acid amplification test (CBNAAT)/Xpert MTB/RIF has advantage over conventional sputum microscopy for the diagnosis of pulmonary tuberculosis (PTB), a substantial proportion of pulmonary cases don't produce sputum (sputum scarce) and the diagnosis remained a predictable challenge for disease confirmation. The present study aimed to evaluate the role of Broncho-Alveolar Lavage (BAL) for diagnosis of PTB in patients who were either non-expectorating or whom sputum were negative for AFB smear or CBNAAT.
Methods: Clinico-radiologically suspected patients of pulmonary tuberculosis who were not producing sputum despite sputum induction (with hypertonic saline) were included in the study from February 2018 to March 2019. BAL samples were collected using flexible bronchoscopy by instillation and subsequent suctioning of normal saline from suspected areas by placing tip of bronchoscope in wedged position within the targeted segments of lungs. The samples were subjected for detection of MTB DNA and rifampicin resistance by using Xpert MTB/RIF(Cepheid,USA) assay and smear microscopy for acid fast bacilli.
Results: Of the total of 264 BAL samples, 21 were positive for MTB DNA by Gene Xpert MTB/RIF and 7 by smear microscopy. All the 7 smear positive samples were also positive by Gene Xpert MTBRIF resulting 14 additional positive by Gene Xpert. All 21 samples were rifampicin sensitive. Amongst the above MTB positive cases, 3 cases presented with pneumonia, 3 cases presented as mass lesion, 2 cases were chronic obstructive lung disease, 1 empyema and 1 pneumoconiosis.
Conclusions: Diagnosis of PTB is difficult in non-expectorating suspected cases. This study has shown the additional diagnostic values of Xpert MTB in BAL samples in this group of cases, who otherwise would have remained undiagnosed for tuberculosis. The higher positivity by Xpert MTB in BAL fluid helps in early detection of Tuberculosis in addition to Rifampicin sensitivity and thus early initiation of appropriate anti-tubercular therapy.

PS-09-593-31 Comparison of Gene Xpert MTB/RIF assay with Multiplex PCR for diagnosis of gastrointestinal tuberculosis (GITB) from ileocecal biopsy samples

M Sharma,[1] K Sharma,[1] S Malik,[2] S Sinha,[2] [1]Postgraduate Institute of Medical Education and Research, Medical Microbiology, Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research, Gastroenterology, Chandigarh, India.
e-mail: megha_sharma_16@yahoo.co.in

Background: Prompt and accurate diagnosis of gastrointestinal tuberculosis (GITB) is a challenge. Conventional techniques lack sensitivity and are time-consuming. The role of Gene Xpert MTB/RIF (GX) in the diagnosis of intestinal tuberculosis is still unclear. Therefore, the present study was undertaken to assessed the diagnostic utility of the GX assay, and to estimated the prevalence of multidrug-resistant (MDR) TB in the north Indian population. We also compared the GX with Multiplex PCR (MPCR) using three targets (IS6110, MPB64 and Protein b) for diagnosing GITB from ileocecal biopsy samples.
Methods: GX and MPCR were performed on ileocecal biopsy samples of 40 patients of suspected GITB and 20 Non-TB patients from control group. rpoB gene sequencing was done for diagnosing Rifampicin resistance in all positive cases.
Results: Out of 40 GITB patients, the GX and MPCR were positive in 7/40 (17.5%) and 34/40(85%) cases, respectively. Out of 7 GX positive cases, 4/7 (57.14%) were Rifampicin (RIF) sensitive cases and 3/7 (42.8%) were Rifampicin resistant. On rpoB gene sequencing of all the positive results by any test, Rif resistance was detected in 3/34 (8.82%) and the rest 31/34 (91.97%) were RIF sensitive. The sensitivity, specificity, positive predictive value and negative predictive value of the GX was 17.5%, 100%, 100%, and 23.55%, respectively. Whereas sensitivity, specificity, positive predictive value, and negative predictive value of MPCR was 85%,100%,100% and 76.92%, respectively.
Conclusions: MPCR followed by rpoB gene sequencing is a promising technique for diagnosis and detection of RIF resistance in patients of GITB. Based on the rpoB gene sequencing the prevalence of Rif-resistant GITB was 8.82%. Future large prospective studies with more number of subjects are required to validate the role of GX in GITB.

PS-09-594-31 Applying a standardised approach to strengthen performances of GeneXpert networks (ASAP-GxNet): strengthen local managerial skills and conduct a standardised impact assessment of the GeneXpert network

R Alagna,[1] LT Sawadogo,[2] A Combary,[2] DM Cirillo,[1]
[1]IRCCS San Raffaele Scientific Institute, Emerging Bacterial Pathogens Unit, Milano, Italy, [2]National TB Programme, National TB Programme, Ouagadougou, Burkina Faso.
e-mail: alagna.riccardo@hsr.it

Background and challenges to implementation: GeneXpert scale-up is a historic step in the process of tuberculosis (TB) elimination. Thousands of GeneXpert platforms have been installed in hard-to-reach health facilities of low resource countries. As a result, patients are now offered better diagnostic than they used to receive. However, the global roll-out of the test has highlighted gaps that have limited impact on the TB care cascade.
Intervention or response: Here we report the description of an innovative GeneXpert network strengthening tool called Applying a Standardized Approach to Strengthen Performances of GeneXpert Networks (ASAP-GxNet) and highlights preliminary challenges, and achievements during the pilot implementation in Burkina Faso.
ASAP-GxNet is a competency-based programme that spans for 6 months composed by an innovative GeneXpert assessment tool as well as a series of short courses and work-based projects to qualitatively improve the network while strengthening the capacity of national GeneXpert Focal Point to oversight the network. To assess the progress, the GeneXpert network's compliance is measured before and at the end of the programme and rated from 0 to 4 stars.
Results and lessons learnt: The innovative assessment tool allowed to comprehensively identify GeneXpert network gaps, assign a score based on the accomplishment of 10 GeneXpert network components as well as prioritize actions needed.
Workshop and work-based projects allowed to clearly define tasks and responsibilities as well as increase awareness of the importance of national GeneXpert focal point role.

[ASAP-GxNet implementation process. Orange: entry and exit assessments; red: workshops; green: 2-mont]

Conclusions and key recommendations: To our knowledge, ASAP-GxNet is the first programme that allows to have an overall picture of the quality of GeneXpert networks and to connect performances with management behaviours. ASAP-GxNet is uniquely positioned to help National TB Programmes to coordinate efforts and needs as well as to inform whether the current GeneXpert network is achieving the expected results.

PS-09-595-31 Xpert MTB/RIF Ultra on fine needle aspirates accurately diagnoses tuberculosis lymphadenitis in an HIV-endemic setting

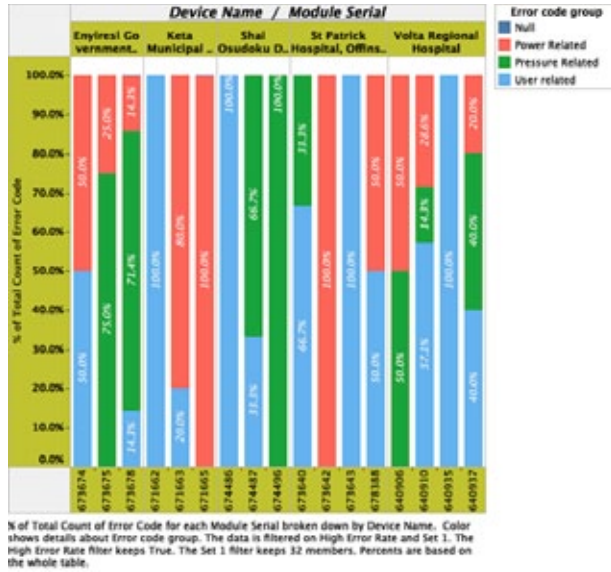
S Minnies,[1] B Reeve,[1] A Whitelaw,[2] P Schubert,[3] C Rautenbach,[2] R Warren,[1] G Theron,[1] [1]Stellenbosch University, Biomedical Sciences, Cape Town, South Africa, [2]Stellenbosch University, Medical Microbiology, Cape Town, South Africa, [3]Stellenbosch University, Anatomical Pathology, Cape Town, South Africa.
e-mail: byronreeve@sun.ac.za

Background: TB lymphadenitis is the most common manifestation of extrapulmonary TB (EPTB), accounting for 35% of cases. Xpert MTB/RIF Ultra (Ultra) is a new test designed for pulmonary TB but its accuracy for TB lymphadenitis is yet to be described.
Methods: Fine needle aspirates (FNAs) from patients with presumptive TB lymphadenitis (n=135) undergoing routine clinical investigation were collected at Tygerberg Hospital, Cape Town. Three passes from a syringe in the site-of-disease were collected and used for cytology and microbiology, including culture, Ultra, and its predecessor Xpert MTB/RIF (Xpert). The diagnostic accuracy [sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)] of Ultra in FNA specimens were reported according to STARD guidelines using liquid culture on FNAs as a reference standard in the primary analysis.
Results: Out of 135 enrolled patients, 57% (75/131) were HIV-positive and 26% (21/82) were confirmed TB-positive with culture as a reference standard. In a head-to-head comparison of Ultra vs. Xpert using culture as a reference standard (n=63), Ultra showed 50% improved sensitivity (94%, 95% confidence interval: 70-100; p=0.002) vs. Xpert (44%, 20-70) but had decreased specificity (74%, 60-86 vs. 100%, 92-100; p< 0.001). PPV was decreased (56%, 35-75 vs. 100%, 59-100; p=0.028) and NPV improved (97%, 85-100 vs. 84%,72-92; p=0.046). When Ultra was compared to Xpert using a composite reference standard (culture and cytology), similar trends were observed.
Conclusions: Ultra shows an improved sensitivity compared to Xpert in FNAs. The nature of Ultra-positive, culture-negative patients, which likely reflects limitations of the reference standard, requires clarification. A negative Ultra result can be used to confidently rule-out TB lymphadenitis.

PS-09-596-31 GeneXpert error codes: an evaluation of their definitions and implications for programme- strengthening efforts

S Kudzawu,[1,2] F Bonsu,[3] N Gous,[4] B Cunningham,[4] H Ganu,[2] F Sorvor,[3] [1]Korle Bu Teaching Hospital, Department of Chest Diseases, Accra, Ghana, [2]Korle Bu Teaching Hospital, Chest Clinic Tuberculosis Reference Laboratory, Accra, Ghana, [3]Ghana Health Service, National Tuberculosis Control Program, Accra, Ghana, [4]SystemOne, LLC, Training, Johannesburg, South Africa.
e-mail: skudzay@yahoo.com

Background: The GeneXpert (Cepheid) has revolutionized the tuberculosis(TB) diagnosis landscape. However, many national GeneXpert TB programs still battle high unsuccessful test rates partly due to frequent error reporting associated with a number of issues.
Error code descriptions linked to potential sources by Cepheid seems not consistent enough.
The study objective was to evaluate error code reporting within the National Ghanaian GeneXpert TB program to better understand error code descriptions and identify areas for strengthening program performance.
Methods: This study retrospectively analyzed result data uploaded on the GxAlert system from 130 GeneXpert devices in Ghanabetween 2016 and 2018.
The error codes were grouped into six categories guided by Cepheid descriptions; User, Power, Temperature and Pressure-related, Non-assigned and others. Analysis was by Tableau Desktop Data Visualization software.
Results: Of 106,204 total test results analyzed, 3,690 errors were reported (average rate of 3.5%). 66.8% of national errors were user-related, 25% pressure and 8.1% power.
Regionally, user-related errors ranged between 40.8%-82.5%, while pressure ranged between 12.8%-32.8% and Power issues between 0.0%-26.4%. The more tests performed on an instrument, the lower the error rate observed. Errors categorized as user-related did not consistently occur across modules of an instrument as expected, but oftentimes restricted to single or few modules.
Conclusions: While predominant errors occurring within the program were user-related, 'true' user errors should report across all modules. In our dataset, there were instances where this was restricted to one or two modules. This suggests a sub-category of module/instrument-related errors which require different corrective action to user-related errors. Cepheid error descriptions need better definition because they do not represent most of the time the source.
It's worth noticing that efficiency is enhanced through frequent use thereby reducing error rates. This is very important as GeneXpert is the first choice for TB diagnosis.



[Chart showing User-related errors restricted to some modules as against all modules in the devices.]

PS-10-C8 Quality assessment and improvement in care

PS-10-597-31 Patient experience in tuberculosis care services in low and-middle-income countries: a systematic review of quantitative studies

D Cazabon,[1] T Pande,[1] P Sen,[2] A Daftary,[3] C Arsenault,[4] H Bhatnagar,[5] M Pai,[3] [1]McGill International TB Centre, Infectious Disease, Montreal, QC, Canada, [2]McGill University, Microbiology and Immunology, Montreal, QC, Canada, [3]McGill University, Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [4]Harvard T.H. Chan School of Public Health, Global Health and Population, Boston, MA, United States of America, [5]McMaster University, Health Sciences, Hamilton, ON, Canada.
e-mail: tripti.pande@mail.mcgill.ca

Background: In 2017, tuberculosis (TB) infected 10.0 million people and killed 1.6 million. Several studies have highlighted complex pathways to diagnosis, large patient loss to follow up and gaps in the cascade of TB care. Patient-centred care is at the forefront of the End TB strategy, yet little is known about patient experience and satisfaction with TB services. Our study aims to systematically review and synthesize quantitative studies on TB patient experience and satisfaction within the healthcare system.
Methods: Five databases were searched: PubMed, Embase, CINAHL, Global health (Ovid) and Web of Science. A medical librarian approved the search strategy,

and databases were searched between January 1st, 2009 and December 31st, 2018. English studies assessing TB patient experience within the healthcare system from the patient perspective, were included. Studies evaluating accessibility, costs, interventions, children (<15 years) and in high-income countries were excluded.
Results: The initial search yielded 4230 studies and after de-duplication 3429 studies remained. Title/abstract screening lead to 392 studies, and after full text review 34 quantitative studies were included. Studies were from the African (14), Asian (14) and South American (6) regions. Preliminary analyses indicate that most studies assessed services in the public sector. The most frequent variables related to satisfaction and patient experience included health worker attitude, health education, facility amenities, and overall satisfaction. Less frequent variables included privacy, adherence counselling, and stigma.
Conclusions: These preliminary findings suggest health workers attitude and health education to be major factors affecting patient's user experience and satisfaction with TB care services. Further analysis of the results will include summary statistics on all variables used to measure patient satisfaction and user experience. Impact of variables on treatment outcomes will also be assessed. Knowledge synthesis of such factors will help influence future policy towards developing a patient-centered TB program.

PS-10-598-31 Patients' perceptions of quality of care in tuberculosis care settings in Chennai

M Periyasamy,[1] S Ovung,[1] D Arumugam,[1] B Watson,[2] SR Dhanapal,[1] AM George,[1] VB Sugumaran,[1] K Dharuman,[1] B Thomas,[1] P Pazhanivel,[1] [1]National Institute of Research in Tuberculosis, Social and Behavioural Research, Chennai, India, [2]National Institute of Research in Tuberculosis, Statistics, Chennai, India. e-mail: basilea.watson@gmail.com

Background: It is important to understand the perceptions of TB patients on what determines the quality of care for better TB treatment adherence which is crucial in TB control. While evaluation is most often done from a top to bottom level little is known about how patients perceive the quality of health services.
Methods: In order to understand patients perception, 72 qualitative interviews were conducted from four different categories such as patients continuing in public, patients continuing in private, patients shifted from public to private and patients shifted from private to public health facilities. The patient interviews were transcribed and translated, open coded and later constructs were developed based on grounded theory approach. This is a part of a tool development process to measure patient's perception on quality of TB care settings in Chennai, India.
Results: Patient's perception on quality of care is dependent on 5 key factors, which included availability of treatment services, attitude of the healthcare providers, information provided on TB, availability of basic amenities and affordability of treatment services. These determinants were used as a framework with detailed questions to prepare a tool to measure patients' perception on quality of care, which is currently being tested among 640 TB patients.
Conclusions: Understanding of key determinants which influence the perception on quality of care among TB patients is crucial in the preparation of a tool which can be used to ensure quality care among TB patients. This needs consideration in order to ensure early diagnosis, treatment initiation and TB treatment adherence.

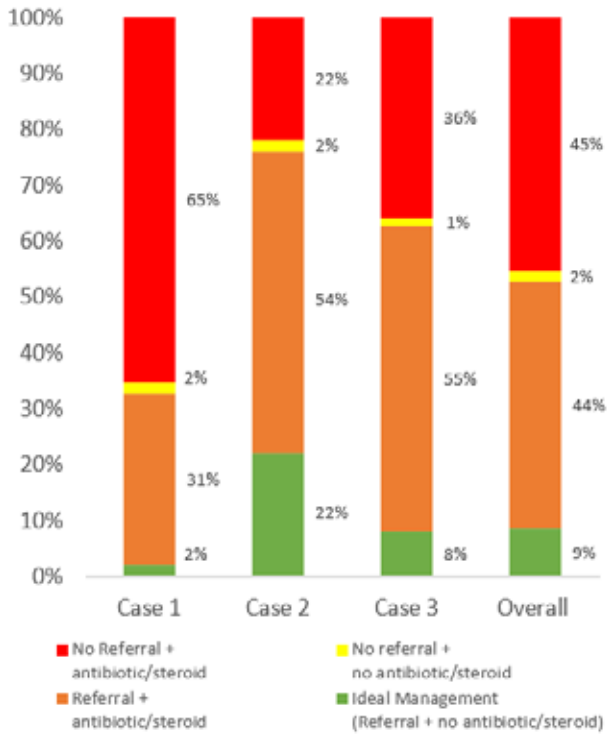
PS-10-600-31 Private sector prescribing practices for tuberculosis symptoms in KwaZulu-Natal, South Africa: a cross-sectional, standardised patient study

A Salomon,[1] J Boffa,[1,2] S Moyo,[3] J Chikovore,[4] T Mkhombo,[3] G Sulis,[1] A Kwan,[5] B Daniels,[6] M Pai,[1,7] A Daftary,[1,8] [1]McGill University, McGill International Tuberculosis Centre, Montreal, QC, Canada, [2]University of KwaZulu-Natal, Centre for Rural Health, Durban, South Africa, [3]Human Sciences Research Council, HIV/AIDS, STIs and Tuberculosis Programme, Cape Town, South Africa, [4]Human Sciences Research Council, HIV/AIDS, STIs and Tuberculosis Programme, Durban, South Africa, [5]University of California, Berkeley, Berkeley, CA, United States of America, [6]The World Bank, Research Development Group, Washington, DC, United States of America, [7]Manipal Academy of Higher Education, Manipal McGill Centre for Infectious Diseases, Manipal, India, [8]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa. e-mail: angela.salomon94@gmail.com

Background: About one-third of South African patients with tuberculosis (TB) symptoms first seek care in the private sector. Little is known about quality of care in these settings. We describe drug-prescribing practices among private general practitioners (GPs) in an urban area of KwaZulu-Natal as part of a standardized patient (SP) study.
Methods: Eight cash-paying SPs presented one of the three cases during unannounced visits to consenting GPs: classic TB symptoms with HIV (case 1), microbiologically confirmed TB without HIV (case 2), and classic TB symptoms with history of TB treatment and HIV (case 3). SPs documented interaction details using standardized questionnaires. We analyzed drug-prescribing (including drug-dispensing) practices as a primary outcome, and ideal case management (referral to clinic or TB test without prescription of antibiotic or steroid) as a secondary outcome.
Results: Over 4 months in 2018, SPs completed 220 interactions with 96 private GPs. SPs were referred or offered a TB test in 52.7% of interactions, but ideal man-

agement occurred in only 8.6% of interactions (Figure). In 208/220 (94.5%) interactions, ≥1 medicine was prescribed (mean=3.83 per interaction) including: antibiotics (87.7%, of which 12% were fluoroquinolones), anti-pyretics (79.6%), cough syrups (44.1%), and steroids (20%). Cotrimoxazole was prescribed in 17.7% interactions and had no association with whether the SP was asked their HIV status. Referral for antiretroviral treatment occurred in 13.5% of 170 interactions where SPs would have been eligible. Case 2 received significantly fewer antibiotics (OR=0.21, 95% CI 0.09-0.49) and steroids (OR=0.37, 95% CI 0.14-1.0) than cases 1 and 3.

Conclusions: Fluoroquinolones, which can trigger drug-resistance, and anti-TB medications, which are available for free in the public sector, were seldom prescribed by private-sector GPs. However, SPs received many other medications, particularly antibiotics, even when TB was microbiologically confirmed. These prescribing practices have implications for TB diagnostic delay and antimicrobial drug-resistance in South Africa.



[Management of SP cases]

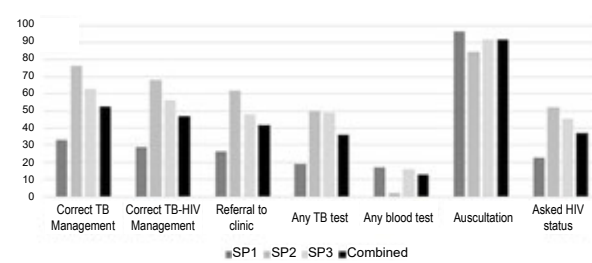
PS-10-601-31 Quality of TB care in South Africa's private sector

J Boffa,[1,2] A Salomon,[1] S Moyo,[3] J Chikovore,[4] T Mkhombo,[3] A Kwan,[5] B Daniels,[6] S Wu,[1] M Pai,[1,7] A Daftary,[1,8] [1]McGill University, McGill International TB Centre, Montreal, QC, Canada, [2]University of KwaZulu-Natal, Centre for Rural Health, Durban, South Africa, [3]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Cape Town, South Africa, [4]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Durban, South Africa, [5]University of California, Health Policy, Berkeley, CA, United States of America, [6]World Bank, Development Research Group, Washington, DC, United States of America, [7]Manipal McGill Centre for Infectious Diseases, Manipal Academy of Higher Education, Manipal, India, [8]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa.
e-mail: angela.salomon@rimuhc.ca

Background: South Africa has the third highest burden of TB and the highest burden of TB-HIV co-infection globally. Efforts to curb TB have focussed on strengthening the public sector. Yet, a recent analysis of patient care pathways reported that 29% of South Africans with active TB symptoms first seek care in the private sector. We utilised the standardised patient (SP) methodology to determine how TB and TB-HIV are managed among private general practitioners in an urban area of KwaZulu-Natal province, South Africa.

Methods: Eight healthy SPs underwent extensive training in one of three case presentations: classic TB symptoms, HIV+ on probing (self-report) (SP1); classic TB symptoms with positive GeneXpert lab report, HIV- on probing (SP2); and classic TB symptoms with history of incomplete TB treatment, HIV+ on probing (SP3). SPs completed 220 interactions with 96 consenting general practitioners. Provider practices were documented through facilitated surveys with SPs immediately following each interaction. We defined correct TB management as any TB test or referral to clinic and correct TB-HIV management as any blood test and any TB test, or referral to clinic.

Results: Overall 53% and 47% of providers correctly managed TB and TB-HIV, respectively. SP1s were less likely to be correctly managed compared to SP2s and SP3s ($p< 0.001$). Providers undertook lung auscultation in 92% of interactions and asked SPs about duration of cough in 83% of interactions. One provider prescribed anti-TB drugs to SP2. Other antibiotics were prescribed in 88% of interactions.



[Clinical Management by Standardised Patient]

Conclusions: While many providers took history (e.g. cough duration) and did physical examination (e.g. lung auscultation), subsequent clinical management of TB and TB-HIV was sub-optimal with regard to test, treat, and referral practices.

PS-10-602-31 Reorganising facility systems to improve retention in care and outcomes of treatment in urban settings: lessons from Kyetume HCIII in Mukono district, Uganda

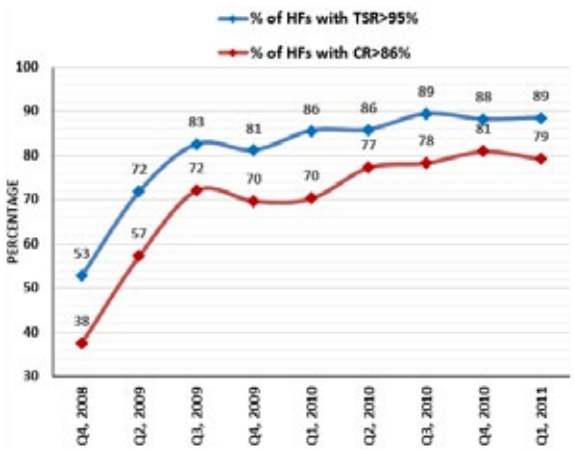
F Nakanwagi,[1,2,3] A Burua,[1] K Mutesasira,[1] J Namutebi,[4] E Tumushabe,[2] A Nkolo,[1] T Nsubuga-Nyombi,[1] [1]University Research Co., LLC (URC)/United States Agency for International Development (USAID) Defeat TB Project, Technical, Kampala, Uganda, [2]Mukono District Health Office, Health, Mukono, Uganda, [3]Kyetume HCIII, Health, Mukono, Uganda, [4]Kyetume HCIII, Health, Kampala, Uganda.
e-mail: fnakanwagi@urc-chs.com

Background and challenges to implementation: TB treatment success rate (TSR)is an indicator of performance of quality TB programs. Mukono district in central Uganda, which has 19 TB diagnostic and treatment units (DTUs), had a TSR of 62% for TB patients initiated in the January-March 2017 cohort. Kyetume Health Centre III in Mukono district had TSR of 44% (Jan-Mar'17 cohort) and gaps identified included: an ineffective patient tracking system to monitor appointments and loss to follow up; no mechanism to follow up missed appointments; patients stopped treatment once they felt better, and health workers were forgetting to request for the follow up sputum smears.
Intervention or response: The USAID Defeat TB project introduced providers to the continuous improvement approach to address gaps in the TB treatment monitoring. Teams identified a specific clinic day for TB treatment refills, provided information about the specific TB clinic day and appointment keeping. Persons with TB disease were scheduled for visits using an appointment book, and phone calls made after each clinic to patients who had missed their appointment. The team used the code "SP" in the unit TB register to identify patients due for sputum follow-up and sputum mugs were given to eligible patients prior to the scheduled visit for sputum follow-up.
Results and lessons learnt: Appointment keeping improved from 48% in October 2017 to 97% (January 19) whereas Treatment Success rate (TSR for all forms) improved from 77% (Oct-Dec'17) to 90% (Oct-Dec'18).
Conclusions and key recommendations: To improve TSR, health facility teams must set up systems that enable recurrent patient tracking; implement more efficient processes of care such as appointment days, provide sputum mugs prior to clinic visits and empower TB patients. These changes will be scaled up to additional DTUS to improve TSR.

PS-10-603-31 Standard of care (SOC) led mentorship improved TB control program in south nations nationalities and peoples region

F Abera,[1] M Godebo,[2] P Reji,[2] M Ashalew,[2] M Yassin,[3] B Tesfamichael,[4] N Birhane,[5] A Atta,[6] D Alemu,[7] [1]South Nations Nationalities and Peoples Regional Health Bureau, TBL Program, Hawassa, Ethiopia, [2]USAID/KNCV TB Foundation, Challenge TB, Hawassa, Ethiopia, [3]USAID/KNCV TB Foundation, Challenge TB, Wolaita, Ethiopia, [4]USAID/KNCV TB Foundation, Challenge TB, Arbaminch, Ethiopia, [5]USAID/KNCV TB Foundation, Challenge TB, Bonga, Ethiopia, [6]USAID/KNCV TB Foundation, Challenge TB, Jinka, Ethiopia, [7]USAID/KNCV TB Foundation, Challenge TB, Hossana, Ethiopia.
e-mail: melaku.gebremichel@kncvtbc.org

Background: A program's success highly depends on presence of efficient monitoring and evaluation system. Thus, Standard of Care (SOC) led mentorship has been implemented in SNNPR to systematically monitor and improve TB program performance.
Methods: SNNP regional health bureau with support from USAID/Challenge TB adapted the standard of care tool that was used by HEAL TB project. Twenty-seven standard quality indicators covering different technical areas were used for baseline assessment, progress monitoring, gap identification, capacity need assessment and data quality assurance.
Excel based analysis tool was developed to easily classify health facilities as poor, moderate and good performers in each technical area. District TB focal and district HMIS focal for whom orientation was given on the tool used to conduct the mentorship since December 2009 on quarterly bases.
Results: About 76% (119) of the woredas conducted at least five round SOC led mentorship since December 2009. The percentage of health facilities with cure rate ≥86% increased from 38% (47/125) in quarter 4, 2008 EFY to 79% (348/439) in quarter 1, 2011 EFY whereas percentage of health facilities with ≥95% treatment success rate among clinically diagnosed TB cases increased from 53% (64/121) in quarter 4, 2008 EFY to 89% (318/359) in quarter 1, 2011 EFY.
Community contribution for TB detection showed sluggish increment from 16.9% (413/2439) in quarter 2, 2009 EFY to 20.8% (744/3565) in Quarter 1, 2011 EFY. Regarding random blinded rechecking (RBR), two-fold increments in percentage of health facilities that participated in RBR and result received for sample was observed when compared to the baseline performance (Q4, 2008) of 41%.
Conclusions: Despite all the challenges, statistical evidences showed the SOC led mentorship program contributed for the improvement of TB control program in the region. However, district health office support and follow-up is critical to get all the potential benefits from SOC approach.



[Figure 1: Progress in percentage of health facilities that achieved the regional treatment outcome t]

PS-10-604-31 Good leadership and quality improvement principles change the TB cascade in Drakenstein subdistrict in Cape Winelands, South Africa

A van Zyl,[1] L Maschilla,[2] S Theron,[2] H Liebenberg,[3] G Jagwer,[4] [1]University Research Co., LLC - South Africa, NGO, Wellington, South Africa, [2]Department of Health, Health, Paarl, South Africa, [3]Department of Health, Health, Worcester, South Africa, [4]University Research Co., LLC - South Africa, NGO, Pretoria, South Africa. e-mail: alicevz@urc-sa.com

Background and challenges to implementation: The USAID Tuberculosis South Africa Project supports the National Department of Health (NDOH) to improve the country tuberculosis (TB) outcomes by scaling up the implementation of continuous quality improvement (QI) methodologies across the TB Care Cascade. All patients who present at health facilities must be screened for TB, but this has not been happening. To address this, the TB Quality Improvement Project (TB QIP) was initiated and piloted in 14 health facilities in this sub district from January 2017-December 2018.

Intervention or response: The USAID TB South Africa Project provided technical assistance to each facility by mentorship, support and in-service training. Leadership commitment ensured QI teams formed comprised of management, health care staff and information officers. Defining and managing the QI vision facilitated ground level staff to incorporate quality principles into their policies, plans and procedures. Ongoing monitoring by the Information Officers provided regular feedback on their facilities TB cascade improvements and gaps.

Results and lessons learnt: During 2017/18 Drakenstein sub district improved TB screening from 48% to 65,6% and presumptive TB cases Increased from 1,730 per quarter to 2,233. Positive TB testing improved from 239 to 305 per quarter and TB treatment initiation averaged at 98% per quarter.

Conclusions and key recommendations: The improved performance in case finding illustrates that good leadership and ongoing mentorship can bring change. To ensure sustainable change, a step by step QI approach must be followed starting with leaders taking ownership and involving all staff from the beginning.

PS-10-605-31 Implementation of quality improvement for the TB programme in South Africa: lessons learnt

L Mvusi,[1] N Ramawela,[1] M Tshabalala,[2] A Fernandes,[1] C Diergaardt,[3] H Ngidi,[4] M Youngleson,[3] N Kamoga,[5] [1]National Department of Health, TB Control and Management, Pretoria, South Africa, [2]Institute for Health Research and Policyealthcare Improvement, Quality Improvement, Pretoria, South Africa, [3]Institute for Healthcare Improvement, Quality Improvement, Cape Town, South Africa, [4]Institute for Healthcare Improvement, Quality Improvement, Durban, South Africa, [5]Institute for Healthcare Improvement, Quality Improvement, Pretoria, South Africa. e-mail: lindiwe.mvusi@health.gov.za

Background and challenges to implementation: South Africa is one of the 30 high burden TB countries globally with a TB incidence of 567 per 100 000 and a high mortality rate of 99 per 100 000 population among HIV positive TB patients. This is driven mainly by the high HIV prevalence with 60% co-morbidity. There is an increase in DR-TB with an MDR-TB incidence of 25 per 100 000 population. Loses across TB care cascade were identified as barriers to attaining the 90-90-90 targets by 2020. QI methodology was implemented in 10 subdistricts to address the leakages along the TB care Cascade from 2017 to 2018.

Intervention or response: Four provinces with high burden of TB disease were selected for implementation - KZN, GP, EC and WC. High burden districts, sub districts and facilities were identified. IHI implementation guides were adapted for the TB programme. Management engagement and champions identified at all levels. Quality improvement, clinical and data management training was conducted for managers and facility staff. Mentoring was conducted through monthly facility support visits and quarterly learning sessions.

Results and lessons learnt: The TB screening rate increased from 68% to 87%, sputum collection improved from 54% to 95%. TB yield increased from 6.6% to 7.8%, there was a 58% increase in the number of children started on treatment. Slight improvement in treatment initiation rate from 93% to 96%. Initial loss to follow up due to patients who could not be traced. Management ownership and team work at all levels is critical for successful implementation.

Quality data is an essential component of quality improvement and for monitoring the success of the programme. Regular reviews of the systems and processes implemented at facility and community levels helps to identify bottlenecks and gaps early for prompt action.

Conclusions and key recommendations: Implementing quality improvement methodology within the TB programme can improve programme performance.

PS-10-606-31 Footfalls and days: journeys of pulmonary drug-resistant TB patients in Mumbai

P Dev,[1] S Kamble,[1] S Shah,[1] Y Dholakia,[1] N Mistry,[1]
[1]The Foundation for Medical Research, TB Department, Mumbai, India. e-mail: fmr@fmrindia.org

Background: Distance matters. Long distances and frequent travel reduces access to care and may affect treatment outcomes. India bears a heavy burden of drug resistant tuberculosis (DR-TB) associated with lengthy diagnosis and treatment durations. The time-distance axis needs to be studied for DR-TB patients to create a patient-centric system.
Methods: A retrospective study using in-depth interviews of 44 pulmonary DR-TB patients residing and seeking care in Mumbai. Care-seeking pathways were constructed to determine the duration from first point of care to initiation of DR-TB treatment. Distances travelled by patients were calculated using a network-based analysis. Data represented as means with ranges was stratified to understand multiple components of pathways.
Results: Overall, 84%(n=37/44) of patients approached a private facility at first point of care. Patients took 10days[1-65days] and travelled 3km[0.01-51km] for first care-seeking. Fifty percent of patients accessed proximal (≤1km) facilities, all being private. Patients then travelled 27km[0-215km] to approach a diagnosing facility and spent 80days[3-414days] for DR-TB diagnosis. Subsequently they travelled an additional 26km[0-173km] to approach the facility which initiated their treatment, spending 9days[0-38days] for its initiation. Nine patients had multiple treatment episodes adding 74km and 155days to their pathway.
Patients traversed 78km[7-509km] during their entire TB care pathway. Total distance travelled (53km vs 81km;p=0.16) and time (79days vs 117days;p=0.22) taken by retreatment patients (n=20) was lesser than that of new patients. Post diagnosis, public system referrals led patients to travel 20km[0.7km-171km] for treatment initiation. Twenty-seven patients (61%) travelled an additional 9km[0.1-92km] to avail investigations in private laboratories.
Conclusions: This study highlights excessive movement of DR-TB afflicted suggesting the restructuring of a fragmented healthcare system to a one-stop window. Placement of health facilities in adequate numbers and at convenient locations should be a part of health system planning.

PS-10-607-31 Health-seeking pathway among pulmonary TB patients in Bandung, Indonesia

BW Lestari,[1,2] S McAllister,[3] N Afifah,[4]
PF Hadisoemarto,[1] R van Crevel,[2] PC Hill,[3]
B Alisjahbana,[5] [1]Universitas Padjadjaran, Faculty of Medicine, Public Health, Bandung, Indonesia, [2]Radboud University Medical Centre, Internal Medicine, Nijmegen, Netherlands, [3]University of Otago, Department of Preventive and Social Medicine, Dunedin, New Zealand, [4]Universitas Padjadjaran, Faculty of Medicine, TB Working Group, Bandung, Indonesia, [5]Universitas Padjadjaran, Faculty of Medicine, Internal Medicine, Bandung, Indonesia. e-mail: nurafifah3393@gmail.com

Background: The private sector provides an estimated 60% of tuberculosis (TB) care in Indonesia, and this might delay adequate TB diagnosis and treatment. We examined patient health care pathways, and possible factors associated with a delay in TB diagnosis in Bandung, Indonesia.
Methods: We recruited consecutive adults diagnosed and treated with pulmonary TB in 30 randomly selected Public Health Centres (PHCs), 5 hospitals, and 320 Private Practitioners (PPs), and collected data sociodemographic and clinical data using structured questionnaires.
Results: A total of 448 TB patients completed the interview, 138 (30.8%) in PHCs, 210 (46.9%) in hospitals and 100 (22.3%) in PPs; the median age was 35 years (IQR 24-49); 56.7% were male. The main reason for seeking care was prolonged cough (92.4% of patients). Patients made a median of 4 visits (IQR 3-6) to health providers before TB was diagnosed. Most patients first visited either private practitioners (36%) or informal providers such as pharmacies (41%). TB diagnosis was mostly made in hospitals (62%), while treatment was mostly provided in PHCs (40%). One third of patients (37%) sought care from more than four healthcare providers (HCP) before diagnosis. The median time was 30 days (IQR 14-61) from onset of symptoms to visiting a formal HCP; 63 days until TB diagnosis, 67 days until start of TB treatment. The pathway was longer for patients finally diagnosed and treated with TB in PHCs (p=0.015). More severe disease and having government insurance were associated with shorter pathways (p< 0.001).
Conclusions: Most Indonesian TB patients visit multiple public and private health care sites and suffer significant delay before diagnosis and initiation of treatment. This will increase transmission, incur significant costs, and hamper treatment outcomes. There is a strong need for better integration of public and private services to help TB control in Indonesia.

PS-10-608-31 The role of quality improvement (QI) in community healthcare worker-supported household TB contact tracing in South Africa

P Hippner,[1] K Velen,[1] R Lessells,[2] K Fielding,[3] C Chetty-Makkan,[1] D Dowdy,[4] R Mukora,[1] H Sohn,[4] S Charalambous,[1,5] A Grant,[3,6] [1]The Aurum Institute, Implementation Research Division, Johannesburg, South Africa, [2]University of KwaZulu-Natal, KwaZulu-Natal Research Innovation and Sequencing Platform, Durban, South Africa, [3]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom, [4]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [5]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [6]Africa Health Research Institute, Africa Centre, Mtubatuba, South Africa.
e-mail: phippner@auruminstitute.org

Background: Tuberculosis (TB) remains a major public health challenge in South Africa (SA) despite progress observed in declining incidence rates. Optimizing existing case-finding strategies is imperative to enable greater momentum for reducing the epidemic. Household contact tracing (HHCT), although a long-standing intervention, has been sub-optimally implemented due to logistical difficulties and lack of a formalized model. We evaluated the use of quality improvement (QI) methodologies for improving implementation of HHCT.
Methods: A QI approach, comprising root cause analysis and use of the Plan-Do-Study-Act cycle, was used to strengthen HHCT implemented by community healthcare workers (CHW) by identifying shortcomings in the contact tracing cascade and addressing these through change ideas. Change ideas included: 1) better documentation of HHCT and 2) changing staff perspectives of their work from linear to systemic processes. Two QI coaches supported seven clinics across three districts in SA representing urban, peri-urban and rural settings. Process indicators from the TB screening cascade were used to assess the impact of the QI intervention.
Results: The QI-supported intervention was implemented for an average of 7.7 months per clinic and in total 488 TB cases were registered during the intervention period with 1,240 contacts; proportion of index cases with any contacts listed in their TB records increased from 63.5% (range 42.5-86.8%) to 74.7% (range 41.7-100%) while the average number of contacts per index case increased from 1.87 to 2.54. Proportion of contacts screened decreased from 33.4% to 28.9% during the intervention.
Conclusions: We observed no significant impact on TB contact screening rates due to inadequate data flow from CHWs to the clinic as well as many contacts living beyond the facility catchment area. There was a trend toward improved TB contact data recording at the clinics. Utilising QI to strengthen CHW-supported HHCT is feasible but additional adaptation and support are needed to maximise its reach.

PS-11-C2 Supporting patients for better TB treatment outcomes

PS-11-609-31 Lessons learnt from the uses of mHealth platform to monitor DOT of multidrug-resistant tuberculosis (MDR-TB) patients in Bangladesh

NA Saki,[1] ST Hossain,[2] MM Morshed,[2] PK Modak,[1] MS Islam,[1] MR Islam,[2] O Cordon,[2] C Welch,[3] [1]NTP, MBDC, DGHS, Dhaka, Bangladesh, [2]MSH, Challenge TB, Dhaka, Bangladesh, [3]MSH, Program Delivery Group, Medford, MA, United States of America.
e-mail: nazis.arefin@yahoo.com

Background and challenges to implementation: Bangladesh is a high tuberculosis (TB) burden country with estimated 5,800 multi-drug resistant TB (MDR-TB) cases and 80% of patients remain undiagnosed. In 2012, community-based programmatic management of DR-TB was introduced. Directly observed treatment, short-course (DOTS) providers use mobile phones with an application to monitor activities and improve management of patients.
Intervention or response: During each DOT session, the mHealth application guides the DOT provider through treatment protocol while recording the patient's treatment data. Location information is also captured using GPS, to verify exactly where each DOTS session was held. We analyzed and demonstrated how the mHealth platform was used for monitoring and supervision of DOT services for MDR-TB patients and improving treatment adherence.
Results and lessons learnt: Between June 2013 and September 2018, the mHealth application monitored 1,893 MDR-TB patients' treatment and their DOT providers' activities. A total of 960 DOT providers treated MDR-TB patients, supervised and monitored by using the application in 42 districts and Dhaka. A total of 680 smart phones were distributed and 1,239 DOTS providers, including government staff, have been trained. Data shows with use of the mHealth platform, over 93% of MDR-TB patients had increased treatment compliance 6%. From January 2017-January 2018, the built-in adverse events monitoring system facilitated successful referral of 172 patients who experienced side effects to the nearest doctor/facility for treatment. Based on the field survey, DOT providers using the monitoring application provided extra advantages over non-app DOT providers, including easy monitoring of patients, tracking side effects of drugs, and better communication linkages. The application also improved the DOTs providers′ performance and technical capacity significantly.
Conclusions and key recommendations: The application provides real-time information regarding DOT and ensures that patients are receiving daily treatment. This DOT monitoring mHealth demonstrates the potential

of enhancing quality of care for MDR-TB patients and can serve as a vital component of patient-centered TB care in Bangladesh.

PS-11-610-31 Video-observed treatment as part of the programmatic introduction of new drugs and regimens in Kyrgyz Republic

M Ahmatov,[1] T Beishenbiev,[1] B Myrzaliev,[1] A Kadyrov,[2] C Kamarli,[3] T Murzabekova,[1] D Egemberdieva,[1] A Ibraeva,[4] N Toktorbaeva,[1] C Shukurali kyzy,[1] [1]KNCV-Challenge TB, Medical, Bishkek, Kyrgyz Republic, [2]National Center of Phthiziology of the MOH Kyrgyzstan, Medical, Bishkek, Kyrgyz Republic, [3]USAID, Medical, Bishkek, Kyrgyz Republic, [4]MoH, Medical, Bishkek, Kyrgyz Republic. e-mail: gunta.dravniece@kncvtbc.org

Background and challenges to implementation: Treatment of drug resistant tuberculosis (DR-TB) lasts for many months. Once released from hospitals patients receive daily directly observed treatment (DOT) at local facilities. The working time is not convenient for patients. Daily visits to the facility to be observed can be seen as a torture, lack of trust for the patient and increases TB stigmatization. A majority of patients are faced with the dilemma of treatment completion versus remaining employed and able to take care of their families. Patient friendly treatment approaches are needed.
Intervention or response: The USAID Challenge TB Project (CTB) implemented by KNCV in Kyrgyz Republic (KR) introduced video observed treatment (VOT). Instead of DOT patients made a daily video record of their drug intake process and shared it with the district nurse. CTB/KNCV developed standard operating procedures and provided trainings for health care workers and patients. To evaluate the acceptability, interviews for patients and health care workers (HCW) were conducted.
Results and lessons learnt: During the seven months of implementation 92 patients were included on VOT. 38 patients used VOT due to long distance to treatment facility, 14 were students or were working, 8 had to take pills several times during the day. 32 patients had other reasons for the use of VOT - extrapulmonary TB, disabilities, conditions after surgery, need to take care of their children, etc. During the piloting 12 patients completed the treatment and one patient was transferred back to normal DOT due to a change of living place. The rest successfully continue treatment. More than 95 % of patients and HCW were satisfied with the VOT.
Conclusions and key recommendations: Both patients and HCW noted the advantages of VOT - patient-friendliness, potential to increase treatment success rates. Based on successful piloting VOT will be handed over to the National TB Program with the further support provided by Red Crescent Society Kyrgyzstan.

PS-11-611-31 Experience using tablet technology for detection and monitoring of hearing loss among patients with MDR-TB in the STREAM clinical trial

I Qawiy,[1] J Komrska,[1] J Nan,[1] L Patel,[1] [1]Vital Strategies, Research Division, New York, NY, United States of America. e-mail: iqawiy@vitalstrategies.org

Background and challenges to implementation: New portable technologies have been introduced in various healthcare systems in low resource settings. While these devices are instrumental in facilitating care, they can present unintended and potentially disruptive consequences. We summarize our experience using tablet technology in Stage 2 of the STREAM clinical trial. Initial training on the tablet and audiometry application, and continuous monitoring and technical support was provided by the Sponsor to all sites.
Intervention or response: We reviewed queries related to the tablet from 12 Stage 2 sites, and challenges identified during site visits. These were categorized into: software, user error, internet connectivity, and supply chain. Queries addressed during Sponsor monitoring visits at sites were excluded from the analysis.
Results and lessons learnt: A total of 19 queries were reviewed. Software issues including tablet operating system updates and audiometry application malfunctions accounted for just under half of the inquires (9 (47%)). User error, including forgotten login information and incorrectly recording test results under the wrong patient profiles, accounted for 5 (26%) of the reported queries. Internet connectivity issues also posed challenges updating the tablet and/or audiometry application systems and uploading audiometry results contributed to 3 (15%) queries. Supply chain issues such as customs clearance delays of annually calibrated headsets used with the tablet contributed to 2 (12%) queries. Hardware issues were not identified as a key challenge affecting the use of the tablet and audiometry application.
Conclusions and key recommendations: Tablet-based technology is important for improving access to audiometry testing in low resource settings, but rollout and implementation can be challenging. The number of queries we reported is likely an underestimate, as these were not systematically collected, and additional queries and challenges were identified during site visits. This highlights the need for ongoing training and support to ensure proper audiometry testing in the context of clinical trials.

PS-11-612-31 Community health workers: a resource to support and improve drug-resistant tuberculosis patients' treatment adherence in Yichang City, China

Q Yang,[1] F Tan,[1] X Liu,[2] Z Yang,[2] C Yang,[3] X Chen,[4] S Hou,[3] [1]Yichang No. 3 Hospital, MDR-TB, Yichang, China, [2]Yichang City CDC, TB Division, Yichang, China, [3]Hubei Provincial CDC, TB Division, Wuhan, China, [4]FHI 360, Program, Beijing, China. e-mail: 279364993@qq.com

Background and challenges to implementation: Treatment for multidrug-resistant tuberculosis (MDR-TB) requires 18-24 months of ambulatory care. Usually MDR-TB patients have a very short hospitalized treatment period at the beginning. Then after discharged from MDR-TB designated hospitals, they have a long-time follow-up treatment in the community. Many MDR-TB patients are easy to be loss-to-follow-up during this period and won't return to designated hospitals for health re-checkup. Hence, community treatment supervision and follow-up from community health workers play a crucial role from MDR-TB patients' treatment adherence, but this work was still very weak.

Intervention or response: Under the support from the USAID Control and Prevention of Tuberculosis (CAP-TB) Project, Yichang No.3 hospital, the MDR-TB designated hospital in Yichang City, has launched the supportive care package for MDR-TB patients since July 2017. Then No.3 hospital extended the care package to communities in Yichang. No. 3 Hospital conducted 4 times of trainings on 20 community health works on care skills. Community health workers are responsible for patients' community treatment management. They built close contact with patients and provided counselling to address patients' educational, physical, psychosocial and financial needs. They supervised and monitored patients' community treatment and remind them returning to hospital for re-checkup regularly and timely.

Results and lessons learnt: From July 2017 to July 2018, Yichang No.3 Hospital diagnosed 55 MDR-TB patients. After enhancing community health workers' follow up, the rate of returning to hospital for regular re-checkup, increased from 62% in 2017 to 88% in 2018.

Conclusions and key recommendations: Community health workers are an important resource for MDR-TB patients. This strategy increased MDR-TB patients' community treatment adherence and monthly/bi-monthly re-checkup rate. Hospital and community work together could provide full course care to MDR-TB patients. This will contribute a better treatment outcome.

PS-11-613-31 Treatment adherence by real-time medication event reminder monitor device in Hyderabad, Telangana State: a cohort study

J Kurada,[1] S Shukla,[1] S Chittiboyina,[2] C Devi,[3] R Adepu,[2] R Ramachandran,[4] R Rao,[5] S Mase,[4] [1]WHO India, RNTCP Technical Assistance Project, Hyderabad, India, [2]Directorate of Public Health Telangana, State TB Cell, Hyderabad, India, [3]Directorate of Public Health Telangana, District TB Cell, Hyderabad, India, [4]World Health Organisation Country Office for India, Tuberculosis, New Delhi, India, [5]Ministry of Health & Family Welfare, Govt. of India, Central TB Division, New Delhi, India. e-mail: kuradaj@rntcp.org

Background and challenges to implementation: Treatment adherence is a major component in management of tuberculosis (TB). Directly Observed Treatment Short course (DOTS) chemotherapy has been the mainstay for monitoring treatment adherence of TB patients in India under the National TB Program. While DOTS, facilitated by treatment supporters, was successful, it also had shortcomings. Daily DOT was not feasible due to barriers as such as stigma, out of pocket travel expenditures, bed ridden patients, hard to reach geographies/resource limited settings.

The current study summarizes program experience with an ICT -based adherence monitoring device called **Medication Event Reminder Monitor Device** (**RT-MERM**).

Intervention or response: RT-MERM is an electronic pillbox that uses cellular connections to remind patients of daily dosing and of medication refill. The tablet strips are placed in the box and it beeps at a fixed time every day, following which it is expected that patient takes medication. It is based on the presumption that opening of the pillbox corresponds with the medication being "in-hand" and ingested. The corresponding patient data records for pill compliance gets synced into an electronic monitoring dashboard. The current study was implemented in 3 TB Units (TUs) of Hyderabad District in Telangana State.

Results and lessons learnt: Out of the 385 drug sensitive TB patients enrolled over 7 months study period (Feb-August 2018), treatment outcomes were analysed and tabulated as below-

Treatment Adherence Monitoring	Outcomes evaluated	Cured	Treatment completed	Loss to follow up	Failure	Regimen changed	Died	Treatment success
RT-MERM	269	101	155	0	1	5	7	256
% Outcomes	%	37.5	57.6	0	0.4	1.9	2.6	95.2
DOTS	3019	1290	1504	38	18	48	121	2794
% Outcomes	%	42.7	49.8	1.3	0.6	1.6	4.0	92.5

[Treatment outcomes comparison for patients on RT-MERM monitoring vs DOTS (Feb'18-August 2018)]

Conclusions and key recommendations: RT-MERM was found to be a low cost, effective, feasible, user friendly method of treatment adherence and as a good alternative to DOTS for TB patients, with encouraging treatment success rates and minimal loss to follow up.

PS-11-614-31 Stops and starts: initial drug regimens do not always reflect treatment received by patients

C Hewison,[1] H Huerga,[2] N Cumburidze,[3] N Khachatryan,[4] Y Tessew,[5] KZ Kyi Lay,[6] N Samieva,[7] S Wanjala,[8] F Varaine,[1] M Bastard,[9] [1]Médecins Sans Frontières, Medical, Paris, France, [2]Epicentre, Scientific Research, Paris, France, [3]Médecins Sans Frontières, Research, Tbilisi, Georgia, [4]Médecins Sans Frontières, Medical, Yerevan, Armenia, [5]Médecins Sans Frontières, Medical, Minsk, Belarus, [6]Médecins Sans Frontières, Research, Yangoon, Myanmar, [7]Medecins Sans Frontieres, Medical, Bishkek, France, [8]Medecins Sans Frontieres, Medical, Nairobi, Kenya, [9]Epicentre, Scientific Research, Geneva, Switzerland. e-mail: cathy.hewison@paris.msf.org

Background: Often analyses of the effectiveness of treatment regimens for multidrug resistant tuberculosis do not consider individual drug durations or interruptions. The frequency of drug stops and changes are likely underestimated and could have an important impact of the attribution of treatment effectiveness to the initial treatment regimen. Reasons for drug changes during treatment are complex and rarely analysed. The endTB project supported by Médicins Sans Frontières was implemented in 6 countries which captured all drug changes and reasons for drugs changes throughout treatment.

Methods: Patient and treatment data from the endTB observational study were entered into an electronic medical record. Patients started on bedaquiline or delamanid between April 2015 and June 2018 are included. We describe: frequency of individual drug stops (temporary or permanent) during treatment (excluding planned stops and those at treatment finish), treatment interruptions (3 or more drugs stopped the same day), most frequently stopped drugs and main reasons for drug stops.

Results: The 575 patients included experienced a total of 2880 non-planned drug changes. The majority of patients (498, 86.8%) had at least one drug stopped at any time during their treatment. The highest frequency of patients experiencing at least one drug stop amongst drugs they received at baseline or at anytime during treatment were patients receiving capreomycin, imipenem-cilastatin, pyrazinamide and linezolid (Table) Patients experienced less stops with delamanid and bedaquiline. The most common reason for drug stops was adverse events (2128/2880, 73.9%). The majority of patients had at least one treatment interruption 341/575 (59.3%). The median number of interruptions was 1 (minimum 1, maximum 6).

Conclusions: Drug stops and treatment interruptions are common in MDRTB treatment and need consideration when analysing effectiveness of treatment regimens. As adverse events are the most common reason for drug stops, the tolerability of drug regimens should be considered when choosing an effective regimen.

Drugs	Cm	Z	Imp/Cln	Lzd	Cfz	Cs	Bdq	Dlm
Number of patients receiving drug at baseline N (% of total patients)	230 (40.0)	153 (26.6)	248 (43.1)	505 (87.8)	469 (81.6)	355 (61.7)	380 (66.1)	233 (38.2)
Number of patients with at least 1 drug stop amongst patients who received drug at baseline (%)	140 (60.9)	90 (58.8)	128 (51.6)	238 (47.1)	195 (41.6)	161 (45.3)	98 (25.8)	89 (38.2)
Number of patient who received the drug at any time N (% of total patients)	296 (51.5)	199 (34.6)	289 (50.3)	542 (94.3)	522 (90.8)	413 (71.8)	419 (72.9)	296 (51.5)
Number of patients who stopped the drug at least once amongst patients who received drug at any time during treatment (%)	168 (56.8)	120 (60.3)	157 (54.3)	250 (46.1)	215 (41.2)	183 (44.3)	105 (25.1)	103 (34.8)
Number of patients who stopped the drug at least once due to due to AE amongst patients who received the drug at anytime (%)	133 (44.9)	68 (34.2)	106 (36.7)	214 (39.5)	172 (33.0)	142 (34.8)	80 (19.1)	79 (26.7)

[Frequency of drug stops amongst drugs at baseline and anytime during treatment for the most frequently stopped drugs, bedaquiline and delamanid]

PS-11-615-31 Starting MDR-TB care off right: patient counselling to reduce initial loss to follow-up in Jingzhou City, China

Y Li,[1] Y Zhang,[1] C Yang,[2] S Hou,[2] L Zhong,[3] Z Xu,[4] L Li,[5] [1]Jingzhou Tuberculosis Prevention and Treatment Institute, TB Department, Jingzhou, China, [2]Hubei Provincial CDC, TB Division, Wuhan, China, [3]FHI 360, Program, Beijing, China, [4]FHI 360, Technical Support, Kunming, China, [5]FHI 360, Program, Kunming, China. e-mail: lijyjy@126.com

Background and challenges to implementation: When the Global Fund exited China in 2014, many MDR-TB patients suddenly had to pay for treatment out-of-pocket. Nearly half of all diagnosed MDR-TB patients did not initiate treatment for economic or psychological reasons. In Jinzhou, the patient cost for MDR-TB ambulatory care has been covered by the local health insurance scheme since 2017. However, the initial loss to follow-up (ILTFU) rate remains high. In August 2018, the USAID Control and Prevention of Tuberculosis (CAP-TB) Project and Jingzhou Chest Hospital launched a patient-centered care and counselling approach to decrease ILTFU and improve treatment outcomes.

Intervention or response: CAP-TB trained nurses and peer educators as counsellors. Following standard steps, counsellors provide one-on-one counselling to all MDR-

TB patients. Counsellors also play a crucial role in supporting presumptive MDR-TB patients as they receive their diagnostic test results. When a patient is confirmed as having MDR-TB, a counsellor will initiate post-test counselling sessions with support from an MDR-TB doctor. Through effective strategic communication with the patients aided by carefully designed educational tools, staff help patients make informed decisions about their treatment. The trained counsellors provide psychosocial support and assist with decision making throughout the treatment process.

Results and lessons learnt: From August 2018 to February 2019, Jingzhou Chest Hospital diagnosed 47 MDR-TB patients, and 87% (41) initiated treatment. The ILTFU rate dropped significantly from approximately 38% (50/133) in 2017 to 13% (6/47) in 2018.

Conclusions and key recommendations: Counselling and peer support can effectively increase patients' willingness to receive treatment, help them understand the implications of poor treatment adherence, allow them to overcome barriers and build self-efficacy for the prolonged course of MDR-TB treatment. Supportive counselling as patients receive MDR-TB results should be incorporated into all MDR-TB care sites in China.

PS-11-616-31 Understanding challenges TB patients face in using digital adherence technologies

B Thomas,[1] V Kumar,[1] M Chiranjeevi,[1] G Ramachandran,[2] P Murugesan,[1] AS Khandewale,[1] D Shah,[3] R Subbaraman,[4] [1]National Institute for Research in Tuberculosis, ICMR, Department of Social and Behavioral Research, Chennai, India, [2]National Institute for Research in Tuberculosis, ICMR, Department of Biochemistry, Chennai, India, [3]Municipal Corporation of Greater Mumbai, Public Health, Mumbai, India, [4]Tufts University, Department of Public Health and Community Medicine, Chennai, India.
e-mail: ramnath.sub@gmail.com

Background: While digital adherence technologies (DATs) have the potential to track adherence and improve TB care some of these technologies could result in inaccuracies of the reported adherence record. Our study of the accuracy of 99DOTS, a cellphone-based adherence monitoring strategy, showed suboptimal negative predictive value (21%) (not calling 99DOTS but actually taking their TB medications). Furthemore the suboptimal specificity (60%) suggests that 99DOTS misses non adherent patients. We present patient-reported reasons for these barriers to engagement with 99DOTS to facilitate strengthening of this approach being rolled out in other countries.

Methods: Of the total 597 patients enrolled for this accuracy study, 159 had taken their TB medications (as confirmed by a positive urine test for isoniazid) but not called 99DOTS to report taking these medication doses (a false-negative medication adherence record). In addition, 25 patients reported calling 99DOTS to report taking a dose, even though they had not taken these medication doses (a false-positive medication adherence record).

Results: The main reasons for taking medication but not calling 99DOTS were phone inaccessibility (53.2%), as many patients had often phones shared with other family members, followed by network problems (28.2%), fatigue of calling everyday (18.6%), travelling away from home (17.3%), forgetting to call (16.7%), problems with charging of phone (12.2%), and lack of privacy (10.3%) to make the call. The main reasons for calling 99DOTS without taking TB medications included call made by a family member assuming medication was taken (36%) and to avoid tracking by HCP(28%).

Conclusions: For 99DOTS to be effective it is important the TB patients have individual access to phones and that the network challenges be addressed, as some phones have wider network coverage than others. Furthermore, regular motivation of patients by healthcare providers regarding engagement with 99DOTS may reduce technology fatigue.

PS-11-617-31 Project TB ECHO in Georgia: ensuring quality TB and specialty care for patients

N Kiria,[1] M Buziashvili,[2] N Lomtadze,[3] Z Avaliani,[4] I Khonelidze,[5] G Kuchukhidze,[5] BB Struminger,[6] [1]National Center for Tuberculosis and Lung Diseases, Clinical, Tbilisi, Georgia, [2]National Center for Tuberculosis and Lung Diseases, Scientific Research, Tbilisi, Georgia, [3]National Center for Tuberculosis and Lung Diseases, Surveillance and Strategic Planning, Tbilisi, Georgia, [4]National Center for Tuberculosis and Lung Diseases, NA, Tbilisi, Georgia, [5]National Center for Disease Control and Public Health, NA, Tbilisi, Georgia, [6]University of New Mexico Health Sciences Center, Infectious Diseases, Albuquerque, Georgia.
e-mail: mari.buziashvili@yahoo.com

Background and challenges to implementation: Despite universal access to tuberculosis (TB) diagnosis and treatment in Georgia, TB patients with co-morbidities from rural and underserved areas of Georgia were required to travel to central TB facilities to receive appropriate treatment and have full access to specialty care. This created geographical hurdles for patients causing delays in appropriate treatment initiation and likely contributing to high rates of lost-to-follow-up (19% of MDR cohort, 2016).

Intervention or response: Project TB ECHO is a pioneering tele-mentoring and distance learning program designed to improve patient care in rural and under-served areas and strengthen healthcare workforce capacity. The mission of Project TB ECHO is to spread knowledge and ensure collaborative problem solving, to develop the capacity to safely and effectively treat complex TB cases, including pediatric tuberculosis.

Results and lessons learnt: The full scale implementation of the project started in 2018, fully substituting the concept of the "Mobile Consilium." Between March 2018 and April 2019 a total 54 successful ECHO sessions were conducted with 399 TB patient cases discussed at the regional facilities with the involvement of multi-disciplinary specialists; five sessions included didactic presentations. It is anticipated that the project will significantly increase the number of patients with full access to different types of specialty care, significantly reducing time between TB diagnosis and initiation of relevant treatment, adverse event management, safety reporting and quality care. Although outcomes of the 2018 cohort are yet to be measured, this intervention is expected to result in a significantly decreased number of lost to follow-up patients and increased treatment success.
Conclusions and key recommendations: Project TB ECHO provides an opportunity of simultaneous attendance of all regional site teams at the committee meeting, and countrywide access to specialty care and consultations, in a patient oriented and cost-effective manner. Project TB ECHO serves as a tool for dissemination of best practices, innovations and sharing of knowledge.

PS-11-619-31 Evaluating the impacts of treatment supporters on tuberculosis care and management in Nigeria: a cohort analysis of treatment outcomes in Osun, a southwestern state

M Alatise,[1,2] T Aina,[1] B Levy-Braide,[3] D Gbadamosi,[1] A Popoola,[1] W Tajudeen,[4] [1]State Ministry of Health, Public Health, Osogbo, Nigeria, [2]State Specialist Hospital, Tuberculosis Referral Center/Chest Clinic, Osogbo, Nigeria, [3]KNCV-Challenge TB, Osun State TB Control Program Unit, Osogbo, Nigeria, [4]Osun State University, Public Health, Osogbo, Nigeria.
e-mail: dr.alatise_adexmed@hotmail.com

Background: Globally in 2017, 10 million people developed tuberculosis (TB) with an estimated 1.6 million TB related deaths recorded. In view of the growing TB burden, exclusively practicing hospital-based daily DOTS is becoming unfeasible and practically inadequate to achieving TB control. Therefore, decentralizing TB care to community level by engaging treatment supporters is important in achieving improved access to care -a necessity in high burden countries.
Methods: This study evaluates impacts of treatment supporters as measured by treatment outcomes recorded through retrospective cohort analysis of all forms of tuberculosis registered and managed in Osun state, Nigeria between January 1st and December 31st, 2016. Data such as patients' information and treatment outcomes were obtained from National standard recording and reporting tools. To investigate and compare the differences in treatment outcomes with the category of patients managed by health workers, Odds ratio and Relative Risk were determined for each outcome.
Results: Annual cure rate, treatment success rate, failure rate and death rate recorded by treatment supporters compared with health workers were 64.2% vs. 68.6% (P=0.012); 85.0% vs. 91.6% (P< 0.0001); 0.8% vs. 1.9% (P=0.009) and 3.5% vs. 7.8% (P< 0.0001) respectively. Also, patients managed by treatment supporters were less likely to achieve treatment success (RR=0.90) and had a higher risk of having unsuccessful outcomes (treatment failure (RR=1.22) and death (RR=2.42)) compared with those managed by health workers.
Conclusions: In this study, treatment supporters recorded poorer treatment outcomes. Also, associations between types of treatment supervisor, the recorded treatment success and death rate in virtually all the cohorts is extremely significant. To improve on the findings, the choice and process of engaging treatment supporters needs to be reviewed and re-evaluated; strict adherence to the standard operating procedure be instituted; and counseling and education of patients and treatment supporters be more frequent throughout course of treatment.

PS-11-620-31 Test, treat, track: high TB treatment adherence by using eCompliance in Dar es Salaam, Tanzania

G Mgode,[1] D Bwana,[2] J Soka,[1] S Batra,[3] A Kahwa,[4] L Mleoh,[5] B Mutayoba,[5] C Cox,[6] L Fiebig,[7] [1]APOPO Sokoine University of Agriculture, APOPO TB Detection, Morogoro, Tanzania, United Rep., [2]MKUTA, MKUTA, Dar es Salaam, Tanzania, United Rep., [3]Operation ASHA, Operation ASHA, New Delhi, India, [4]National Medical Research Institute, Muhimbili Medical Research Centre, Dar es Salaam, Tanzania, United Rep., [5]Ministry of Health, Community Development, Gender, Elderly and Children, National TB and Leprosy Program (NTLP), Dodoma, Tanzania, United Rep., [6]APOPO Sokoine University of Agriculture, Operational Headquarters, Morogoro, Tanzania, United Rep., [7]APOPO Sokoine University of Agriculture, TB Detection, Morogoro, Tanzania, United Rep.. e-mail: lena.fiebig@apopo.org

Background: The new global "Find.Treat.All#EndTB" initiative underlines an old principle in TB control: efforts to find more TB cases need to be paired with efforts to ensure all patients are correctly treated and reliably cured."Test, Treat, and Track", a joint project by APOPO, MKUTA, OpAsha and TB clinics, combines enhanced case finding using TB detection rats and confirmation tests, patient tracing and tracking by community health workers (CHW) and a pilot of 'eCompliance' technology to monitor treatment adherence. Here, we aim to present first experiences using eCompliance.
Methods: Since July 2017, all newly diagnosed TB patients in 9 participating government and private clinics in Temeke district, Dar es Salaam, have been registered on eCompliance upon their informed consent. eCompliance consists of customized software that runs on tab-

lets, incorruptible finger print verification of providers and patients for monitoring of drug intake, and a data dashboard. It is used by 9 nurses (hospital-based directly observed therapy (DOT), and 15 MKUTA CHW (home-based DOT).

Results: By end March 2019, 2,747TB patients have been enrolled. Patient mobility was high, 960 patients (35%) moved out the study area while under treatment. The devices were well accepted by patients and providers and considered easy to handle; however, training and daily support was needed to solve technical challenges in the beginning. The patients' TB treatment adherence (% doses taken) increased over the course of the project: in 2017 quarters (Q) 3 and 4 adherence was 65%. In 2018 Q1 (77%), Q2 (89%), Q3 (88%) and Q4 (86%) whereas in 2019 Q1 (94%).

Conclusions: The first results showing an improvement in treatment adherence over the study period are encouraging, especially since all TB patients irrespective of potential risk factors are considered including those with adherence issues or disabilities who may not be eligible for other electronic DOT.

PS-11-621-31 Has the case-based, web-based TB notification system (Nikshay) strengthened the referral feedback mechanism in Delhi?

R Arora,[1] A Khanna,[2] N Sharma,[3] V Khanna,[4] K Shringarpure,[5] K Selv,[6] KD Sagili,[7] [1]Maulana Azad Medical College, RNTCP Referral Unit, New Delhi, India, [2]State TB Office, RNTCP, Delhi, India, [3]MAMC, Community Medicine, Delhi, India, [4]District TB Office, RNTCP, Delhi, India, [5]Medical College of Baroda, PSM, Baroda, India, [6]PGIMER, Community Medicine, Chandigarh, India, [7]The Union South East Asia Office (USEA), TB and Communicable Diseases, Delhi, India.
e-mail: arorareema1569@gmail.com

Background and challenges to implementation: Notification, timely initiation of treatment and follow up for completion of treatment course are important for elimination of Tuberculosis in any country. The referral and feedback mechanism of national Tuberculosis control programme of India has been changed from paper-based to case-based, web-based (Nikshay) system since 2018. The current study was carried out to assess the effect of Nikshay on strengthening the referral feedback mechanism in India.

Intervention or response: This retrospective cohort study was conducted in a medical college referral unit of a tertiary care hospital, National Capital Territory of Delhi, India. Data for conventional referral system using postcard/phone/email/referral form (July 2017-December 2017) and Nikshay (July 2018-December 2018) was extracted from the referral register and the portal respectively and compared for receipt of feedback on treatment initiation, and median duration for receipt of feedback.

Results and lessons learnt: A total of 1328 and 2597 patients have been referred out through conventional and Nikshay referral system respectively. Of this, 65.9% (875/1328) and 96.5% (2507/2597) were referred within Delhi and the remaining were referred out of Delhi respectively.

Feedback on treatment was received from 92.1% (806/875) and 78.6% (356/453) for Delhi and outside Delhi referrals using conventional referral system respectively. The same using Nikshay system was 21.8% (547/2507) and 84.4% (76/90) for Delhi and outside Delhi referrals respectively.

Conclusions and key recommendations: The low feedback using Nikshay needs to be further researched for improving the feedback and better tracking of each patient. Standard operating procedures must be drafted and implemented for effective referrals and tracking. Detailed qualitative study for in-depth understanding of the program barriers and enablers is the way forward.

PS-11-622-31 Areas at risk for childhood tuberculosis in the municipality of São Paulo, Brazil (2006-2017)

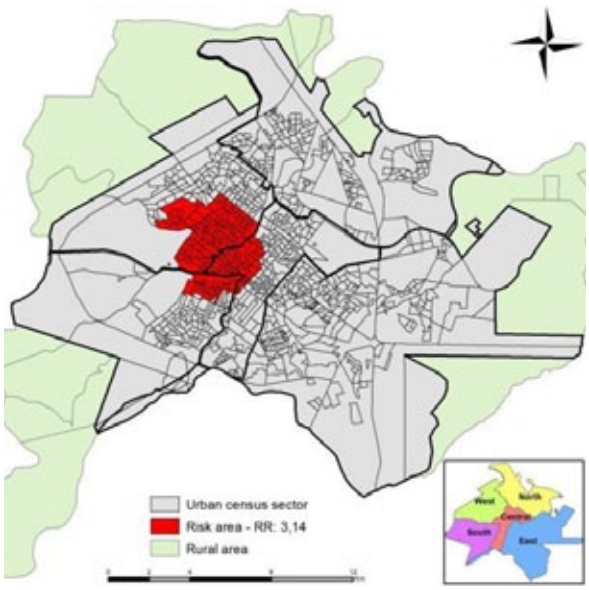
Y Mathias Alves,[1] T Zamboni Berra,[1] LL Limirio Souza,[1] AC Vieira Ramos,[1] AT Inomata Bruce,[1] L Terenciani Campoy,[1] F Lima dos Santos,[1] I Simionato de Assis,[1] J Dália Alves,[1] RA Arcêncio,[1] [1]University of São Paulo, Ribeirão Preto College Nursing, Ribeirão Preto, SP, Brazil.
e-mail: ricardo@eerp.usp.br

Background: Childhood tuberculosis is estimated at approximately one million cases worldwide. Tuberculosis is one of the 10 leading causes of child deaths around the world, accounting for 130,000 deaths per year in this population. The major challenge related to childhood tuberculosis is its diagnosis, because the diagnostic techniques used in adults have low sensitivity and specificity in children. The aim was to identify areas of risk for childhood tuberculosis.

Methods: An ecological study was carried out in Ribeirão Preto-SP. The study population is comprised of cases of tuberculosis in children younger than 15 years of age reported in the TBWeb between 2006 and 2017. The notified cases were geocoded and for the detection of the areas of spatial risk of cases of childhood tuberculosis. The relative spatial risks and their respective confidence intervals were estimated at 95%. The software SaTScan version 9.4 was used with the statistical technique of scanning. The thematic map was built using ArcGis software version 10.5.

Results: 96 cases of childhood tuberculosis were reported, 90 cases were eligible for geocoding (93.75%). A spatial risk area (p: 0.006) (Figure 1), which presented a risk relative of 3.14 (95% CI = 2.05-4.84) involving 167 census tracts in the Central, West and South districts, 33 cases of childhood tuberculosis, a population of 17,794 children under 15 years of age.

Conclusions: Through the Scan Statistics, a risk area for infant tuberculosis was identified in the Central, West and South districts, where it is possible to observe areas with high detection rate of pulmonary tuberculosis cases, high proportion of residents per household, low index of Human Development and greater concentration of favelas. The detection of areas at risk is important for health surveillance and its measures can guide public policies in the area and contribute to improving children´s access to and accessibility to health services.



[Areas of spatial risk for childhood tuberculosis, Ribeirão Preto, São Paulo, Brazil (2006-2017)]

PS-12-C1 TPT: How can we increase uptake?

PS-12-623-31 Programmatic challenges in expanding TB preventive therapy among child contacts in India

D Balasubramanian,[1] SK Mattoo,[1] R Ramachandran,[2] KS Sachdeva,[3] [1]Ministry of Health & Family Welfare, Central TB Division, New Delhi, India, [2]World Health Organisation, TB Control Programme, New Delhi, India, [3]Ministry of Health & Family Welfare, Govt. of India, Central TB Division, New Delhi, India.
e-mail: deep19882000@gmail.com

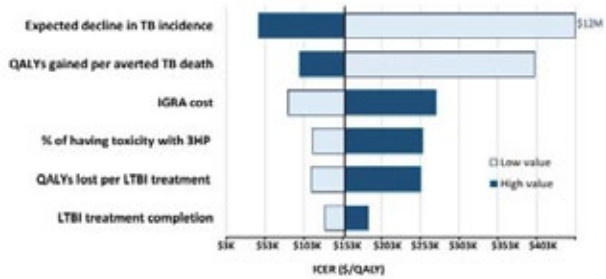
Background and challenges to implementation: India is committed to targets set for 2022 in UN High level meeting on TB. The coverage of TB preventive therapy (TPT) among child contacts of TB patients has been sub-optimal traditionally. The National TB programme (NTP) is looking to expand the coverage of TPT among existing eligible population, prior to scaling it up as per new WHO recommendations.
Intervention or response: In order to understand the challenges, a survey was conducted among 14 States randomly accounting for 50% of country´s population. All states noted sub-optimal documentation of the activity, two-thirds felt lack of monitoring of activity was impeding progress and atleast 1/3rd has issues in logistics related to drugs. In order to address this, the programme made suitable modifications in recording format in treatment card and reporting mechanisms, along with systematic efforts in strengthening monitoring through periodic feedback.
Results and lessons learnt: As a result of the systematic response, the documentation of number of children provided TPT increased 115% from 38,745 in 2017 to 83,109 in 2018 achieving a 23% coverage among the eligible beneficiaries.
Conclusions and key recommendations: The key to successful implementation is effective adoption of pillars of End TB strategy, Government stewardship and accountability, with monitoring and evaluation and ensuring uninterrupted supply of drugs.

PS-12-624-31 Determinants of cost effectiveness of targeted testing and treatment for latent tuberculosis infection in California, Florida, New York and Texas

Y Jo,[1] I Gomes,[1] S Shrestha,[1] A Hill,[2] S Marks,[2] D Dowdy,[1] [1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [2]Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination, Atlanta, GA, United States of America.
e-mail: yjo5@jhu.edu

Background: Targeted testing and treatment (TTT) for latent tuberculosis infection (LTBI) is a priority to eliminate tuberculosis in the United States (US), but the cost-effectiveness of TTT may depend on assumptions by modelers about cost, TB progression, and health outcomes.
Methods: We used a transmission model to estimate numbers of persons tested by interferon-gamma release assay (IGRA) and completing 3 months of rifapentine and isoniazid (3HP) under various TTT scenarios in California, Florida, New York and Texas. We estimated the incremental cost effectiveness ratio (ICER, measured as cost per quality-adjusted-life-year [QALY] gained) of TTT in key populations—non US-born, diabetic, HIV-positive, homeless and incarcerated—by state and evaluated relationships between key model parameters and estimated cost-effectiveness. We varied the expected decline in TB incidence over the next 30 years (without TTT) from 0% to 5% per year, QALYs gained from averted deaths by +/- 50%, IGRA costs from $50 to $264, probability of LTBI treatment toxicity from 0.4%

to 11.2%, QALYs lost from LTBI treatment from 0 to .007, and LTBI treatment completion by +/-20%. Parameter values were informed by the published literature and medical claims databases. We report costs in 2016 dollars, adjusted by cost-of-living.
Results: Key determinants of cost-effectiveness included expected decline in incidence, QALYs gained per averted TB-related death, and toxicity from 3HP (Figure). Considering TTT among non-US-born individuals in California (baseline estimate: $152,000/QALY gained), varying the projected decline in incidence (without TTT) from 0% to 5% annually changed the estimated ICER to $42,000 and $12 million per QALY gained, respectively. Halving the estimated number of QALYs gained per averted TB death increased the ICER to $398,000 per QALY gained.
Conclusions: TTT cost-effectiveness is strongly affected by assumptions about future TB trends and QALYs gained from averted deaths. Better empirical estimates to inform these values in different epidemiological contexts are needed.



[Figure 1. One-Way Sensitivity Analyses on the Cost-Effectiveness of Targeted Testing and Treatment (TTT) for Latent Tuberculosis Infection (LTBI) in California]

PS-12-625-31 Comparison of tuberculin skin tests and QuantiFERON Gold in-tube tests in a high TB-burden setting: a population-based, prospective cohort study

L Zhu,[1] P Lu,[1] W Lu,[1] [1]Center for Disease Control and Prevention of Jiangsu Province, Department of Chronic Communicable Disease, Nanjing, China.
e-mail: lilyam0921@163.com

Background: QuantiFERON (QFT) and tuberculin skin tests (TST) are commonly used for the diagnosis of the latent tuberculosis infection (LTBI). However, there is uncertainty regarding diagnostic utility of boths testsin high TB-burden settings with universal Bacillus Calmette-Guerin (BCG) vaccination.
Methods: We compared TSTs and QFT results in a prospective cohort study in rural Danyang County, Jiangsu Province. Relative operating characteristic curves were used to ascertain the best performing cutoff-value of the TST. Five year follow-up was examined to identify active tuberculosis patients and the prognostic value of both tests.
Results: Between July 1-30, 2013, 5405 participants were included in the analysis. Sensitivity (73.1%) and specificity (72.7%) was greatest when using a 10 millimeter induration. 2045 (37.8%) participants were TST positive whereas 1107 (20.5%) were QFT positive. 817 (40%) of 2045 TST positive participants also had positive QFT tests. Overall agreement between the TST and the QFT was moderate (71.9%; kappa=0.344, P< 0.0001). During five-years of follow-up, 12 individuals progressed to active tuberculosis. Among participants QFT positive at baseline, 8 (0.7%) developed tuberculosis over follow-up equating to an annual tuberculosis incidence rate of 144.9 per 100000 persons (95% CI, 44.7-245.1). QFT positivity was strongly predictive of tuberculosis progression (RR, 7.8, 95% CI, 2.4-25.8, P< 0.0001 compared to QFT negative participants). 7 (0.3%) TST-positive participants developed active tuberculosis, an annual incidence rate 68.5 per 100000 persons (95% CI, 17.8-119.2). This was not statistically predictive of disease progression (RR, 2.3, 95% CI, 0.7-7.2, P=0.242) compared to TST negative participants.
Conclusions: The QFT performed substantially better than the TST in predicting active incident tuberculosis and should be preferred in settings like China where BCG vaccination is universal.

PS-12-626-31 Introduction of 12-dose, weekly preventive treatment regimen in Bangladesh and experience from the field

MT Rahman,[1] MS Islam,[2] F Hossain,[1] S Alam,[1] AJ Faisel,[1] S Hamid,[2] O Cordon,[3] T Roy,[4] H Hussain,[5] [1]Interactive Research and Development, Challenge TB Project, Dhaka, Bangladesh, [2]DGHS, National Tuberculosis Control Program, Dhaka, Bangladesh, [3]Management Sciences for Health, Challenge TB Project, Dhaka, Bangladesh, [4]Interactive Research and Development, Country Director, Dhaka, Bangladesh, [5]Interactive Research and Development, IRD Global, Singapore, Singapore.
e-mail: toufiq.rahman@ird.global

Background and challenges to implementation: In 2018, Bangladesh committed to enrolling 969,300 individuals on preventive treatment (PT) by 2022. It is crucial to expand the PT program among all age groups at risk of developing tuberculosis (TB). We aimed to develop an effective programmatic approach for PT in Dhaka, Bangladesh.
Intervention or response: Between February 2018 and January 2019, we collected a list of bacteriologically positive index pulmonary TB (PTB) patients from 12 DOT centers in Dhaka. We enumerated the household contacts of index patients and counseled them to visit the health facility. We performed symptomatic verbal screening for TB, clinical evaluation, and chest X-ray among the contacts. We ruled out active TB in individuals who did not have suggestive lung lesions, identified all eligible contacts, and counseled them for PT. Among the contacts who consented, we began PT using a 12-

dose, weekly Isoniazid and Rifapentine regimen and followed them until treatment completion. We also initiated anti-TB treatment among contacts with TB.

Results and lessons learnt: During the study period, we visited households of 883 index patients and counseled all 3,193 household contacts to visit the health facility. A total of 2,149 (67%) contacts visited, and we performed CXR on 1,804 (84%) to rule out active TB. We identified 39 (2%) contacts with TB and began anti-TB treatment. We counselled 1,673 (93%) contacts that were eligible for PT and began PT on 1,216 (73%) contacts who consented. The mean age of participants was 27, and 56% were female. A total of 1,175 contacts (97%) completed PT with no serious adverse events.

Conclusions and key recommendations: The convenient weekly regimen, shorter treatment duration, and minimal side effects resulted in a higher adherence among those enrolled for PT. The approach seems feasible to scale up at the national level and can be used to reach the committed target for PT.

PS-12-627-31 Isoniazid preventive therapy in healthy under five-year-old household TB contacts in East Jakarta, Indonesia

FA Putri,[1] N Salama,[2] AM Zaki,[3] M Luciana,[4] N Kaswandani,[5] [1]IRD Global, Indonesia, Tangerang Selatan, Indonesia, [2]East Jakarta District Health Office, Transmittable Disease Control, Jakarta Timur, Indonesia, [3]Muhammadiyah, Muhammadiyah Against TB in Children, Jakarta Pusat, Indonesia, [4]DKI Jakarta Provincial Health Office, Transmittable Disease Control, Jakarta Pusat, Indonesia, [5]Universitas Indonesia, Pediatrics, Jakarta Pusat, Indonesia. e-mail: fauziah.putri@ird.global

Background and challenges to implementation: Regimen available in Indonesia for tuberculosis (TB) preventive treatment is 6 months of isoniazid preventive therapy (IPT). Even though IPT for child household contacts aged < 5 years old has been part of Indonesian national TB guidelines, its coverage is still very low. In 2017, of the estimated 71,500 child contacts who were eligible for treatment, only 6,080 had been initiated on treatment (8.5%).[1]

Intervention or response: This project was funded by TB REACH Wave 5. We started the project by training doctors and nurses from health facilities in East Jakarta. In total there were 200 physicians and 165 nurses trained from 89 Puskesmas (public primary health care facilities) and 7 private clinics in East Jakarta. This training was aimed to increase health care workers' knowledge on childhood TB, its diagnosis and treatment, and also on the importance of preventive treatment for children aged < 5 years old.

We also trained the health cadres who worked under Aisyiyah to do the household contact investigations.

We use TB scoring system developed by Indonesian Pediatric Society to rule out active TB. Tuberculin skin test (TST) was performed if the reagent was available.

Results and lessons learnt: This project ran from Q2 2017 to Q2 2018. From the beginning of the project, the uptake of IPT started to increase in East Jakarta with 96 children were initiated on treatment. The peak of the project activity was in Q4 2017 where 553 children were initiated on IPT (Graph 1). During the project period, there was a shortage of reagent for TST across all Puskesmas. Due to this shortage, some children received TST while some others did not.

Conclusions and key recommendations: Training health care workers paired with household contact investigation are effective methods to increase the uptake of TB preventive treatment.

[Graph 1. Isoniazid Preventive Therapy in Children <5 Years Old in East Jakarta]

PS-12-628-31 Treatment adherence and patient satisfaction with electronic remote directly observed treatment and conventional in-person directly observed treatment for tuberculosis contacts with latent infection

S-H Chen,[1] I Wang,[2] C-C Huang,[1] Y-J Liu,[3] C-H Lee,[4] [1]Taipei City Government, Department of Health, Taipei, Taiwan, [2]Taipei Medical University, School of Medicine, College of Medicine, Taipei, Taiwan, [3]Wanfang Hospital, Taipei Medical University, Division of Pulmonary Medicine, Department of Internal Medicine, Taipei, Taiwan, [4]Wanfang Hospital, Taipei Medical University, Division of Pulmomary Medicine, Department of Internal Medicine, Taipei, Taiwan. e-mail: chleetw@tmu.edu.tw

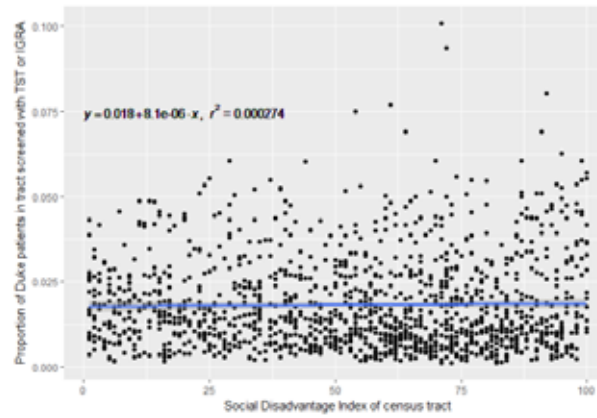
Background: Treatment of latent tuberculosis (TB) infection (LTBI) is an important strategy for active disease prevention. Although directly observed treatment (DOT) programs were recommended to reinforce treatment adherence, conventional in-person DOT (CDOT) programs are challenged by patient dissatisfaction over problems of convenience and privacy. The present study assessed treatment adherence of electronic remote DOT (EDOT) and CDOT programs from patients' perspectives.

Methods: A two-part questionnaire was presented to 240 TB contacts with LTBI who either completed or quit a 9-month isoniazid treatment regimen along with mandatory DOT monitoring during January 2014 to December 2017.
Results: Adherence rates for treatment were higher (p = 0.001) in the EDOT group (66.60%) than the CDOT group (61.42%). The treatment withdrawal rate of the EDOT group was significantly lower compared to the CDOT group [adjusted odds ratio (OR) 0.11 (95% confidence interval (CI): 0.01~0.89)]. Satisfaction with time scheduling and privacy issues was superior in the EDOT group. A strong belief in the risk of progression to active disease [OR 0.13 (0.02~0.96)] and the impact of adherence on the treatment efficacy [OR 0.26 (0.08~0.85)] were also independent predictors preventing patients from withdrawing from treatment.
Conclusions: The LTBI treatment completion rate of the EDOT program was higher than that of the CDOT program. Participants in the EDOT group voiced greater satisfaction with time scheduling and protection of privacy. Treatment completion rates were influenced by the strength of opinions towards the risk of disease progression and impacts of adherence on the treatment efficacy.

PS-12-629-31 No impact of social disadvantage on geography of latent tuberculosis screening

L Farrow,[1] J Bonnewell,[1] K Dicks,[1] G Cox,[1] J Stout,[1]
[1]Duke University Medical Center, Medicine-Infectious Diseases, Durham, NC, United States of America.
e-mail: laura.farrow@duke.edu

Background: Targeted testing and treatment of latent tuberculosis infection (LTBI) is a key element of tuberculosis (TB) elimination in the United States. Foreign-born persons from endemic areas are a key population for targeted testing, but socioeconomic factors may limit healthcare utilization, including LTBI screening.
Methods: We used the DEDUCE interface to query the electronic medical records of all patients presenting to Duke University Health System from 1/1/2010-11/1/2017. Latent tuberculosis screening was identified using CPT codes for the tuberculin skin test (TST) and/or interferon gamma release assays (IGRA). Patients' home addresses were mapped to census tracts; demographic data for these tracts were obtained from the 2016 American Community Survey 5yr estimate. Higher-risk foreign born persons were defined as those born in Africa, Asia, or Latin America. Social disadvantage of each census tract was assessed using the 2015 Social Deprivation Index, a composite index shown to correlate with poor health outcomes such as mortality, low birth-weight, and avoidable hospitalizations.
Results: 36,825 patients received 48,419 TSTs and 5,366 received 5,746 IGRAs during the study period. Patients residing in census tracts with a greater proportion of higher-risk foreign-born persons were marginally more likely to be tested for LTBI (r^2=0.1, p< 0.001 for correlation), but social deprivation had no relationship with likelihood to be tested for LTBI (p=0.91).
Conclusions: LTBI screening was significantly but weakly associated with a greater proportion of higher-risk foreign born persons in a given census tract, and social deprivation did not seem to modify this effect. Continued efforts to improve LTBI screening across socioeconomic groups are necessary.



[Correlation of Social Disadvantage Index with Duke patients screened for LTBI per census tract]

PS-12-630-31 Polymorphisms in interferon genes and risk of latent Mycobacterium tuberculosis infection in contacts of tuberculosis cases in Brazil: a retrospective cohort study

M Arriaga,[1,2] JM Cubillos-Angulo,[1,2] KF Fukutani,[1,2] TR Sterling,[3] AL Kritski,[4] BB Andrade,[1,2,3] Beatriz L. A. Müller Daniela M. P. Ramalho Pryscila F. C. Miranda Adriana S. R. Moreira Antonio Ruffino-Netto Jose R. Lapa e Silva Martha M. Oliveira [1]Fundação Oswaldo Cruz, Instituto Gonçalo Moniz, Salvador, BA, Brazil, [2]Multinational Organization Network Sponsoring Translational and Epidemiological Research (MONSTER) Initiative, Clinical Research, Salvador, BA, Brazil, [3]Vanderbilt University School of Medicine/Division of Infectious Diseases, Medicine, Nashville, TN, United States of America, [4]Universidade Federal do Rio de Janeiro/Programa Acadêmico de Tuberculose, Faculdade de Medicina e Complexo Hospitalar HUCFF-IDT, Rio de Janeiro, RJ, Brazil.
e-mail: mbag711@gmail.com

Background: Approximately 1.7 billion individuals are infected with Mycobacterium tuberculosis. The only effective strategy to prevent active tuberculosis (TB) in adults is treatment of latent TB infection (LTBI). Current studies suggest that host genetic factors play a key role in determining the susceptibility to LTBI, but biomarkers like genetic polymorphisms is not yet fully understood.

Methods: We designed a retrospective study to tested genotype as risk factors for tuberculin skin test (TST) in contacts of active TB cases. Contacts of pulmonary TB cases were screened for longitudinal evaluation up to 24 months after diagnosis the TB index case, with clinical examination and serial TST, between 1998 and 2004 at a referral center in Brazil. Data and biospecimens were collected from 482 individuals who were contacts of 145 active TB index cases. Positive TST was defined as induration ≥5mm at baseline or in the month 4, 12 or 24. Independent associations were tested using logistic regression models.
Results: Among the 482 contacts, 296 had TST positive. Multivariable regression analysis demonstrated that household contact (OR:8.1, 95%CI: 1.2-52.7), SNPs in IRF7 (OR:2.2, 95%CI: 1.0-4.6), and IFIT1 genes (OR: 5.3, 95%CI: 1.5-18.5) were independently associated with positive TST. IFI16 polymorphism was also associated with TST positive (OR:0.04, 95%CI: 0.01-0.3). Bayesian network analysis confirmed the associations between IFI16, IFIT15, IFIT1 and IRF7 polymorphisms and positive TST. Recessive genetic models showed that with two copies of A increase protective association between rs1633256 and positive TST (OR= 0.09, 95%CI: 0.02-0.41) and with two copies of G from rs304478 increase the risk significantly to positive TST (OR= 2.28, 95%CI: 1.06-4.91).
Conclusions: These results provide strong evidence for associations between polymorphisms in several IFN genes and susceptibility to LTBI in Brazil. Therefore, the presented findings are the basis for future studies to delineate the molecular events underlying these associations.

PS-12-631-31 Latent tuberculosis in pregnant women: a patient perspective

L Jansson,[1] J Shedrawy,[2] K Lönnroth,[2] J Bruchfeld,[1,3] A Kulane,[2] [1]Karolinska University Hospital Solna, Infectious Diseases, Stockholm, Sweden, [2]Karolinska Institutet, Public Health Sciences, Stockholm, Sweden, [3]Karolinska Institutet, Infectious Diseases, Stockholm, Sweden. e-mail: lena.m.jansson@sll.se

Background: Since 2016 pregnant women from tuberculosis (TB) high endemic countries are screened for active and latent TB (LTBI) in Stockholm County. Preventive treatment is usually prescribed after delivery. The aim of the study was to explore how women diagnosed with LTBI during pregnancy understood and experienced their diagnosis and treatment.
Methods: 16 semi-structured interviews with women on treatment for LTBI were analysed using content analysis with an inductive approach.
Results: None of the women were familiar with LTBI before and when diagnosed they assumed it was active TB. This assumption caused a lot of worry about who they might have infected and how it would affect the baby. They showed great ability to search for and understand information regarding the condition. There was a great fear of being stigmatized so they only told one or a few people about the LTBI. While waiting to be treated some women got a cough, causing anxiety about the TB becoming active. Once treatment was initiated the women were highly motivated to complete it. However, they found it difficult to take the medication on an empty stomach and were worried about harming their babies through breastfeeding while on treatment. No logistical barriers were identified.
Conclusions: To our knowledge this study is the first to explore how being diagnosed with LTBI during pregnancy affects the patients, including their perception of LTBI. The findings suggest that the most important motivational factor was for medical staff to provide reliable information about the condition and treatment to help patients overcome concerns and misconceptions. Nurses and doctors need to be aware of the patients' fear of being infectious and stigmatized.

PS-13-C8 World tour: innovations in finding "missing persons" with TB

PS-13-632-31 Engagement of the private sector in ending TB in Uganda: a private health provider perspective

A Ocero,[1] M Kweyamba,[2] R Makabayi Mugabe,[3] A Nkolo,[1] E Birabwa,[4] [1]USAID/URC Defeat TB Project, Health Systems Strenghtening, Kampala, Uganda, [2]National TB and Leprosy Control Programme, Public Private Mix, Kampala, Uganda, [3]USAID/URC Defeat TB Project, Operations Research (OR), Kampala, Uganda, [4]USAID Uganda, TB, Kampala, Uganda.
e-mail: aocero@urc-chs.com

Background and challenges to implementation: The 2015 Uganda National TB Prevalence survey indicates that over a third of TB patients made first contact with the health system through private-for-profit clinics, pharmacies and drug shops. Private-for-profit units continue to play a passive role in TB management. The USAID Defeat TB project is working with private practitioners to strengthen their role in TB care. Therefore, an understanding of factors that would enhance private practitioners' involvement in the national TB response was necessary.
Intervention or response: 25 private practitioners who attended a TB management training in June 2018, were engaged using a participatory approach to determine the influence of financial and non-financial incentives on private practitioner involvement in TB management. In addition, key informant interviews were conducted with respondents from the society of Uganda Private Practitioner Association.

Results and lessons learnt: Facilitators for private practitioner engagement in TB management were: technical support, capacity building from the National TB Program; provision of screening and diagnostic tools; linkage to the national sample transportation system; proximity to slummy areas that are TB hotspots; and anticipation of future financing by government. Important barriers were: lack of support supervision from the district local government; lack of access to TB medicines and laboratory supplies; and the lack of appreciation by government.
Conclusions and key recommendations: Formal recognition mechanisms and the engagement of private practitioners in TB program planning and implementation at national and sub national level will improve private sector involvement in TB services. Strengthening TB service linkages between the public and private sectors will improve the quality-of-care along the TB diagnostic and treatment cascades.

PS-13-633-31 The role of cough monitors in active case finding among people attending the general out-patient department: an experience from India

S Pandurangan,[1] S Mohanty,[1] AK Pandey,[1]
[1]International Union Against Tuberculosis and Lung Disease, TB Care and Control, New Delhi, India.
e-mail: sripriya14@gmail.com

Background and challenges to implementation: India has approximately 27% of the total global burden of TB cases, and 33% of global deaths from TB. In order to move towards the target of TB elimination by 2025, multi-pronged strategies to be adopted for TB detection and notification. This study focuses on the effectiveness of enhancing the screening of patients attending the government hospitals. In India, half of the TB patients seek treatment from public sector but all patients reaching Government hospitals for other services do not get adequately screened for TB due lack of awareness and overcrowding at the health facilities which leads to delay in diagnosis.
Intervention or response: To address the gap of delay in diagnosis, a cough monitor was deployed in the waiting area of outpatient health facility of the district hospital. The cough monitor screened all the clients visited the public health facility for symptoms of TB and identified presumptive TB patients were fast tracked to the diagnostic centre.The data from the quarterly reports were analysed for the yield of TB patients from this intervention.
Results and lessons learnt: The fast-tracking intervention was initiated in 125 high loaded district hospitals across the project districts during the period April 2018 - Dec 2018. In a quarter nearly 133 additional presumptive TB cases were identified in each district resulting into diagnosis of 25 additional TB patients in each district. The project facilitated smear examination and chest X-ray for smear negative cases. Of the identified TB patients, 15% were clinically diagnosed TB patients.

Indicators	Numbers	%
No. of hospitals with cough monitors	125	
Number of presumptive TB patients identified	50218	
Number of presumptive TB patients examined	43815	87%
Number of TB patients diagnosed (all forms of TB)	9123	21%
Number of patients initiated on DOTS	7912	87%

[Fast tracking intervention]

Conclusions and key recommendations: The results of the intervention clearly depicts there is a significant increase in the examination and detection rates in the intervention districts.
Thus, an additional effort by placing a cough monitor at the out-patient department of the hospital enables early identification of presumptive TB patients and there by helps in identifying the missing TB patients.

PS-13-634-31 Using geographic information systems as a tuberculosis programme management tool

E Hasker,[1] Y Assoumani,[2] A Mzembaba,[3] AZ Lapaix,[4] N Ortuno-Gutierrez,[5] B de Jong,[6] [1]Institute of Tropical Medicine, Public Health, Antwerpen, Belgium, [2]Damien Foundation, Comoros, Moroni, Comoros, [3]National TB Control Program, National, Moroni, Comoros, [4]National TB Control Program, Grande Comore, Moroni, Comoros, [5]Damien Foundation, Projects, Brussels, Belgium, [6]Institute of Tropical Medicine, Biomedical Sciences, Antwerpen, Belgium. e-mail: nimer.ortunogutierrez@damiaanactie.be

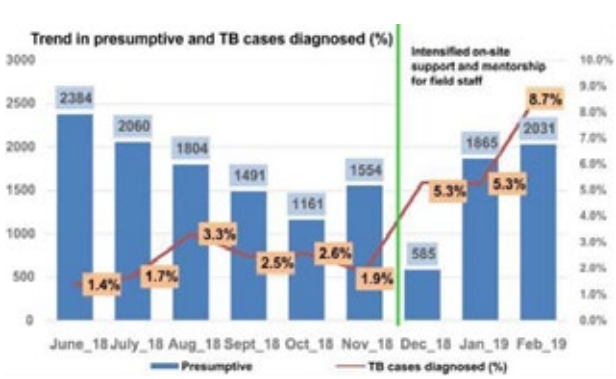
Background and challenges to implementation: The Comoros are a small island nation in the Indian ocean. Roughly half of the total population of approximately 800,000 live on the main island, Grande Comore. Despite a relatively low estimated incidence of 35/100,000, the tuberculosis (TB) treatment coverage rate achieved nationwide remains below 50%.
Intervention or response: TB data is routinely collected through standard WHO type registers, on Grande Comore these data are entered in an MS Access database. The database has a standardized list of district and village names, each of the villages have been georeferenced. A query was added to allow to draw up a list of all villages, with their geographic coordinates, estimated population sizes and numbers of TB cases for a specified period.
We used this query to plot villages and numbers of TB cases for the period 2014-2018 on a map in Quantum GIS. A nurse at national level was trained in doing this. We also conducted a further analysis in Satscan to map TB incidence. Our aim was to identify areas with high or low case notification.

Results and lessons learnt: On the map in Quantum GIS we could identify areas of high case notification on the west coast and low case notification on the east coast of the island. The Satscan analysis confirmed these results, taking into account the distribution of the population. On the west coast we identified two high incidence clusters with incidence rates ratios (IRR) of 2.3 (p= < 0.0001) and 3.6 (p =0.056) and on the east coast one low incidence cluster with IRR of 0.26 (p < 0.0001).
Conclusions and key recommendations: Geographic information systems allow for cluster-specific TB program management, with relevant software available free of charge and requiring little training. Active case finding can distinguish under detection from heterogeneous distribution of TB on Grande Comore, and allows for in-depth investigation of transmission hotspots.

PS-13-635-31 Targeted active TB case finding approaches in urban setting: a case study of Malawi

M Mmanga,[1] J Mpunga,[1] B Shigut,[1] K Mbendera,[1] I Dambe,[1] H Chafulumira,[1] [1]Ministry of Health, National TB Control Program, Lilongwe, Malawi.
e-mail: mmangamadalitso@gmail.com

Background and challenges to implementation: In Malawi, 32% of incident TB cases were not diagnosed in 2017 (Global TB report, 2018). This informed the program to go beyond passive TB case finding rather embarking on active case finding as a key strategy in finding missing people with TB in urban population.
Intervention or response: Mobile diagnostic units equipped with Genexpert and digital X-ray were deployed in five targeted urban communities. Individuals above 15 years of age were screened using symptomatic and chest X-ray (CXR), those found with cardinal sign(s) of TB and abnormal CXR had to undergone Genexpert test.
Results and lessons learnt: From June 2018 to February 2019 an analysis was performed with categorical data for the first six months (June to November, 2018) as a pilot phase; staff had received basic TB training and quarterly onsite technical support.



[Figure 1: Trend in presumptive and TB cases diagnosed]

The implementation phase (December 2018 to February, 2019), after performance review led to changes on programmatic approaches; in site selection, training on chest X-ray interpretation, sputum collection techniques and onsite mentorships. The results (Figure 1) showed that, in the first 6 months, 25,297 people were screened, of which 17% were presumptive TB, 94 TB cases diagnosed (371 per 100k screened) and yield was 2%. Post changes results for the last 3 months of implementation showed 21,322 people were screened of which 20% were TB presumptive, 293 TB cases diagnosed (1374 cases per 100k screened) and the yield was 7%. The yield significantly increased after implementing a package of additional interventions in all sites (p < 0.0001, 95% CI: 2.53 - 4.06) and had a positive causal effect on the yield.
Conclusions and key recommendations: These results have indicated the significance of continuous on job technical support and mentorship for field staff for a sustainable improvement on quality of chest X-ray imaging, interpretation and yield of TB among presumptive in high urban populations.

PS-13-636-31 Intensified case finding among high risk populations in Calabarzon, Philippines

K Dalawangbayan,[1] J Dycoco-Cam,[1] M Articona,[1] T Rodrigo,[2] E Bontuyan,[2] R Cruz,[1] P Daru,[1] [1]University Research Co., LLC (URC), TB/Infectious Diseases, Manila, Philippines, [2]USAID Philippines, Infectious Disease, Manila, Philippines. e-mail: kdalawangbayan@urc-chs.com

Background and challenges to implementation: Despite the increasing trend of case detection in Philippines, there is a still a huge gap between notified and estimated TB cases.
Intervention or response: In 2018, mobile community intensified case finding activities (ICF) were conducted in the CALABARZON (region IV A) with support from different levels of health offices, funding agencies and development partners. The ICF aimed to screen high risk populations such as elderly, 4Ps (conditional cash transfer beneficiaries), diabetics, and inmates and transport groups. The high risk populations were screened by using mobile x-ray at the community level, the presumptive were further confirmed by Gene Xpert test.
Results and lessons learnt: Out of 84,290 individuals screened with chest x-ray in 2018, 10,432 were found to have findings suggestive of TB. Of these TB presumptive, 6,750 (64.7%) were tested using Xpert MTB/RIF. A total of 959 tested positive for MTB of which 29 are also Rifampicin resistant. However, A total of 3,802 TB cases were enrolled including clinically diagnosed TB (76.7% of total cases. enrolled).The number needed to screen estimated is 88 (among bacteriologically confirmed cases). This is similar to the results obtained in the National TB Prevalence Survey in 2016. Rough estimates on cost incurred per patient detected is high.

Conclusions and key recommendations: Mobile community case finding can serve as a complementary activity to reach people who do not go to health facilities. To enhance the ICF, uniform reporting across facilities, validation of reports as well as inclusion of the high risk groups among data collected can help in analyzing the reports. Tracking mechanism must be enhanced and social and behavior change campaigns strengthened to increase testing rate among TB presumptive identified during screening.

PS-13-637-31 Private sector contribution to active tuberculosis case finding in Lagos Nigeria: the SHOPS Plus model

B Olusola-Faleye,[1] F Nwagagbo,[1] M Toriola,[1] A Iroko,[1] I Okekearu,[2] O Sokoya,[3] E Ekanem,[4] E Baruwa,[4] T Odusote,[5] C Obanubi,[5] [1]Abt Associates/ SHOPS Plus, International Development Division, Lagos, Nigeria, [2]Abt Associates/ SHOPS Plus, International Development Division, Abuja, Nigeria, [3]Lagos State Ministry of Health, Directorate of Disease Control, Lagos, Nigeria, [4]Abt Associates, International Development Division, Rockville, MD, United States of America, [5]United States Agency for International Development, Office of HIV/AIDS and Tuberculosis, Abuja, Nigeria.
e-mail: bolanle_olusolafaleye@shopsproject.com

Background and challenges to implementation: Nigeria's Lagos State has the largest and dynamic private health sector (estimated at over 5000) providing care to about 60% of the population. The private sector includes hospitals/clinics, stand-alone laboratories, community pharmacists (CPs) and the patent medicine vendors (PMVs). Despite efforts by the Lagos State TB Control Program (LSTBLCP) to improve private sector TB notification, less than 5% of the private sector notify TB cases to the LSTBLCP.
The USAID-funded SHOP PLUS model beginning in October 2017, is an innovative private sector approach using multi-cadre networks to increase TB case notification.
Intervention or response: The SHOP PLUS model is 22 multi-cadre networks of private providers consisting of trained clinical facilities (hospitals, clinics and nursing homes), laboratories, CPs and PMVs. Each network member is expected to screen clients for TB regardless of their reason for accessing services. Providers identify presumptive TB clients and test for TB by Xpert MTB/RIF assay, smear microscopy or chest X-ray. CPs and PMVs collect sputum samples or refer TB presumptives to networked clinical facilities for diagnosis. Diagnosed cases are referred to clinical facilities (may/may not charge consulting fees) for treatment with government procured drugs (no drug charge). Each network is supported by a local intermediary organization whose network officers provide mentoring and supportive supervision, coordinate referrals and support sputum transportation.
Results and lessons learnt: A total of 794,316 clients visited the 22 networks (October 2018 to February 2019) of which 114,584 (14.4%) were screened for TB. Screening yielded 10,528 (9.2%) presumptive TB clients of which 10,080 (95.7%) were tested for TB. A total of 979 TB cases were detected which contributed 24.1% (979/4,065) of the total TB case notification to the LSTBLCP within the implementation period
Conclusions and key recommendations: A multi-cadre private provider network conducting TB screening of their clients can increase TB case detection and notification.

PS-13-638-31 Reaching the missing cases among key populations through active case finding (ACF) campaign in Jharkhand, India

R Dayal,[1] S Nayak,[2] R Yeole,[3] [1]State TB Cell, Health, Medical Education & Family Welfare, Ranchi, Jharkhand, India, [2]The Union South East Asia, Tuberculosis, New Delhi, India, [3]WHO RNTCP Technical Assistance Project India, Tuberculosis, Ranchi, India. e-mail: nayaks@rntcp.org

Background and challenges to implementation: Missing TB cases and drug-resistant TB are two major challenges in TB control and demand actions to halt the transmission cycle. Jharkhand, a tribal state, misses approximately 35% TB cases every year. Facility based TB screening is the main pillar of TB diagnosis in Jharkhand. With India's aim to END TB by 2025, Active Case Finding (ACF) is recognized as a key strategy for early diagnosis and treatment to reduce the transmission of infection.
Intervention or response: ACF was conducted during September 2018 in 24 districts of Jharkhand among nearly 10% of its 37 million populations. The method included mapping of areas with key population (Slums, Migrants, Miners, Hard to reach, tribal, stone crushers, prisons, asylums etc.), sensitizing administrators, capacity building of community volunteers, strengthening lab capacity along with specific monitoring tools.
Community volunteers systematically screened selected key population, ensured examination (Microscopy/Chest X-ray/CBNAAT) of identified presumptive cases and treatment initiation of diagnosed patients.
Results and lessons learnt: The ACF campaign reached 0.56 Million households covering a population of 3 Million, identified 17158 (NNS=178) presumptive and diagnosed 1067 TB cases.
The campaign showed 18% rise in TB Notification i.e. 3686 in September 2018 against 3121 in September 2017. The annualized incidence during campaign month was 120 per 100,000 populations against 101 in corresponding month of 2017 and significantly that of key population was 427.
Overall increase in total TB cases was 4% i.e. 37919 in 2018 against 36300 in 2017. Additionally, 10 cases were found as Drug Resistant TB.

Conclusions and key recommendations: Facility based screening is inadequate to find the missing cases from the community. ACF is essential to reach the unreached and break the transmission chain. Integration of facility and community based case finding is crucial for achieving the objectives of End TB strategy 2025 of India.

PS-13-640-31 High tuberculosis case detection yield at low costs: systematic screening at two tertiary care hospitals in Hai Phong, Viet Nam

TT Do,[1] NV Nguyen,[1] HV Le,[1] HB Nguyen,[1] HT Nguyen,[2] LV Pham,[3] TTT Dong,[4] RJ Forse,[5] AJ Codlin,[6] LNQ Vo,[7,8] [1]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [2]Hai Phong International General Hospital, Board of Directors, Hai Phong, Viet Nam, [3]Hai Phong University of Medicine and Phamarcy Hospital, Board of Directors, Hai Phong, Viet Nam, [4]Friends for International TB Relief, Operations, Hanoi, Viet Nam, [5]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [6]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [7]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [8]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam. e-mail: thuthuong0308@gmail.com

Background and challenges to implementation: A major challenge to ending tuberculosis (TB) are the estimated 4 million 'missing cases.′ However, these missed individuals include people who were diagnosed and treated, but never notified to National Tuberculosis Programs (NTP).

Greater efforts are needed to improve detection, treatment and reporting of TB patients outside of the NTP network in Viet Nam.

Intervention or response: As part of the TB REACH-funded Zero TB Viet Nam project, we piloted a new public-private mix model (PPM) in one public and one private general hospital in Hai Phong. Participants were verbally screened for TB symptoms by nurses in the waiting areas of key outpatient departments at the two hospitals. Symptomatic individuals were referred for chest x-ray (CXR) screening, and if eligible, received diagnostic testing using smear, Xpert MTB/RIF, Tosoh TRCReady-80 and Bactec MGIT culture. People with TB were linked to treatment with the Provincial TB Program.

The project paid a modest monthly stipend for conducting verbal screening activities and performance-based incentives for each recorded CXR, sputum test result and new TB patient enrolled onto treatment.

Results and lessons learnt: 3,356 people with TB symptoms were screened by CXR, and 446 of these individuals had CXR abnormalities (13.3%). 523 sputum tests were performed for people with symptoms and/or CXR abnormalities, resulting in the diagnosis of 104 people with TB (19.9%). 97 of these people (93.3%) were initiated on treatment with the Provincial TB Program. The crude cost of implementing these activities was $1,588.70, which translates to a crude cost-utility of $16.38 per TB notification.

Conclusions and key recommendations: While additional evaluation is needed, this PPM model produced a high yield of TB for a low cost per notification. To end TB in Viet Nam, the NTP should expand the scale and scope of PPM provider engagement for diagnosis, notification and management of TB patients in tertiary care facilities outside of the NTP network.

PS-13-641-31 Finding the missing TB cases through synergistic facility and community-based intensified TB case finding (ICF) in a high-density urban township in Lusaka, Zambia

C Chungu,[1] P Lungu,[2] S Nyimbili,[2] R Chimzizi,[2] A Silumesii,[3] C Mwale,[4] B Tambatamba,[4] W Mbewe,[5] M Muyoyeta,[6] K Zyambo,[1] [1]Ministry of Health, Lusaka District Health Office, Lusaka, Zambia, [2]Ministry of Health, National TB Control Programme, Lusaka, Zambia, [3]Ministry of Health, Public Health, Lusaka, Zambia, [4]Ministry of Health, Provincial Health Office, Lusaka, Zambia, [5]Ministry of Health, Kanyama First Level Hospital, Lusaka, Zambia, [6]Center for Infectious Disease Research In Zambia, TB Programs, Lusaka, Zambia. e-mail: chalilwe@yahoo.com

Background and challenges to implementation: Tuberculosis (TB) remains one of the leading causes of morbidity and mortality globally. Zambia is one of the thirty high TB burden countries worldwide (TB incidence rate: 361 per 100,000, HIV prevalence ≈11.8%). About 42% of TB cases are missed annually.

Intervention or response: We aimed to determine the yield from health facility and community intensified TB case finding (ICF) using sensitive TB diagnostic tools in a high density urban township in Lusaka.

TB ICF was conducted for ten days in June 2018 at Kanyama First Level Hospital and its catchment community preceded by community TB awareness campaigns and re-orientation of health staff. TB symptom screening was followed by Computer Aided Detection (CAD) assisted chest x-ray both in the community and at the hospital. All patients with a score > 60% had sputa collected and couriered to the hospital laboratory for Xpert/MTB Rif test.

Results and lessons learnt: At the hospital, 7,267 clients were symptom screened and 1,228 (17%) were TB presumptive. Of these, 54 were bacteriologically confirmed and 98 clinical TB cases representing 12% yield from presumptives, and 2% from the total facility attendance. In the community, 1,518 TB presumptives were identified with 12 bacteriologically confirmed and 39 clinically diagnosed representing 3.4% yield from presumptives. Overall, 2,746 TB presumptives were identified with 7.4% (203/2,746) diagnosed and initiated on treatment. About 33% (66/203) were bacteriologically con-

firmed and 67% (137/203) clinically diagnosed. Males accounted for 36% (73/203) and females 64% (130/203). TB/HIV co-infection rate was 39.4% (80/203). The TB cases diagnosed was twice what the hospital routinely notifies. Approximately 75% (152/203) of cases were diagnosed through hospital ICF while 25% in the community.

Conclusions and key recommendations: Health facility TB ICF coupled with heightened community TB awareness is a good approach to finding missing TB cases in high TB burden countries to achieve the End TB targets.

PS-13-642-31 Lessons from active case finding for tuberculosis in Cambodia, 2016-2018

MT Eang,[1] RM Singh,[2] T Sivanna,[1] LC Lay,[1] S Deng,[3] F Morishita,[4] [1]National Centre for Tuberculosis and Leprosy Control, Ministry of Health, Phnom Penh, Cambodia, [2]World Health Organization, Communicable Disease, Phnom Penh, Cambodia, [3]World Health Organisation, Communicable Disease, Phnom Penh, Cambodia, [4]World Health Organisation, End TB and Leprosy Unit Division of Communicable Diseases, Manila, Philippines. e-mail: mao@online.com.kh

Background: Cambodia's national tuberculosis programme (NTP) has been at the forefront of innovations to reach populations that are poor, and hard to reach. Since 2005, the NTP has been conducting active case finding (ACF) for TB. Over the past decade ACF has evolved considerably and become an important complimentary programme strategy to passive case finding. Between 2016 and 2018, six projects (one ACF and five semi-ACF) were implemented in communities (villages and pagodas) targeting multiple high-risk populations.

Methods: We reviewed the aggregated TB screening data from six projects. Descriptive analyses were carried out to assess the effectiveness of different screening approaches by comparing key performance indicators including number screened, tested and diagnosed, as well as % of yield for all forms and bacteriologically-confirmed TB.

Results: A total of 169,801 people were screened through the six TB screening projects. Of them, 59,476 (35%) were tested by either sputum smear microscopy or Xpert test, or both. The direct yield of TB was 6,809 (4.0%, 95% Confidence Interval [CI]: 3.9% - 4.1%) for all forms of TB and 2,797 (1.65%, 95% CI: 1.59% - 1.71%) for bacteriologically-confirmed TB. In particular, higher yield in percentage was observed in the projects with the combined use of CXR and Xpert as well as in the projects that targeted the elderly and symptomatics. The treatment success rate from ACF targeting the elderly and symptomatics was 90%.

Conclusions: In Cambodia, ACF and semi-ACF for TB that were embedded in communities showed a high yield of TB both in number and percentage, without compromising treatment outcomes, which demonstrated the effectiveness of the approaches. Inclusion of multiple risk groups, particularly the elderly, in community-based TB screening should be expanded in Cambodia, and it could be replicated in other countries where the prevalence of TB among older age groups is high.

PS-13-643-31 Factors influencing active tuberculosis case finding policy development and implementation: a mixed-methods study

O Biermann,[1] K Viney,[1,2] M Caws,[3] S Atkins,[1,4] K Lönnroth,[1] [1]Karolinska Institutet, Public Health Sciences, Stockholm, Sweden, [2]Australian National University, College of Health and Medicine, Canberra, ACT, Australia, [3]Liverpool School of Tropical Medicine, Clinical Sciences, Liverpool, United Kingdom, [4]Tampere University, Faculty of Social Sciences, Tampere, Finland. e-mail: olivia.biermann@ki.se

Background: The World Health Organization emphasizes that active case-finding (ACF) for early detection of tuberculosis (TB) is an important but complex part of the intervention package needed to achieve the Sustainable Development Goal target to End TB by 2030. Available evidence is limited and mainly describes barriers and facilitators for ACF implementation. This study explored factors influencing ACF policy development and implementation.

Methods: We conducted a mixed-methods study including 39 interviews with national and global experts from non-governmental and civil society organizations, funding bodies, ministries of health and universities and a cross-sectional interviewer-administered survey with 23 National TB Program managers from the 30 high-burden countries. Data were analysed using framework analysis. We compared the results from the interviews and the survey and merged the data during the interpretation of the results.

Results: The data shows that most experts and National TB Program managers agree on the importance of ACF for ending TB. Experts described the influence of different stakeholders on ACF policy development (e.g. governments and donors) and the influence of available systems and structures (e.g. from other types of screening or serving vulnerable groups) on implementation. The National TB Program managers provided a nuanced view on ACF policy development and implementation in high-burden countries, e.g. by weighing different types of barriers and facilitators against each other. The survey results also highlight the reliance on World Health Organization guidance in policy development, closing the gap between evidence and policy, while leaving a gap between policy and practice.

Conclusions: The presented framework allows policymakers and implementers to transparently and systematically analyse influencing factors for ACF policy development and implementation in their own contexts and can thereby empower them to informed action, reaping the potential benefits of ACF.

PS-14-C10 They're out there somewhere: TB case finding strategies

PS-14-644-31 Diagnostic capacity for DR-TB after three years of the EndTB strategy

T Nguyen,[1] K England,[2] [1]Duke University, Public Policy Studies, Durham, NC, United States of America, [2]Médecins Sans Frontières, Access Campaign, Geneva, Switzerland. e-mail: kathleen.england@geneva.msf.org

Background: In 2015, the End TB strategy outlined specific polices for increasing diagnostic capacity across all high TB burden countries. The policies prioritized rapid molecular diagnosis using Xpert MTB/RIF over smear microscopy as the initial test for TB and universal drug susceptibility testing (DST) for rifampicin resistant TB. Further, the strategy emphasized capacity building to evaluate 2nd-line drug resistance.
Methods: Data reported by countries in the WHO TB data base for the years 2015-2017 with regard to the number of testing facilities having capacity for smear microscopy, GeneXpert MTB/RIF, 2nd-line drug Line Probe Assay (LPA) and culture DST were evaluated for 48 high TB, HIV-TB, and MDR-TB burden countries.
Results: While all countries (except South Africa) increased in the number of Xpert testing facilities, surprisingly 28 countries also added new microscopy centers. Only 16/48 (33%) countries increased culture testing for patient treatment monitoring. With the deployment of new drugs and regimens, evaluating patients for resistance to 2nd-line drugs is critical.
However, 13/48 (27%) countries lack in-country 2nd-line testing using LPA or conventional DST testing. DST for new and repurposed drugs (LZD, CFZ, BDQ, and DLM) remains unaccessible at country level.
Conclusions: In the era of alternative treatment regimens using newer drugs, capacity building for the diagnosis of drug resistance to all relevant anti-TB drugs used in treatment must become a high priority for all countries.

PS-14-645-31 Losses in the sputum referral chain: the case of Mpulungu district, Northern Province Zambia

B Mwansa,[1] J Bwembya,[2] P Ndubani,[3] R Goma,[1] F Kasongo,[1] W Siame,[1] F Chibinga,[4] L Mulenga,[5] R Kumar,[2] [1]Ministry of Health, Mpulungu District Health Office, Mpulungu, Zambia, [2]Zambart, Eradicate TB Project, Lusaka, Zambia, [3]Frontiers Development and Research Group, Research, Lusaka, Zambia, [4]PATH, Eradicate TB Project, Kasama, Zambia, [5]African Society for Laboratory Medicine, Eradicate TB Project, Lusaka, Zambia. e-mail: briamwansa@yahoo.com

Background: A good referral system for sputum specimens from non-diagnostic to diagnostic sites for examination can ensure timely tuberculosis (TB) diagnosis in resource-limited settings where access to laboratory services are limited. Mpulungu District Health Office in Zambia investigated the sputum referral chain to identify points at which losses of specimens occurred in the district.
Methods: This was a cross-sectional study. Primary data were collected through observations and interviews with 22 TB service providers. We tracked the number of sputum specimens referred from 10 non-diagnostic sites to the 3 diagnostic centres, and number of results received by examining the data in the presumptive TB and laboratory registers from April to September 2018. Proportions of specimens and lab results at every stage of the referral cascade were calculated using Epi Info v7.
Results: A total of 307 presumptive TB patients were recorded at non-diagnostic facilities. Of these, 209 (68%) submitted sputum samples, and 205 (98%) sputum specimen samples were referred to diagnostic facilities. Of the referred sputum samples, 149 (73%) were received at diagnostic facilities, 146 (97%) were examined, and 49 (33%) results were received by the referring facilities. The mean sample turn-around time was 4 days (SD = 3.4). Barriers in the referral cascade included: inadequate staff oriented in sputum specimen referral, negative staff attitudes towards sputum collection, and lack of packaging material, transport, and a specimen-tracking system.
Conclusions: There are losses at every stage of the sputum referral chain in Mpulungu district, and the largest losses occur between release of laboratory results, and their receipt at referring facilities. Lack of orientation in sputum specimen referral, transport, packaging materials, and tracking systems were the main barriers. The district health office should introduce a motorbike courier system, train staff in sputum collection and transportation and develop quality indicators for every stage of the referral chain.

PS-14-646-31 Geospatial patterns of Xpert MTB/RIF testing among PEPFAR-supported people with HIV receiving ART in Nigeria

M Peterson,[1] P Hall,[2] M Okoye,[3] I Audu,[3] B Odume,[3] NS Shah,[1] C Nichols,[4] A MacNeil,[1] [1]U.S. Centers for Disease Control and Prevention, Global Tuberculosis Branch, Atlanta, GA, United States of America, [2]U.S. Centers for Disease Control and Prevention, International Laboratory Branch, Atlanta, GA, United States of America, [3]U.S. Centers for Disease Control and Prevention, Laboratory Branch, Abuja, Nigeria, [4]United States Agency for International Development, Strategic Information, Evaluation, and Informatics, Washington, D.C., DC, United States of America. e-mail: odt4@cdc.gov

Background: Nigeria had over 300,000 missed tuberculosis (TB) cases in 2017. Accurate and timely evaluation for TB is of particular concern in high-risk populations including people living with HIV (PLHIV). Xpert MTB/RIF is the recommended primary diagnostic test for PLHIV undergoing evaluation for TB. Nigeria has aimed to address this by planning to deploy Xpert instruments in all 774 local government areas (LGAs). We sought to describe geographic trends in MTB/RIF testing need among PLHIV on antiretroviral therapy (ART) to identify gaps and inform interventions.

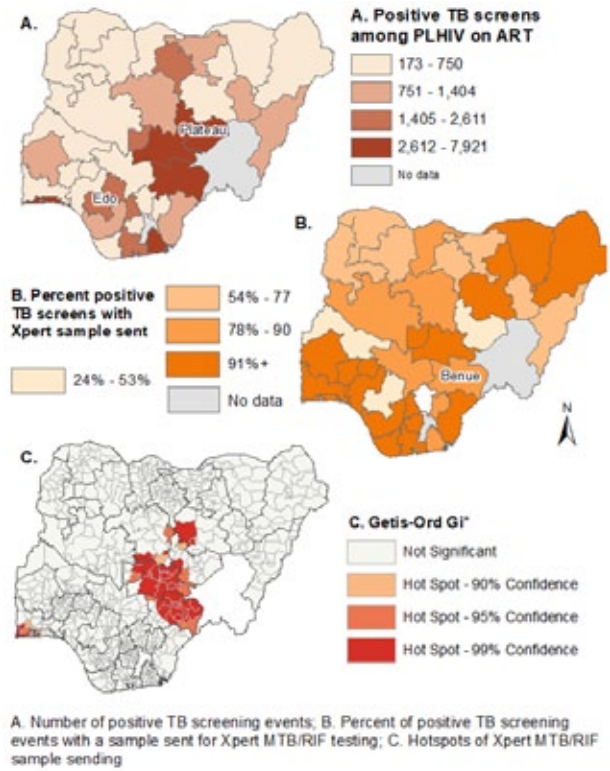
Methods: We analyzed data on PLHIV receiving ART in the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) program from October 2017-September 2018, which represented 80% of UNAIDS-estimated ART patients in Nigeria. We mapped the aggregate number of positive TB symptom screening events and proportion of these with MTB/RIF specimens sent, at state and LGA levels. Getis-Ord Gi* analysis was applied at LGA-level to identify areas with high concentrations of MTB/RIF specimen referral.

Results: Number of positive TB symptom screens among PLHIV was highest in Benue and neighboring states. Less than 25% of positive screens had samples submitted for Xpert MTB/RIF testing in Edo and Plateau, two states that also reported high numbers of positive screens.

Southern and northeastern states reported less positive TB screens, but higher proportions with MTB/RIF samples sent. MTB/RIF requests were concentrated in states with more positive TB screening events, demonstrating a clustered pattern of requests.

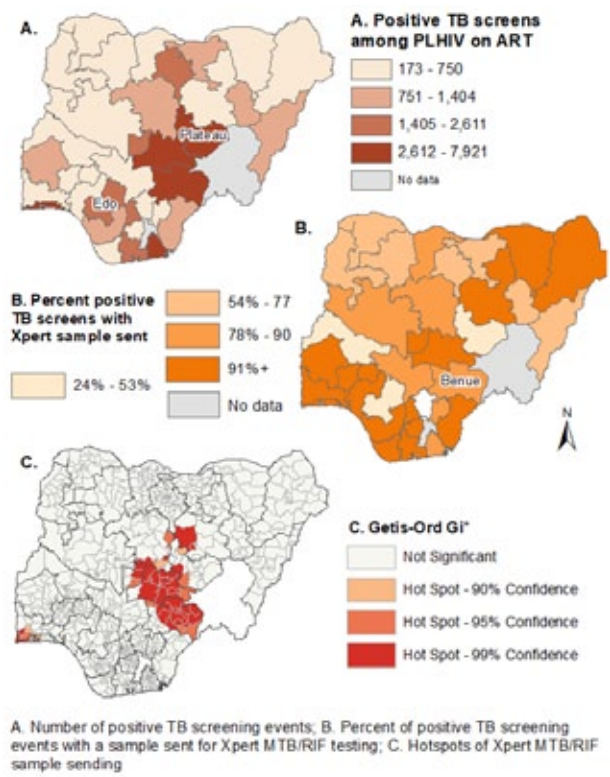
Conclusions: Xpert MTB/RIF use among PLHIV treated in PEPFAR sites is non-homogenous in Nigeria, and overall testing concentrations coincide with states that have more positive TB symptom screens.

However, the proportion of PLHIV with positive screens receiving Xpert MTB/RIF diagnostic testing within some states remains sub-optimal. Efforts to improve TB diagnosis in PLHIV should ensure sufficient capacity for MTB/RIF testing, including data-driven placement of machines where need is greatest.



A. Number of positive TB screening events; B. Percent of positive TB screening events with a sample sent for Xpert MTB/RIF testing; C. Hotspots of Xpert MTB/RIF sample sending

[Geographic distribution of Xpert MTB/RIF diagnostics among PLHIV receiving ART in Nigeria]



A. Number of positive TB screening events; B. Percent of positive TB screening events with a sample sent for Xpert MTB/RIF testing; C. Hotspots of Xpert MTB/RIF sample sending

[Geographic distribution of Xpert MTB/RIF diagnostics among PLHIV receiving ART in Nigeria]

PS-14-647-31 Boosting GeneXpert utilisation in rural India

T Garg,[1] D Sen,[2] M Varyani,[2] S Kumar,[2] M Bhardwaj,[2] [1]Innovators in Health, Research, Patna, India, [2]Innovators in Health, Operations, Patna, India. e-mail: tgarg@innovatorsinhealth.org

Background and challenges to implementation: Drug Susceptibility Testing (DST) is essential to a high-quality treatment program, and urgently needed to control the spread of DRTB. The increasing availability of GeneXpert machines has the potential to transform access to DST. However, the GeneXpert infrastructure runs the risk of chronic underutilization in rural contexts. E.g., in rural Indian state of Bihar, 37 Xpert machines tested 35,850 samples in 2018, a rate of 969 samples/Xpert/yr.
Intervention or response: A GeneXpert machine was installed to support an active-case-finding (ACF) program in three blocks (pop. 1.02 million, 630 sq. km.) of the Samastipur district (pop. 4.3M, 96% rural) in Bihar. Community health workers (CHWs) screened patients in the field to identify presumptive TB patients. All presumptive DRTB patients, presumptive EPTB patients, and pediatric patients received upfront Xpert testing, while patients with an abnormal chest X-ray and Bac+ patients received it after microscopy.
We estimated a demand of 2500 tests/yr. Staffing 2 technicians allowed up to 12 hours of operation. CHWs collected sputum samples at patients' homes, and a courier brought samples to the facility. This eliminated a crucial barrier to access, and allowed better control over volume and timing. Refrigerating sputum smoothed demand spikes. The Xpert software was linked to electronic medical records to efficiently track samples and update records.
Results and lessons learnt: From September 2017 to March 2019, 3907 samples were tested, an annualized rate of 2468 tests/yr. 907 samples (23%) were positive for TB, of which 87 (9.6%) were rifampicin-resistant (5.4/100,000 pop./yr.) In comparison, the district Xpert machine tested 2428 samples during the same period, or 1534 tests/yr. There were 128 DRTB cases (2.5/100,000 pop./yr.)
Conclusions and key recommendations: Utilization of the Xpert infrastructure can be significantly boosted by closer integration with frontline case-finding and diagnosis, reducing referral and travel burden, distributed sputum collection, and end-to-end electronic record management.

PS-14-648-31 Impact of power optimisation on the functionality of GeneXpert MTB/RIF machines in IHVN-supported TB diagnostic facilities in Nigeria

M Iwakun,[1] O Akinmulero,[1] J Ogwu,[1] S Peters,[1] A Agbaje,[2] N Ndembi,[1] A Abimiku,[3,4] [1]Institute of Human Virology, Clinical Laboratory Services Department, Abuja, Nigeria, [2]Institute of Human Virology, Program Management, Abuja, Nigeria, [3]Institute of Human Virology, International Research Center of Excellence (IRCE), Abuja, Nigeria, [4]University of Maryland School of PharmacyInstitute of Human Virology at the University of Maryland School of Medicine, Medicine, Maryland, United States of America. e-mail: miwakun@ihvnigeria.org

Background and challenges to implementation: Nigeria is ranked 7th among the 30 high burden TB countries by the World Health Organization. In 2016, Nigeria adopted the GeneXpert MTB/RIF test, a TB diagnostic molecular assay which detects the presence of the TB bacteria and resistance to the Rifampicin drug as an initial diagnostic for presumptive TB patients. However, there is a sub-optimal use of the GeneXpert MTB/RIF machines in Nigeria which arise from lack of adequate power, module issues, amongst others.
Intervention or response: A total of 50 GeneXpert MTB/RIF laboratories were identified to have major power issues as a hindrance to work efficiency and were included in this study. Sites which had other issues including module functionality issues, HR issues, and sample transport issues amongst others were excluded from this study. The sites included in the study were then provided with solar panels, inverters, and inverter batteries as an alternative source of power. A total of 24 sites were optimized in quarter 2, 2018 and 26 sites in quarter 3, 2018.
Results and lessons learnt: The total samples tested before and after the intervention were measured. There was increment in samples tested from 5,573 in quarter 1 to 7,607, 8869 in quarters 3and 4, 2018 for the 24 sites optimized. There was increment in samples tested from 4,657 in quarter 2 to 8,405 samples in quarter 3, 2018.
Conclusions and key recommendations: The results show that the output and the functionality of the GeneXpert machines can be increased with access to constant power. As Nigeria does not have access to constant power, it is recommended that alternative power sources that ensures the provision of constant power should be made available in facilities where GeneXpert machines are installed.

PS-14-649-31 The impact of sensitisation and use of TB diagnostic algorithms to optimise Xpert MTB/RIF utilisation in Maputo City, Mozambique

D Jaintilal,[1] A Teixeira Chongo,[2] S Guilengue,[3] KM Morais,[3] S Lobo,[4] HE Coelho Hamene,[5] L De Morais,[1] M Urrego,[6] K Azam,[1] [1]American Society for Microbiology, International Affairs, Maputo, Mozambique, [2]Ministry of Health, Central Laboratory Department, Maputo, Mozambique, [3]Direccao de Saude da Cidade de Maputo, Medical Assistance Department, Maputo, Mozambique, [4]Direccao de Saude da Cidade de Maputo, DSCM, Maputo, Mozambique, [5]Ministry of Health, National Tuberculosis Control Program, Maputo, Mozambique, [6]American Society for Microbiology, International Affairs, Washington DC, DC, United States of America. e-mail: kie.azam@live.com

Background and challenges to implementation: The Xpert MTB/RIF has been rolled out in Mozambique since 2011. In 2016 the National Tuberculosis Program recommended the use of Xpert MTB/RIF as first tool to diagnose TB in all health facilities where the GeneXpert instrument is available. Maputo City has 13 GeneXpert sites but bacteriological confirmed TB case detection rate is below 50% and GeneXpert utilization is below 60% of the installed capacity

Intervention or response: In December 2018 one, two days workshop for clinicians and one, five days workshop for laboratory technicians were conducted in Maputo City to sensitize, explain the diagnostic algorithms and standard operational procedures in order to improve TB and MDR-TB case detection. Comparison of retrospective of Xpert MTB/RIF results four months prior and after the workshop was conducted to assess the impact of the workshop. Data from September 2017 through April 2018 was also compafrom to evaluate trends in the same period from previous year

Results and lessons learnt: Four months after the intervention there were 13038 Xpert MTB/RIF performed with positivity rate of 9% against 10981 tests four months prior to intervention with 13% positivity rate. There was an increase in number of tests performed after the intervention. In the same period of previous years (2017/2018) there was a decrease in tests performed from September/December 2017 (7951 tests) to January/April 2018 (7696) which demonstrates the impact of the workshop in increasing the number of patients tested for TB using GeneXpert

Conclusions and key recommendations: Training and sensitization can increase the utilization of GeneXpert for TB diagnsotics but care must be taken to prevent losses in positivity rates.

PS-14-650-31 Increased diagnostic yield of rifampicin-resistant TB patients by rapid expansion of GeneXpert and using it as initial test in Bangladesh

N Arefin Saki,[1] PK Modak,[1] MS Bashar,[1] M-U Alam,[2] MS Islam,[1] [1]National Tuberculosis Control Program, DGHS, Dhaka, Bangladesh, [2]Interactive Research and Development, Health, Dhaka, Bangladesh. e-mail: nazis.arefin@yahoo.com

Background and challenges to implementation: Bangladesh is one of the 30 high-burden multidrug-resistant TB (MDR-TB) countries with annual incidence of 5800 among notified pulmonary TB patients. The estimated proportion of rifampicin/multidrug-resistant TB (RR/MDR-TB) is 1.6% and 29% among new and previously treated TB patients respectively. Until 2017, GeneXpert testing was only limited to presumptive MDR-TB and smear-negative TB cases due to limited number of machines. Between 2014 and 2017, RR/MDR-TB case diagnosis remained almost static (range: 944-994) with ~80% missing cases.

Intervention or response: With funding support from The Global Fund, Bangladesh expanded GeneXpert implementation from 51 machines in 2017 to 193 machines in 2018. National program also revised the diagnostic algorithm offering all presumptive TB patients X-ray followed by GeneXpert and where X-ray was not available GeneXpert was offered as initial test. However, this algorithm was applicable only for the areas equipped with GeneXpert while the rest were using microscopy as initial test. We examined the contribution of GeneXpert expansion and new algorithm towards RR/MDR-TB case detection and categorized the patients by history of exposure to TB treatment.

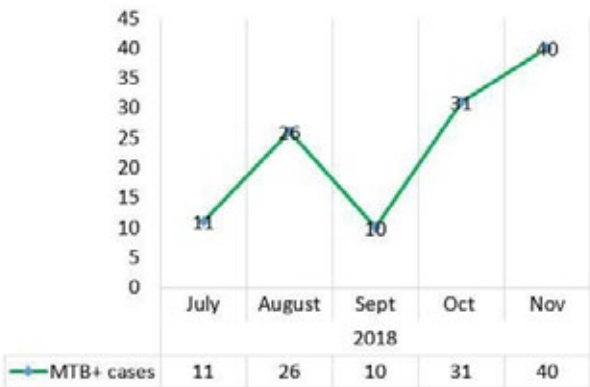
Results and lessons learnt: 1356 RR/MDR-TB patients were detected in 2018, compared to 968 patients in 2017, a 40% increase. With GeneXpert expansion and implementation of new algorithm, the proportion of new TB cases among all RR/MDR-TB cases detected increased to 40.6% from 17.3% in one year, while the proportion of 2-month non-converters and treatment failures decreased from 41% to 22.1% in the same year. These findings highlight the burden of undetected RR/MDR-TB cases among newly diagnosed TB patients who are not initially tested using GeneXpert and being treated with wrong regimen with opportunity to further transmission.

Conclusions and key recommendations: Combating RR/MDR-TB through early diagnosis and finding the missing cases requires testing all presumptive TB using GeneXpert initially. We recommend further expansion and increased investment in GeneXpert implementation.

PS-14-651-31 Finding additional TB patients through improved access to GeneXpert testing in Wakiso district

R Mangeni,[1] K Mutesasira,[1] A Nkolo,[1] M Joloba,[2] E Birabwa,[3] A Kakeeto,[4] [1]University Research Co., LLC (URC), USAID Defeat TB Project, Kampala, Uganda, [2]National Tuberculosis & Leprosy Control Program, National Tuberculosis Reference Laboratory, Kampala, Uganda, [3]USAID, USAID/Defeat TB Project, Kampala, Uganda, [4]Wakiso District Local Government, Health Department, Wakiso, Uganda. e-mail: mangenironald63@gmail.com

Background and challenges to implementation: The TB testing algorithm in Uganda requires all presumptive TB patients to access a genexpert test to increase TB case detection. Genexpert has a sensitivity of 90%.Few Presumptive TB patients accessed genexpert test due to limited number of machines (8) serving 242 facilities within Wakiso district. Samples sometimes were not examined and yet Wakiso District being Urban with mobile population, contributes to high number of TB patients in urban settings. The USAID-Defeat TB project embarked on a plan to increase the number of TB patients detected through improving number of sample referred and tested using genexpert in Wakiso district.
Intervention or response: Wakiso is an Urban district surrounding Kampala city. The USAID Defeat TB mapped the diagnostic and treatment units, identified a need of 3 back up sample riders, and developed tools for improved sample Tracking. The interventions included; Increased frequency of visits (3 time a week) by backup riders, designated sample storage areas at room temperature, and indicating a code "GXP" lab register for referred samples.
Results and lessons learnt: A threefold increase in TB patients (118 TB patients) from referred samples over a period of 5 months from July to November 2018.A code "GXP" in the Laboratory TB register helped to track referred samples. A designated area for sample storage ensured samples were safely prepared for transportation. Increased riders' visits to facilities stimulated health workers to collect and refer sputum samples.



[Number of additional TB patients detected through improved access to genexpert testing]

Conclusions and key recommendations: Improved access to genexpert test helps to find missing persons with TB. Sputum sample referral tracking system should be enhanced with a code "GXP" in the Laboratory TB register. A designated area for sample storage at room temperature in facilities without refrigerators is important for timely preparation of samples for transportation.

PS-14-652-31 Improving diagnosis of TB-HIV co-infected patients with Xpert MTB/RIF Ultra Assay in Yangon Region, Myanmar

T Naing,[1] WW Nyunt,[2] Z Myint,[2] H Aung,[1] V Harris,[3] K Kao,[3] ST Aung,[4] MM Moe,[2] [1]Clinton Health Access Initiative, (CHAI), Yangon, Myanmar, [2]National Tuberculosis Programme (NTP), Ministry of Health and Sports, Yangon, Myanmar, [3]Foundation for Innovative New Diagnostics, (FIND), Geneva, Switzerland, [4]National Tuberculosis Programme (NTP), Ministry of Health and Sports, Nay Pyi Taw, Myanmar. e-mail: tnaing@clintonhealthaccess.org

Background: In March 2017, Xpert MTB/RIF Ultra cartridge of higher sensitivity was endorsed by WHO as a replacement for the current Xpert MTB/RIF cartridge in the diagnosis of TB and rifampicin resistance. The aim of this pilot study is to investigate whether this higher sensitivity in HIV positive TB patients and children can apply in Myanmar local context and to determine the programmatic guidance and appropriate algorithm for transition from Xpert MTB/RIF to Ultra cartridge
Methods: All presumptive or confirmed TB patients who are HIV positive from (33) townships in Yangon region were enrolled in the study between July and December 2018. Routine samples from children with presumptive TB were also enrolled for secondary data analysis. Patients were tested with Xpert MTB/RIF Ultra as a replacement test for Xpert MTB/RIF. Trace and TI results were repeated testing with both assays and culture. Chi-square test was used for statistical analysis in compared with 6-month prior Xpert MTB/RIF data. This study also reported on the experiences and challenges of piloting rollout of Ultra.
Results: There were total 1804 tests enrolled of which 66 failed (4%) in the study. Ultra increased the detection rate by 10.4% (95% CI, 5.4-15.2) in presumptive HIV patients and 2.4% (95% CI, 0.5-5.3) in smear negative children than Xpert MTB/RIF. Greatest yield in bacteriologically diagnosed cases was in smear negative cases in both groups. Repeated testing of trace results generated no additional data or information and no significant impact on clinical management. TI results were too limited to draw the conclusion.
Conclusions: Overall, the transition of Ultra in Myanmar can be prioritized and adopted on PLWHIV, children and smear negative cases to maximize the diagnostic benefits that have been observed in the pilot. Trace result should be managed as per WHO recommendation in vulnerable population groups without repeating the testing.

PS-14-653-31 Exploring challenges of GeneXpert utilisation in Bangladesh

AH Khan,[1] MAH Salim,[2] PK Modak,[3] N Arefin,[4] RS Banu,[5] MS Islam,[6] [1]National Tuberculosis Control Program, Epidemiology, Dhaka, Bangladesh, [2]National Tuberculosis Control Program, NTP, Dhaka, Bangladesh, [3]National Tuberculosis Control Program, Laboratory, Dhaka, Bangladesh, [4]National Tuberculosis and Leprosy Programme, PMDT, Dhaka, Bangladesh, [5]National Tuberculosis and Leprosy Control Programme, NTP, Dhaka, Bangladesh, [6]National Tuberculosis and Leprosy Control Programme, MBDC, Dhaka, Bangladesh.
e-mail: mandentpbd@gmail.com

Background: Bangladesh started to use Xpert MTB/RIF test since 2012. Starting from 4 machines in 2012, total194 machines (847 modules) were placed in 164 sites by 2018. NTP introduced a new diagnostic algorithm in sites with Xpert. Low utilization of Xpert was observed in most sites.
Methods: A questionnaire was introduced for periodic assessment. 1st assessment was done in October 2018 and second one in March 2019. A questionnaire was sent to all sites to collect data on the number of tests performed and functional status of the machines including actions taken to make the machine functional. The objective was to identify the barriers for optimum utilization of the Xpert MTB/RIF test.
Results: Compiled site assessment data shows that during first assessment 700 modules were in the field, 650 (93%) of them found functional and 50 (7%) nonfunctional. In March 2019, including new machines placed in between total 847 modules were in the field, 793 (94%) were functional and 54 were (6%) nonfunctional. Test per functional module was 32 and 30 respectively in October and March. Fully nonfunctional machines were 5 in October, all of which were made functional in between but 4 new machines were found nonfunctional during March. In October assessment 21 sites performed less than 10 tests in a month, whereas only 5 sites in March. In 49% sites Medical Technologist were supported by the Government and remaining by the NGO partners. Medical Technologists supported by partners were fully dedicated and utilization rate was higher on those sites. Main reasons for low utilization were noncompliance with algorithm, lack of dedicated Human resources, nonfunctional UPS and Laptop.
Conclusions: Effective utilization of this new technology remains challenging. To resolve problem of nonfunctional modules, UPS and Laptop need regular monitoring and prompt action. Dedicated Medical Technologist need to be placed in each sites.

PS-14-654-31 Addressing the diagnosis challenge of extra-pulmonary TB in Afghanistan: the role of GeneXpert

GQ Qader,[1] MK Seddiq,[2] M Zafari,[2] DA Safi,[1] N Ahmadzada,[2] MK Rashidi,[1] MK Ayoubi,[2] MM Aseresa,[3] GP Suarez,[3] [1]Management Sciences for Health (MSH), Challenge TB Project (CTB), Kabul, Afghanistan, [2]Ministry of Public Health (MoPH), National TB Program (NTP), Kabul, Afghanistan, [3]Management Sciences for Health (MSH), Technical Excellence Group, Arlington, VA, United States of America.
e-mail: gqader@msh.org

Background and challenges to implementation: The primary goal of GeneXpert (GX) technology is to detect drug sensitive (DS) and drug resistance (DR) TB. Extra-Pulmonary TB (TB meningitis) has been a challenge for National TB Program (NTP). Meningitis is prevalence in Afghanistan and in 2017, 3,551 Afghans died of meningitis. The USAID- funded Challenge TB (CTB) project assisted NTP to use GX to detect DR and DS TB from body fluids. The aim of this assessment was to explore the yield of TB in body fluids.
Intervention or response: The CTB project assisted NTP to train clinical staff to refer pleura, abdomen and cerebrospinal fluids (CSF) of presumptive TB patients for GX testing. The laboratory staffs were trained on preparation of materials for testing. We used standard recording and reporting forms to document results. The data from 27 GX machines was collected and reviewed by technical team from NTP and CTB.
Results and lessons learnt: In 2018, 442 GX tests of body fluids conducted. Of them, CSF was 108 (24.4%), other body fluids were 323 (73.1%) and 11 (2.5%) were lymph-node pass. GX detected 15(13.9%) TB cases and one RR-TB among CSF, 24 (7.4%) TB among other body fluids and one (9.1%) TB among lymph node pass. The TB case notification was 13,888 in 100,000 meningitis patients and 7,185 in 100,000 patients with accumulations of fluid in their pleural, abdomen or lymph node pass. The positivity rate for CSF fluid was twice of sputum smear microscopy detection. The average sputum smear microscopy rate for pulmonary presumptive TB patients was 7% in 2017. Yield of TB among CSF fluid was 3.5 times higher than sputum smear testing.
Conclusions and key recommendations: TB-meningitis is highly prevalent among meningitis patients (CSF) and other body fluids in Afghanistan and GX technology is effective diagnostic tool. Thus, we recommend GX testing of CSF among all meningitis cases and other body fluids.

ABSTRACT PRESENTATIONS FRIDAY 1 NOVEMBER 2019

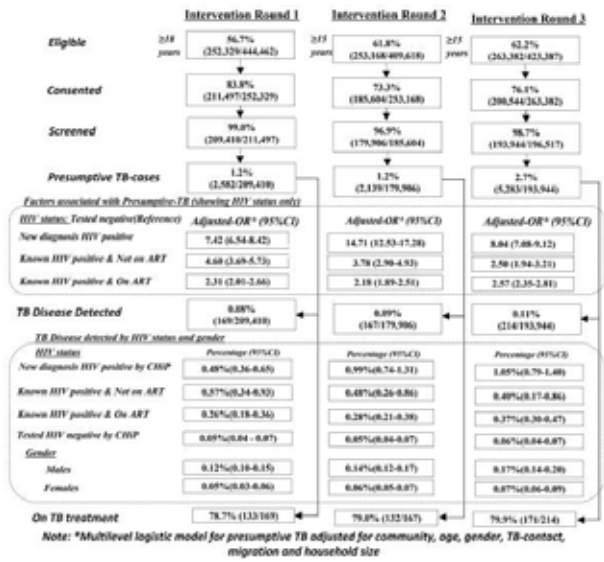
ORAL ABSTRACT SESSIONS (OA)

OA-12-C8 Active TB case finding: one size does not truly fit all: part 2

OA-12-388-01 Outcomes of household-based, community TB case finding from the HPTN 071 (PopART) study in Zambia

T Gachie,[1] A Schaap,[1,2] E Sakala,[3] M Phiri,[3] K Shanaube,[3] S Fidler,[4] R Hayes,[2] L Telisinghe,[5] S Floyd,[2] H Ayles,[3,5] [1]Zambart, Data, Lusaka, Zambia, [2]London School of Hygiene & Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [3]Zambart, Research, Lusaka, Zambia, [4]Imperial College London, HIV Clinical Trials Unit, London, United Kingdom, [5]London School of Hygiene & Tropical Medicine, Clinical Research, London, United Kingdom.
e-mail: thomas@zambart.org.zm

Background: Household-based active TB case finding (ACF) may facilitate reaching the first End-TB Global Plan 90-90-90 target. We present ACF outcomes from eight Zambian HPTN 071 intervention communities.
Methods: Between 01/2014-12/2017, Community HIV-care Providers (CHiPs) conducted three intervention rounds (IRs) during which CHiPs visited all community households, enumerating all members; (444,462 (IR1), 409,618 (IR2) and 423,387 (IR3)). Consenting individuals aged ≥18years (IR1) and ≥15years (IR2 and IR3) were offered HIV testing and TB symptom screening (cough≥2weeks, night sweats or unintentional weight loss≥1.5 Kilograms); presumptive-TB (pr-TB) was defined as any positive symptom. CHiPs collected sputum for Xpert/smear from pr-TB cases, captured TB test results and treatment start data. For each IR we; summarise the ACF cascade; explore factors associated with pr-TB using multilevel logistic regression and characterise TB disease cases.
Results: Of those screened for TB in IRs1-3 (N=209,410, 179,906 and 193,944 respectively), 1.2%, 1.2% and 2.7% were identified as pr-TB cases (Figure1). Regression analysis showed that community, age, sex, migration, household contact with a TB patient, household size and HIV status were associated with pr-TB across all IRs (Figure1, showing HIV status only). TB disease yield was 81/100,000 (95% confidence Interval [95%CI] 69-94/100,000), 93/100,000 (95%CI 80-108/100,000) and 110/100,000 (95%CI 96-126/100,000) in IRs1-3; highest among new CHiP HIV diagnoses, followed by known HIV-positive individuals not on ART and known HIV-positive individuals on ART, compared to those tested HIV-negative by CHiPs, across all IRs. TB disease yield was approximately two times higher among men than women in all IRs (Figure 1). In IRs1-3, 78.7%, 79.0% and 79.9% of TB Disease cases started treatment (Figure1).
Conclusions: Household-based, community-wide universal HIV testing and treatment with ACF in high HIV prevalence settings can improve TB detection among groups (men, people living with HIV) known to be hard to reach and at greatest risk for TB.



[Figure 1: TB Cascades for HPTN 071 intervention rounds in Zambia.]

OA-12-389-01 Catch care cure: towards TB 90 90 90 using community-based interoperable digital information systems

A von Delft,[1,2] N Wilson,[3] C Bill,[4] M Kitenge,[5,6] M Spani,[7] L Malgas,[8,9] C Goliath,[10] A Heekes,[1,2] V Mudaly,[1,3] A Boulle,[1,2] [1]University of Cape Town Faculty of Health Sciences, School of Public Health and Family Medicine, Cape Town, South Africa, [2]Western Cape Government: Health, Health Impact Assessment Directorate, Strategy and Health Support, Cape Town, South Africa, [3]Western Cape Government: Health, Health Programmes, Cape Town, South Africa, [4]Philani, Maternal, Child Health and Nutrition Project, Cape Town, South Africa, [5]Stellenbosch University Faculty of Medicine and Health Sciences, Division of Epidemiology and Biostatistics, Cape Town, South Africa, [6]Médecins Sans Frontières, Khayelitsha, Cape Town, South Africa, [7]Masincedane Community Service, Nomzamo, Cape Town, South Africa, [8]The Caring Network, Bishop Lavis, Cape Town, South Africa, [9]Touching Nations, Delft, Cape Town, South Africa, [10]Western Cape Government: Health, Metro Health Services, Cape Town, South Africa.
e-mail: vuzumsi@gmail.com

Background and challenges to implementation: Tuberculosis (TB) is the leading cause of death in South Africa, with only 68% of people with active TB accessing appropriate care. Western Cape Government Health developed an innovative Digital Information System to help close gaps in the TB 90 90 90 (i.e. 'Catch Care Cure') cascade.

Intervention or response: Community Health Workers (CHWs) visit households systematically, providing integrated Community-Oriented Primary Care (COPC), and screening and referring patients using an innovative homegrown mHealth App (Catch & Match) and interoperability layer. Patient-level data from all other electronic health sources (e.g. clinics, hospitals, laboratories and pharmacies) are integrated by the Provincial Health Data Centre (PHDC) and made accessible to clinicians via the Single Patient Viewer at Primary Healthcare facilities. CHWs receive automated notifications if their patients are matched to existing health records and if they attended healthcare facilities after being referred.

Results and lessons learnt: In 2018, 131 CHWs attended to 28241 individuals across four sites, matching 53% to the PHDC using a unique provincial identifier and related demographic information. 3% of individuals were identified as having possible TB based on mandatory digital TB symptom screening, automated household exposure flagging (all ages) and/or TB referrals (prompted by the App or CHW initiated). 57% had evidence of being tested, and of the 60% diagnosed with TB, 92% were started on treatment (outcome data pending).

Conclusions and key recommendations: CHWs could screen and support more than 90% of household members and people with TB respectively, while delivering integrated person-centered care. Testing among those at increased TB risk remained too low, despite an alarmingly high yield of active TB, reinforcing WHO recommendations for expanded testing and provision of TB preventive therapy. Integrated digital information systems can aid decision making by CHWs, support linkage to care and provide real-time disease dashboards which can be used for monitoring, planning and targeted actions across a wide spectrum of care.

OA-12-390-01 Finding the missing people with tuberculosis through sports: a case in Makadara sub-county in Nairobi, Kenya

S Musau,[1] T Kiptai,[1] V Nyambati,[2] J Nga'ng'a,[1] G Wandeyi,[1] J Mutua,[3] B Ulo,[1] [1]Amref Health Africa in Kenya, Global Fund TB Project, Nairobi, Kenya, [2]Ministry of Health, Nairobi County Government, Health, Nairobi, Kenya, [3]National Tuberculosis, Leprosy and Lung Disease Program (NTLD_P), TB Program, Nairobi, Kenya.
e-mail: samsonmusau81@gmail.com

Background and challenges to implementation: Kenya is among 14 high burden countries for TB, TB/HIV and Multi-drug Resistant TB (MDR-TB). The country is missing about 50% of estimated people with TB. Men are the most affected (883/100,000) and have been demonstrated to have poor health seeking behaviors. Football attracts huge crowd comprised mainly of men. Sports are sub-optimally utilized to reach men for health education and TB screening.

Intervention or response: In November 2018, Amref in collaboration with NTLD_P and Football Kenya Federation (FKF) supported a four day tournament in Nairobi, Makadara Sub-County. Through FKF representatives, 8 out of 24 (Under 20 years) popular teams with likelihood of attracting many people were selected. Teams were provided with branded sports attire. Publicity targeting intended participants and general populations was done through road-shows, mass and social media. CHVs carried out door to door mobilization and distribution of IEC materials. Health education, symptomatic TB screening, chest x-ray (CXR), referral of symptomatic persons and HIV counselling and testing was carried out. Individuals were encouraged to seek TB screening at health facilities.

Results and lessons learnt: A total of 1,984 people were screened for TB, 1,059 (53%) being men. Out of the total 457 presumptive people, 353 (77%) accessed diagnostic services through sputum test and CXR.

Nine (9) TB cases were identified, 3 among 135 people done CXR and 6 from 218 that underwent GeneXpert test. Majority (78%) of the 9 TB cases identified were men. Out of 400 people counselled and tested for HIV, 3 tested positive. Health facilities in the sub county reported increase in number of people seeking TB screening services after the tournament.

Conclusions and key recommendations: Sport is a great avenue for reaching out to men with health messages and screening services. Multi-sectoral approach is im-

portant to ensure acceptance and ownership. Mobilization by CHVs is key in ensuring linkage of community to health services.

OA-12-391-01 Challenges and opportunities in tuberculosis case finding using a seed-and-recruit model: the Cambodian experience

SC Choub,[1] AKJ Teo,[2] S Tuot,[3] C Ly,[1] S Ong,[1] C Ork,[1] M Smelyanskaya,[4] S Yi,[2,3,5] [1]KHANA, KHANA, Phnom Penh, Cambodia, [2]National University of Singapore and National University Health System, Saw Swee Hock School of Public Health, Singapore, Singapore, [3]KHANA, Center for Population Health Research, Phnom Penh, Cambodia, [4]Stop TB Partnership, Stop TB Partnership, Geneva, Switzerland, [5]Touro University California, Center for Global Health Research, Vallejo, CA, United States of America. e-mail: csokchamreun@khana.org.kh

Background and challenges to implementation: In 2017, approximately 40% of tuberculosis (TB) cases were undiagnosed in Cambodia. Active case finding with a seed-and-recruit model engages TB survivors to increase case finding through referrals of presumptive TB in their social network. We piloted the model in 2017, and it empirically demonstrated good case detection yields and is positively accepted by policymakers and community stakeholders. Yet, there was an insufficient number of seeds recruited in some project sites which impacted the yield of TB cases. Some seeds and recruiters were not able to mobilize presumptive TB for testing due to competing personal priorities and distance to health facilities.

Intervention or response: We addressed these challenges by expanding the criteria of seeds recruitment to include key populations for TB. Also, we have incorporated a mobile screening program in collaboration with the Cambodian Anti-tuberculosis Association to bring services closer to the rural communities. Frequent monitoring visits were also conducted to improve communication and reinforce support to the field staff. The improvised intervention is currently implemented in 12 districts in Cambodia.

Results and lessons learnt: Targets for the indicators were determined based on the TB burden, total population, urban-rural classification, and the number of health facilities in the selected districts. In the first quarter of the pilot phase, we achieved 57%, 87%, and 27% of the targeted number of people to be screened, tested and diagnosed with TB (all-forms), respectively.

Compared to the pilot phase, we achieved 77%, 109%, and 71% of the targeted number of people to be screened, tested and diagnosed with TB (all-forms), respectively, in the first quarter of the scale-up phase (Table 1).

Conclusions and key recommendations: The success of the model hinges on the close collaboration between the national and local authorities, health providers, and the communities. We recommend a constant exchange of experience, rigorous monitoring and evaluation to improve the results of the program.

	Pilot phase			Scale-up phase		
	Targets	Achievements	Percentage (%)	Targets	Achievements	Percentage (%)
Number of people screened	846	1211	143	23128	17872	77
Number of people tested	763	664	87	7108	7756	109
Number of people diagnosed with TB (all-forms)	304	82	27	399	285	71

[Targets achievements between pilot and scale-up phase of active case finding with a seed-and-recruit model]

OA-12-392-01 Full scale focused campaign against tuberculosis (FFCAT): experience from the Philippines

R Cruz,[1] H Ybanez,[1] C Candari,[1] P Sarmiento,[1] P Daru,[1] [1]University Research Co., LLC (URC), TB/Infectious Diseases, Manila, Philippines. e-mail: rcruz@urc-chs.com

Background and challenges to implementation: Recent data from the Philippines shows that TB case notifications remain low compared to the disease incidence rates. USAID supported TB Platform project has designed several strategies to support the Government of the Philippines (GOP) to assist with improving the TB control in the country. Full Scale Focused Campaign Against Tuberculosis (FFCAT) was piloted in Calapacuan, one of the Barangay in Central Luzon to increase case finding and TB awareness.

Intervention or response: The FFCAT was designed with several activities to perform in the specific area continuously for 5 days long. A temporary diagnostic center equipped with mobile X-ray van and sputum smear microscopy facility was established in the middle of the Barangay. The FFCAT was started with community assembly followed by Focused Group Discussion (FGD), special campaign called "Bandello", House to house visit, active screening of symptomatic, diagnosis and treatment of TB patients. The program was actively supported by DOH, Local government Unit (LGU), Provincial Health Unit, Rural Health Unit and all other TB stakeholders.

Results and lessons learnt: A total 2,200 house hold were visited and 9723 people were screened by the Barangay health workers, 793(8%) symptomatic were identified, 197 (25%) patients X-ray were suggestive to Tuberculosis and 26(3%) DS-TB were identified. Again, 166 presumptive were self-reported as impact of huge campaign, out of them 37 (22%) have X-ray suggestive to TB and 4(2%) TB patients were diagnosed. The

main Challenge observed is the turn-around time (TAT) for the release of official X-ray results is approximately 1-2weeks. The immediate impact shows very good but the cost per patient diagnosis is much higher.
Conclusions and key recommendations: The cascade of care from screening, diagnosis and treatment will be consolidated through the effort of the LGU. The FFCAT implementation will be scaled up and implemented in the other Municipalities by the support of DOH and LGUs.

OA-12-393-01 The impact of patent medicine vendors in increasing tuberculosis case detection among hard-to-reach dwellers in selected potential districts in Nasarawa state, Nigeria

M Onuoha,[1] B Uguge,[1] D Egbule,[2] A Danjuma,[3] O Akpomiemie,[2] A Idris Tari,[2] [1]KNCV Tuberculosis Foundation, Challenge TB Project, Abuja, Nigeria, [2]KNCV Tuberculosis Foundation, Challenge TB Project, Nasarawa, Nigeria, [3]Nasarawa State TB Control Program, Department of Public Health, Nasarawa, Nigeria.
e-mail: maxwell.onuoha@kncvtbc.org

Background: Despite the high burden of tuberculosis in Nigeria, case detection is generally low and even lower in hard-to-reach settings and maybe due to non-availability or inadequate formal health facilities. Studies on health seeking behaviour of patients with chronic cough revealed that 60% of respondents seek first level care from patent medicine vendors (PMVs)—a constant feature in Nigeria's informal health sector. This study assesses the impact of PMVs in increasing TB case detection among hard-to-reach dwellers in two hard-to-reach districts in Nasarawa state, Nigeria.
Methods: We identified twenty patent medicine vendors in collaboration with the leadership of the National Association of Patent and Proprietary Medicine Dealers (NAPPMED) in two districts, namely Nasarawa and Wamba. The 20 PMVs were trained on identification of presumptive TB, documentation and referral to DOTs facilities. The documentation tools and client's education materials in the local language (Hausa) were provided. Periodic visits and phone-call follow up to PMVs were made. Bi-monthly performance reviews were held and incentives were provided based on number of presumptive and TB cases reported. We reviewed the contribution of the PMVs to the total TB case finding between January 2018 and December 2018 in the two districts.
Results: In 2018, out of the total presumptive TB cases (3641) identified in the two districts, 1177 (32%) were from the PMVs in these hard-to-reach districts. Of all the 424 TB cases notified from these districts, 108 (25%) were diagnosed from successful referrals by the PMVs. The bacteriologic positivity rate of the presumptive TB clients referred by the PMVs was 9%.
Conclusions: PMVs present a great opportunity for finding persons with tuberculosis especially among the poorest people who dwell in hard-to-reach settings. Expanding access to TB screening services to the informal private health care providers will contribute in closing the gaps in TB case detection in Nigeria.

OA-12-394-01 Effectiveness of referral coordinators in bridging human resource gap for active tuberculosis case finding in Osun state, Nigeria

B Levy-Braide,[1] AM Adebayo,[2] D Gbadamosi,[2] A Adedotun,[2] S Batur,[3] M Onoh,[3] R Eneogu,[3] B Nsa,[3] [1]KNCV Tuberculosis Foundation, Programs, Osun, Nigeria, [2]Ministry of Health, State Tuberculosis and Leprosy Control Program, Osogbo, Nigeria, [3]KNCV Tuberculosis Foundation, Programs, Abuja, Nigeria.
e-mail: b.levybraide@gmail.com

Background and challenges to implementation: Osun state was estimated to have a TB burden of 6,574 in 2017, but only 25% treatment coverage was achieved. A major gap in finding the missing cases at the health facility (HF) is the human resource required to actively screen and refer presumptive TB cases for diagnosis and linkage to treatment. We aimed to critically evaluate the role and effectiveness of TB referral coordinators (RFC) in active case finding in Osun state.
Intervention or response: A one-year pre (PIP1) and post-intervention (PIP2) study were conducted between April 2017 to March 2018, and April 2018 to March 2019 respectively in 6 high volume facilities in Osun State. In both periods, standard guidelines and SOPs were available for health care workers (HCW) and routine onsite supervision was conducted. However, in the PIP2, HCW willing and committed to finding the missing cases were selected and trained as RFC from each facility. Monthly meetings were conducted with a representative from each service delivery points (SDPs). Some facilities used WhatsApp groups to monitor and facilitate real-time referrals and linkages.
Results and lessons learnt: Results and lessons learned In PIP1, 1548 presumptive cases were identified, 370 TB patients were diagnosed and 260 (70%) of them were placed on treatment. In the PIP2, 3110 were presumptive cases, 495 were diagnosed and 492 (99%) were placed on treatment. There was a 100% increase of presumptive cases referred for diagnosis in PIP2 (p-value=$\leq$ 0.001). Also, HCWs were more involved and had a better knowledge of TB compared to PIP1.
Conclusions and key recommendations: The presence of RFC increased awareness and knowledge of TB across different SDPs, strengthened HR for health and ensured effective referrals and linkage to treatment. Hence, there is a need to deploy RFC in high volume HF because this approach shows great potential in increasing TB case finding.

OA-12-395-01 Yield in active TB case finding in facility-based and community-based approaches in Mozambique

M Polana,[1] C Saeze,[1] P Mambo,[2] A Balate,[3] T Ferreira,[4] A Jaramillo,[5] R Frescas,[4] J Cardoso,[3] H Muquingue,[2] [1]Jhpiego Mozambique, TBIC/WPS, Maputo, Mozambique, [2]Jhpiego Mozambique, Monitoring and Evaluation, Maputo, Mozambique, [3]Jhpiego Mozambique, HTC, Maputo, Mozambique, [4]Jhpiego Mozambique, Project Management, Maputo, Mozambique, [5]Jhpiego Mozambique, National Directorate, Maputo, Mozambique.
e-mail: mico.polana@jhpiego.org

Background: Mozambique aims to eliminate tuberculosis (TB) by 2030, however as the country ranks 19th among countries most affected, this will be challenging. To eliminate TB, detection rates must increase from current levels. Two different approaches to identify individuals with TB were assessed for effectiveness, based on active case finding (ACF) yield; one is facility-based ACF, using cough officers (CO), the other community-based ACF, using lay counselors (LC), both implemented by trained lay-persons. While health facility CO screen only for TB, LC provide an array of health services, including HIV counselling and testing.
Methods: Data from log books and registers were abstracted from both LC and CO approaches. ACF yield was the percentage of individuals confirmed with TB among those with presumptive TB. Descriptive statistics were used to analyze the data.
Results: Data from February 2016 to February 2019 were analyzed; 382 CO screened 65,416 clients in 106 facilities, identifying 49,531 (75.7%) clients with presumptive TB; of these, 10,553 (21.3%) were confirmed as TB; there were 30 (0.28%) cases of multi-drug resistant TB (MDR-TB). 220 LC screened 1,545,579 clients in 38 districts, identifying 5,625 (0.4%) clients with presumptive TB; of the 1,649 (29.3%) that went to a health facility, 875 (53,1%) were confirmed with TB (no MDR-TB).
Conclusions: Both approaches are important ACF strategies that should be fully deployed to reduce the number of unregistered and untreated TB cases. Both were shown to significantly contribute to detect TB; even more importantly, they show that lay-persons with proper training can help alleviate the burden of TB detection. Among those screened by LC and referred to facilities, the likelihood of disease is relatively high compared with those identified by CO. It is important to note that CO contribute to infection control by prioritizing suspected cases, often in crowded settings, for isolation and rapid diagnosis.

OA-13-B1 Genotyping: state of the art

OA-13-396-01 Targeted next-generation sequencing methodology for characterising high-prevalence multidrug-resistant Mycobacterium tuberculosis mutations

LT Daum,[1] JD Rodriguez,[1] S Ndlovu,[2] NM Mbelle,[2] PB Fourie,[2] GW Fischer,[1] [1]Longhorn Vaccines & Diagnostics, Molecular Biology, San Antonio, TX, United States of America, [2]University of Pretoria, Department of Medical Microbiology, Pretoria, South Africa.
e-mail: longhorn-vandd@sbcglobal.net

Background: Next-generation sequencing (NGS) is the established method for genetic characterization of *Mycobacterium tuberculosis* (MTB) mutations conferring multi-drug resistance (MDR). However, NGS remains cost prohibitive and requires extensive library preparation. Using a panel of South African clinical isolates, we developed a simplified, targeted PCR method for detecting high prevalence MDR-specific mutations in the *rpoB* (rifampin), *katG* (isoniazid), *gyrA* (Fluoroquinolone), and *pncA* (pyrazinamide) genes and compared results to those obtained by whole-genome sequencing (WGS).
Methods: Four targeted PCR assays were designed and optimized for: *1) rpoB* including the rifampin-resistance determining region, *2) katG* spanning the S-315-T resistance mutation, *3) gyrA* including quinolone-resistance determining region, and *4)* the complete *pncA* gene. Using Illumina MiSeq, targeted PCR results were evaluated using clinical isolates (*N = 16*) from South Africa and compared to WGS.
Results: Of 16 clinical isolates analyzed by targeted sequencing, 12 (75%) harbored a S-450-L mutation, 3 (19%) contained a D-435-L, and 1 had a less prevalent Q-423-K rifampin resistance-conferring mutation in the *rpoB*. Analysis of *KatG* revealed 11 isolates (69%) harbored a S-315-T isoniazid-conferring mutation, 10 (63%) contained a Fluoroquinolone-resistance mutation in *gyrA*, and 11 (69%) contained a *pncA* gene mutation. All mutations obtained by targeted sequencing were confirmed by WGS.
Conclusions: Targeted NGS detected MDR-TB in 11 (69%) African isolates. In one MDR isolate, a less prevalent Q-423-K *rpoB* resistance-conferring mutation was detected. Targeted sequencing detects a broader range of resistance-conferring mutations than GenXpert, and is more cost-effective, particularly in low-resource areas where culture or WGS are impractical.

OA-13-397-01 Disputed rifampin mutations in Mycobacterium tuberculosis and treatment outcomes of tuberculosis

W-H Lin,[1] T-Y Chiang,[1] M-H Wu,[1] H-Y Tsai,[1] H-H Chan,[1] R Jou,[1,2] [1]Center of Disease Control, Tuberculosis Research Center, Taipei, Taiwan, [2]National Yang-Ming University, Institute of Microbiology and Immunology, Taipei, Taiwan. e-mail: rwj@cdc.gov.tw

Background: To strengthen our drug-resistant tuberculosis (DR-TB) management program, we analyzed treatment outcomes of DR-TB cases with disputed *rpo*B mutations in multidrug-resistant (MDR) and rifampin-resistant (RR) *Mycobacterium tuberculosis* isolates.
Methods: This is a population-based cohort study. One *M. tuberculosis* isolate was analyzed for each case. During 2014-2018, 837 DR-TB were confirmed using phenotypic agar-based drug-susceptibility testing (DST) and the *rpo*B gene sequencing. Isolates with disputed *rpo*B mutations were further tested using the minimum inhibitory concentrations (MICs) method. Treatment outcomes were obtained from the National TB Registry.
Results: Of the 837 DR-TB cases, isolates of 96 (11.5%) cases harbored disputed *rpo*B mutations. Types of *rpo*B disputed mutations were as following: Leu511Pro (N=19), Asp516Tyr (N=15), His526Leu (N=11), His526Leu+wild-type(wt) (N=1), His526Asn (N=5), Leu533Pro (N=33), Leu533Pro+wt (N=1), Leu511Pro+Leu533Pro (N=1), Asp516Tyr+Leu533Pro (N=2), Leu511Pro+His526Gln (N=2), Leu511Pro+Met515Val (N=1), Leu511Pro+Met515Leu (N=2), Leu511Pro+ Asp516Ala (N=1), Leu511Pro+ Asp516Gly (N=1) and His526Asn+Asp516Gly (N=1).
In this study, we analyzed 60 cases with treatment outcomes including 44 (73.3%) new cases and 16 (26.7%) previously treated cases. The agar-based DST results showed 49 (81.7%) resistant isolates (MICs 0.25 to 16 μg/ml), and 11 (18.3%) susceptible isolates with MICs (≦0.12 to 2 μg/ml), respectively. We found 61.5% (16/26) isolates, harboring Leu533Pro mutation, had low MICs (0.25 to 1 μg/ml). Of the 49 cases with resistant isolates, 31 (63.3%) cases had successful treatment outcome and no one treated with rifampin-containing regimen, 15 (30.6%) cases died, 3 (6.1%) cases were not evaluated. Of the 11 cases with susceptible isolates, 9 (81.8%) cases had successful treatment outcome including 1 case treated with rifampin-containing regimen. The treatment success rate of 60 cases (66.7%) with disputed mutations was significantly lower than that of 692 MDR-TB cases (82.4%) treated ($p < 0.05$).
Conclusions: Disputed *rpo*B mutations are not rare and follow-up phenotypic MIC determination is recommended for guiding treatment of DR-TB.

OA-13-398-01 Genotypic characterisation of "inferred" rifampicin mutations in genotype MTBDRplus assay and its association with phenotypic susceptibility testing of Mycobacterium tuberculosis

R Singhal,[1] D Anthwal,[2] G Kumar,[1] J Arora,[1] M Bhalla,[1] V Myneedu,[1] R Sarin,[3] S Haldar,[4] [1]National Institute of TB & Respiratory Diseases, Microbiology, New Delhi, India, [2]Translational Health Science and Technology Institute, Center for Bio-design and Diagnostics, Faridabad, India, [3]National Institute of TB & Respiratory Diseases, Tuberculosis and Chest, New Delhi, India, [4]Postgraduate Institute of Medical Education and Research, Department of Experimental Medicine and Biotechnology, Chandigarh, India. e-mail: drritugo@gmail.com

Background: Drug resistant tuberculosis diagnosis has been revolutionized with the emergence of rapid molecular techniques such as the Genotype MTBDR*plus* assay. In this assay, the *Mycobacterium tuberculosis* (*M. tuberculosis*) isolate that fails to hybridize to atleast one *rpoB* wild-type or any specific mutation probe is designated as rifampicin (RIF)-resistant. However, in this condition, specific mutation(s) type and its association to phenotypic drug resistance remains unknown. In this study, we sought to identify such 'inferred mutations' in *M. tuberculosis* isolates and their association with phenotypic resistance.
Methods: Ten thousand *M. tuberculosis* isolates were screened to identify 'inferred mutations' in Genotype MTBDR*plus* assay. Among these, n=203 isolates with 'inferrred mutations' were subjected to phenotypic drug susceptibility testing (DST) and sequencing.
Results: Among these n=203 isolates, 139 (68.5%) were resistant and 64 (31.5%) were sensitive in phenotypic RIF-DST. Sequencing showed that the presence of 'inferred mutations' was not always associated with phenotypic RIF-resistance at standard drug concentrations. Common mutations associated with discrepant phenotypic RIF-sensitivity results were D516Y (26.5%), H526N (17.2%), L511P (15.6%) and L533P (6.2%) whereas, RIF-resistant isolates had S531W (22.6%), D516Y (15.7%), L511P (10.8%) and H526N (10.3%) as most common mutations. Additionally, 19 novel mutations were found in this study after extensive data mining.
Conclusions: The recommendation of the Genotype MTBDR*plus* assay to diagnose RIF resistance based on the presence of 'inferred mutations' permits the detection of significant RIF-resistant isolates. Incorporation of additional mutation probes such as S531W in the assay can further increase the specificity and ease of detection of RIF-resistance. Susceptible phenotypic DST results in such cases amounts to delayed diagnosis of resistance, prolonged infection followed by less effective treatment outcomes. This highlights the need to redefine MGIT cut-off concentrations for RIF-phenotypic DST. Further studies are needed to establish the significance of type of mutation with clinical/treatment outcomes.

OA-13-399-01 Efficacy of genotype MTBDRsl assay to exclude fluoroquinolone and second-line injectable drug resistant Mycobacterium tuberculosis in a multidrug-resistant tuberculosis clinical trial

ME Kitata,[1] A Van Deun,[2] E Nduwamahoro,[2] J Keysers,[2] WB De Rijk,[2] E Diro Ejara,[3] L Rigouts,[2] BC de Jong,[2] G Torrea,[2] on behalf of STREAM Collaboration [1]University of Gondar, College Veterinary Medicine and Animal Sciences, Gondar, Ethiopia, [2]Institute of Tropical Medicine, Biosciences, Mycobacteriology Unit, Antwerp, Belgium, [3]University of Gondar, College of Medicine and Health Sciences, Gondar, Ethiopia. e-mail: gtorrea@itg.be

Background: STREAM 1 was a randomised non-inferiority phase 3 trial comparing a 9-11 month "short regimen" versus the WHO 2011 20 month "long regimen" for MDR-TB patients sensitive to fluoroquinolones (FQs) and second line injectables (SLIs). The Hain MTBDRsl line probe assay (LPA) was used to detect resistance to FQs and SLIs. We assessed the ability of the LPA (V1.0) to exclude baseline second line drugs (SLD) resistance.
Methods: Results of LPA performed on sputum in the site laboratories from MDR-TB patients screened for enrolment to the trial which were reported to be sensitive or inconclusive were compared with indirect phenotypic drug-susceptibility testing (pDST) performed in the central lab (Antwerp). Sequencing of gyrA/B genes was done for discordant cases and those with inconclusive LPAs. The association between inconclusive LPA results and bacillary load was determined.
Results: From 406 patients LPA and pDST results were analysed, of which 17 (4.2%) had inconclusive FQ LPA results (2/17 resistant by sequencing); for SLIs, 36 (8.9%) of 408 of the results compared were inconclusive on LPA. The negative predictive values (NPV) to exclude FQ and SLI resistance were 98.7% and 99.5%, respectively, with higher proportion of missed resistance among inconclusive (11.8% for FQ and 8.3% for SLI) than susceptible LPA (1.3% for FQ, 0.5% for SLI). The majority of inconclusive LPA for SLD (74.0% for FQ; 73.7% for SLI) were associated with no-AFB and low bacillary load compared to those with conclusive results (19.5% for FQ; 26.7% for SLI) ($p < 0.001$).
Conclusions: We conclude that MTBDRsl LPA V.1 is a reliable tool to exclude SLD resistance given the high accuracy and NPV for resistance. The inconclusive results should not be considered to be sensitive, in view of their association with resistant pDST, in countries with high prevalence of SLD resistance.

OA-13-400-01 Diagnostic accuracy of centralised assays for TB and drug resistance detection: a systematic review and meta-analysis

M Kohli,[1] E MacLean,[1] S Schumacher,[2] M Pai,[1] C Denkinger,[3] [1]McGill University, Epidemiology, Montreal, QC, Canada, [2]FIND, TB, Geneva, Switzerland, [3]Centre for Infectious Diseases, Infectious Diseases, Heidelberg, Germany. e-mail: mikashmikohli@gmail.com

Background: Diagnosis of TB is a crucial step in the cascade of care. Many diagnostic companies have recently entered the realm of molecular testing for TB and drug resistance detection using high throughput molecular platforms such as Abbott, Bruker-Hain, Becton Dickinson etc. This systematic review aims to analyse these tests for TB and drug resistance detection.
Methods: A comprehensive search of various databases for relevant citations was performed. A culture-based reference standard was used for the evaluation of TB detection. Resistance detection was compared against a phenotypic reference standard, sequencing as a reference standard as well as a composite reference standard.
Results: A total of 21 studies contributed to 27 unique datasets (provided data for more than one index test). Of these, 10 datasets were contributed by Abbott RealTime MTB; 7 by Abbott RealTime RIF/INH assay, 5 by FluoroType MTB assay, 3 by FluoroType MTBDR, 1 by BD Max MDR-TB assay and 1 by Cobas 6800/8800 MTB assay. Meta-analysis for TB detection showed that Abbott RealTime MTB assay demonstrated a sensitivity of 96%, with a specificity of 97%. FluoroType MTB assay demonstrated a sensitivity of 92%, with a specificity of 99%. Abbott RealTime RIF/INH assay had a sensitivity of 94%, with a specificity of 100% for rifampicin resistance detection and 89% sensitivity with a specificity of 99% for isoniazid resistance detection. FluoroType MTBDR, BD Max and Cobas assay demonstrated a high sensitivity (> 95%) and specificity (> 97%) for TB detection. FluoroType MTBDR and BD Max assay demonstrated optimal diagnostic accuracy for drug resistance testing (>95% sensitivity, >98% specificity).
Conclusions: In patients with pulmonary TB, these centralized molecular assays demonstrate promising diagnostic accuracy for TB detection, RIF resistance and INH resistance detection. However, there is a need for more well-designed diagnostic accuracy studies for each of these assays.

OA-13-402-01 In host population dynamics of M. tuberculosis during treatment failure

R Vargas,[1,2] L Freschi,[2] M Farhat,[2,3] [1]Harvard Medical School, Department of Systems Biology, Boston, MA, United States of America, [2]Harvard Medical School, Department of Biomedical Informatics, Boston, MA, United States of America, [3]Massachusetts General Hospital, Pulmonary and Critical Care Medicine, Boston, MA, United States of America. e-mail: roger_vargas@g.harvard.edu

Background: Understanding the within-host dynamics of TB's causative agent, *Mycobacterium tuberculosis* is vital for antibiotic treatment and vaccine design. At long timescales, signatures of positive selection associated with antibiotic resistance have been characterized, but epitope regions appear to be under purifying selection. Little is known about the selection acting on the Mtb genome during short time scales, such as single infections. We hypothesized that employing a longitudinal sampling scheme from humans with active TB disease would aide in unraveling these dynamics.
Methods: We obtained longitudinally collected clinical Mtb isolates that underwent Whole-Genome Sequencing (WGS) from 307 subjects to investigate Mtb diversity during the course of active TB disease. We excluded cases suspected of reinfection or contamination to analyze data from 200 subjects, 167 of which had paired isolates taken 2 or more months apart meeting criteria for treatment failure. Using technical and biological replicate samples, we defined an allele frequency threshold attributable to in-host evolution.
Results: Of the 167 patients with treatment failure, 16% developed resistance amplification between sampling. The majority of amplification occurred among isolates that were genotypically resistant at the outset, 8% of susceptible cases versus 24% of resistant cases (p-value = 0.00585). Low abundance resistance variants at a purity of 19% or higher in the first isolate predicts the fixation of these variants in the subsequent sample with 46% sensitivity and 95% specificity. We examine genes under selection within-host and confirm by assessing phylogenetic convergence across a genetically diverse sample of 10,895 public isolates.
Conclusions: We demonstrate a framework that makes use of average depth WGS data to study how Mtb population diversity changes over time. Knowledge of minor variants can be used to inform antibiotic treatment regimens in patients with TB. In-host variation also displays a signature of positive selection stemming from innate immunity which is critical for vaccine development.

OA-14-C1 Towards TB elimination: the missing 30 million LTBI treatments

OA-14-403-01 Preventing tuberculosis in contact children with three-month rifampicin-isoniazid and six-month isoniazid preventive therapy in four African countries

V Schwoebel,[1] KG Koura,[1,2] M Adjobimey,[3] S Gnanou,[4] A Goupehou Wandji,[5] J-C Gody,[6] A Roggi,[1] A Trébucq,[1] [1]International Union Against Tuberculosis & Lung Disease, TB/HIV, Paris, France, [2]Université Paris 5 Sorbonne, MERIT IRD, Paris, France, [3]Programme National de lutte Antituberculeuse, Centre National Hospitalier Universitaire de Pneumo-Phtisiologie-Cotonou, Cotonou, Benin, [4]Programme National de lutte Antituberculeuse, TB de l'Enfant, Ouagadougou, Burkina Faso, [5]Programme National de lutte Antituberculeuse, Hôpital Laquintinie, Douala, Cameroon, [6]Centre Hospitalier Universitaire de Bangui, Complexe Pédiatrique, Bangui, Central African Republic. e-mail: vschwoebel@theunion.org

Background: Despite evidence-based recommendations, contact investigation is poorly implemented in many low-income settings and less than 25% of eligible children are estimated to access tuberculosis preventive therapy (PT) worldwide. The Titi study aimed to demonstrate the feasibility and document the effectiveness of contact investigation and PT with both standard and shorter regimen for children in routine programmatic conditions in Benin, Burkina Faso, Cameroon and Central African Republic.
Methods: Children under 5 years living at home with adult patients consecutively diagnosed with smear-positive pulmonary tuberculosis (SS+PTB) in 13 urban participating centers were enrolled after parent's informed consent. Children were evaluated during home and clinic visits using standardized questionnaire, clinical examination, tuberculin skin test and chest X-Ray. Children free of active TB were offered PT with 6-month isoniazid (6H) in Benin or 3-month rifampicin-isoniazid (RH75/50) regimen in other countries. Children were followed-up every month during PT, and every three months after completing PT during 12 months.
Results: The ratio of children under 5 years to notified SS+PTB varied by country from 0.7 to 1.0. In total, 1 965 children were enrolled, of whom 56 (2.8%) had active TB at inclusion. Among the 1 761 children (89.6%) who started PT, 1 643 (93.3%) completed treatment. Mild adverse reactions, mostly digestive, were reported in 2% of children, leading to treatment termination in 2 (0.1%), and one child died on 6H for hepatitis of unknown cause. One case of incident TB was reported 12 months after completing 3RH regimen (0.05 per 100 person-years) and was possibly due to a late TB infection.
Conclusions: Home visit is key to enable registration and first clinical evaluation of children in contact with contagious PTB. PT of contact children under 5 years

with both 3RH and 6H is applicable, well tolerated and effective for preventing active TB in programmatic conditions in low-income settings.

OA-14-404-01 Comorbidities, serious adverse events, and treatment outcomes with 12-dose isoniazid-rifapentine treatment

S-H Wang,[1] N Nwana,[2] R Webb,[3] S Bamrah Morris,[2] M Lobato,[2] J Jereb,[2] R Moro,[2] T Chorba,[2] S Mase,[4] C Ho,[2] The ,3HP Post-Marketing Assessment Group
[1]The Ohio State University, Inernal Medicine, Columbus, OH, United States of America, [2]Centers for Disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Atlanta, GA, United States of America, [3]University of Mississippi, Internal Medicine, Jackson, GA, United States of America, [4]World Health Organization, Tuberculosis, New Dehli, India.
e-mail: wang.1055@osu.edu

Background: Latent TB infection (LTBI) treatment with 12-dose isoniazid-rifapentine (3HP) has high treatment completion rates, but more data on serious adverse events (SAE) will inform treatment practice. The U.S. Centers for Disease Control and Prevention conducted 3HP post-marketing surveillance to monitor SAE and treatment discontinuation. We investigated the associations between co-morbidities and SAE and treatment discontinuation.
Methods: Prospective observational cohort. Patient demographic and clinical information and weekly symptom/adverse event (AE) review were collected from 16 U.S. program sites from 2011-2013; 10 of these sites, at 3HP treatment initiation, provided information on co-morbidities/ medications. We performed analyses to describe frequencies of AE (any symptom/laboratory abnormality reported during 3HP treatment), and multivariable logistic regression to identify factors associated with SAE (death, hospitalization, emergency department visit) and treatment discontinuation (< 11 doses 3HP, including those lost to follow-up) by medications and co-morbidities.
Results: Medication use and co-morbidities were collected for 2,389 patients; of these, 782 (32.7%) reported AE. Mental health conditions, hepatitis, chronic lung disease, or smoking were associated with treatment discontinuation, while self-reported alcoholism, diabetes, HIV, or chronic renal disease were not (Table).
Relative risk (RR) of treatment discontinuation increased with any concomitant medication [**1.39** (**1.14-1.70**)]. Proton pump inhibitors [**1.73** (**1.12-2.66**)], H1 blockers [**1.90** (**1.18-3.07**)], serotonin and norepinephrine reuptake inhibitors [**2.97** (**1.68-5.24**)], or duloxetine [**3.77** (**2.06-6.87**)] were associated with treatment discontinuation, while diabetic medications [1.18 (0.74-1.89)], calcium channel blockers [1.33 (0.84-2.13)], or statins [1.51 (1.00-2.29)] were not. 33/2,389 (1.4%) reported SAE. In multivariate analyses, concomitant medication was associated with SAE [**4.69** (**2.22, 9.91**)] and treatment discontinuation [**1.39** (**1.14-1.70**)]. No deaths were reported.
Conclusions: In our cohort, certain co-morbidities/medications modestly increased risk of treatment discontinuation. Patients with these co-morbidities/medications may need intensified monitoring for AE and SAE. These findings are limited by study design and data collection in programmatic settings.

Co-morbidity[1]	Frequency of co-morbidity	Treatment discontinuation RR (95% CI) (n=421)
Excess alcohol (≥2 drinks/day)	211	1.22 (0.89, 1.68)*
Diabetes	176	1.30 (0.91, 1.85)
Chronic renal disease	30	1.57 (0.76, 3.26)
HIV-infected	27	0.58 (0.15, 2.23)
Chronic viral hepatitis	58	1.76 (1.07, 2.89)
Chronic lung disease	78	1.92 (1.27, 2.89)
Mental health disease	127	1.73 (1.22. 2.46)
Smoker (ever)	534	1.53 (1.23, 1.89)**

[1]Co-morbidity
*reference no history of excess alcohol use
**reference non-smoker

[Table. Relative risk of discontinuation of 3HP treatment associated with co-morbidities (N=2,389)]

OA-14-405-01 Opportunities and challenges for occupational TB screening in high-incidence countries: insights from a qualitative study of healthcare workers in Cape Town, South Africa

R Nathavitharana,[1] A Van der Westhuizen,[2] H Mishra,[3] A Sampson,[3] E Nardell,[4] G Theron,[3] [1]Harvard Medical School, Infectious Diseases, Boston, MA, United States of America, [2]Stellenbosch University, Medicine, Cape Town, South Africa, [3]Stellenbosch University, Microbiology, Cape Town, South Africa, [4]Harvard Medical School, Global Health Equity, Boston, MA, United States of America.
e-mail: rnathavi@bidmc.harvard.edu

Background: Healthcare workers(HWs) have at least twice the risk of latent tuberculosis infection(LTBI) compared to the general population. However, occupational health systems in high-incidence countries are often overburdened and, despite the growing emphasis on LTBI treatment in high-risk populations, data on HWs in high-incidence countries are scarce. We conducted a qualitative study to determine HW perspectives related to occupational TB screening at Tygerberg Hospital, Cape Town, South Africa.
Methods: We conducted fourteen in-depth interviews with junior and senior nurse and physician stakeholders, as part of a study evaluating the correlation between rebreathed air exposure and HW acquisition of LTBI. Using an inductive approach, we performed open coding to identify emergent themes and selective coding

to identify relevant text citations. We analyzed themes using the COM-B (capability, opportunity, motivation ->behaviour change) framework.

Results: Six emergent themes were analyzed according to COM-B domains(Table). Within Capability, the themes were responsibility, which included HWs considering the relative importance of their own actions versus the hospital's policies to protect HWs from TB transmission, and the strong duty of care that made them sometimes forget to protect themselves while remaining conscious of the need to reduce transmission risk to patients. Within Opportunity, although all HWs identified a high risk of TB transmission due to unsuspected TB and recognized gaps TB infection control (IC) measures, almost none had undergone workplace TB screening. Regarding motivation, all HWs endorsed the need for TB screening, including LTBI, and almost all were willing to consider LTBI treatment, particularly if it was shorter and if re-exposure risk could be reduced.

Conclusions: All stakeholders identified the high risk of occupational TB and the need for TB screening. While the majority were willing to consider LTBI treatment, an occupational health intervention to implement screening should be accompanied by strengthening TB-IC in order to reduce the risk of exposure.

Theme	Quotations
CAPABILITY - Self-responsibility versus the responsibility of the hospital to protect HWs	"You are responsible for your own protection, so I should wear a mask every day, but sometimes I don't." (Senior doctor, paediatrics) "You expect to be safe in your work environment." (Junior doctor, paediatrics)
CAPABILITY - Strong duty of care	"Yes, safety comes first to me but sometimes I forget that and then I just focus on getting the patient stable, right or not." (Junior nurse, surgery) "I think from a sort of moral, ethical perspective, we should probably screen medical staff for the health of our patients as well." (Senior doctor, paediatrics)
OPPORTUNITY - High risk of TB transmission due to unsuspected TB	"They have TB without the nurses knowing, so it's easy to infect the other patients if they are not on treatment." (Junior Nurse, TB ward) "So, on average it will take us sort of about 24 to 36 hours to diagnose a patient with TB here, I think.... So there is no day here when I don't think I am exposed to TB." (Senior doctor, medicine)
OPPORTUNITY - Gaps in TB Infection Control (TB-IC)	"I know it's [isolation rooms with negative pressure] expensive, I know this hospital is old." (Senior nurse, Obstetrics) "What really I think should be happening is patients should sort of be screened at triage already and patients with possible TB or have TB should be going to a completely different area." (Senior doctor, medicine)
MOTIVATION - Need for TB screening	"Regular testing is not, no, it's not encouraged all that much, from what I have noticed." (Junior doctor, Obstetrics) "I think they must do it [screening] for free for us. You see, because we work with the patients in their hospital. So you can get it [TB] at any time." (Junior nurse, Obstetrics)
MOTIVATION - Willingness to take LTBI treatment	"One day my immune system may become weaker, that TB is going to be active. So, if there is something to destroy that bacteria, I would want it." (Senior Nurse, TB ward) "Even if you use treatment to get rid of latent infection, you will just maybe come in contact with it again." (Junior doctor, Obstetrics)

[Themes related to HW TB screening organized according to COM-B framework domains]

OA-14-406-01 Comorbidities and risk of adverse events with four months of rifampin or nine months of isoniazid for latent tuberculosis infection: results from two randomised controlled trials

JR Campbell,[1,2] F Fregonese,[2] M Bastos,[2] VJ Cook,[3] R Ruslami,[4] M Adjobimey,[5] P Hill,[6] H Al-Jahdali,[7] A Trajman,[8] D Menzies,[2] The 4v9 RCT Team [1]McGill University, Department of Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]University of British Columbia, Faculty of Medicine, Vancouver, BC, Canada, [4]Universitas Padjadjaran, Faculty of Medicine, Bandung, Indonesia, [5]Centre National Hospitalier Universitaire de Pneumo-Phtisiologie, Prevention, Cotonou, Benin, [6]University of Otago, Centre for International Health, Dunedin, New Zealand, [7]King Saud University, Department of Medicine, Riyadh, Saudi Arabia, [8]Federal University of Rio de Janeiro, Internal Medicine Post-Graduate Program, Rio de Janeiro, RJ, Brazil.
e-mail: jonathon.campbell@mail.mcgill.ca

Background: Safety data from phase 2 (NCT00170209) and phase 3 (NCT00931736) randomized controlled trials (RCT) of four-months of daily rifampin (4R) and nine-months of daily isoniazid (9H) showed 4R is safer than 9H for latent tuberculosis infection (LTBI). Safety has not been evaluated specifically among patients with co-morbidities. The objective was to perform a safety analysis on subgroups of patients with co-morbidities from the phase 2 and phase 3 RCTs.

Methods: Patients receiving at least one treatment dose were included. Adverse events (AE) were defined as grade 1-4 rash or any grade 3-5 adverse event that led to permanent treatment discontinuation and were judged related to the study drug by a three-person panel blinded to study drug. Co-morbidities included: people living with HIV (PLHIV), diabetes, other immunocompromising conditions (e.g. immune-suppressing medications), and alcohol intake >1 drink per week or smoking (current or ex) because these were correlated. We calculated the risk difference (RD) for adverse events between individuals randomized to 9H and 4R.

Results: The analysis included 268 PLHIV, 198 people with diabetes, 219 people with other immunocompromising conditions, and 1482 people who were current or ex-smokers or had alcohol intake >1 drink per week. For patients with other conditions, 134 (61%) were using concomitant medications (e.g. TNF-α inhibitors). Overall, patients with any co-morbidity had an AE risk 2.2% (95% CI 0.9%, 3.5%) higher if receiving 9H than if receiving 4R (**Table**). AE risk with 9H was highest for patients with diabetes and highest with 4R among patients with other immunocompromising conditions. Overall, AE risk with 9H (p=0.07) and 4R (p=0.39) were not statistically different between patients with and without co-morbidities.

	Randomized to Isoniazid		Randomized to Rifampin		
Patient Characteristic	Number Received Drug	Events (%)	Number Received Drug	Events (%)	Risk Difference per 100 (Isoniazid - Rifampin)
HIV	138	5 (3.6%)	130	1 (0.8%)	2.9 (95%CI -0.6 to 6.3)
Diabetes	91	5 (5.5%)	107	1 (0.9%)	4.6 (95%CI -0.5 to 9.6)
Other Immuno-compromising Condition	105	3 (2.9%)	114	6 (5.3%)	-2.4 (95%CI -7.6 to 2.8)
Alcohol >1 Drink Per Week or Current- or Ex-Smoker	737	24 (3.2%)	745	6 (0.8%)	2.5 (95%CI 1.0 to 3.9)
Any Co-Morbidity	1071	37 (3.5%)	1096	14 (1.3%)	2.2 (95%CI 0.9 to 3.5)
No Co-Morbidity	2134	39 (2.4%)	2184	36 (1.6%)	0.7 (95%CI -0.2 to 1.5)

[Incidence and Risk Difference of Adverse Events Between Treatments]

Conclusions: Rifampin appears to be well tolerated among patients with co-morbidities. Caution should be exercised when using isoniazid and rifampin among patients with diabetes or other immunocompromising conditions, respectively.

OA-14-407-01 Evaluating human resource needs for the latent tuberculosis cascade of care: how much healthcare worker time does it take?

H Alsdurf,[1,2] O Oxlade,[2] D Menzies,[2] ACT4 Trial Team [1]McGill University, Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]McGill International TB Centre, Research Institute of McGill University Health Centre, Montreal, QC, Canada.
e-mail: hannah.alsdurf@mail.mcgill.ca

Background and challenges to implementation: Although the End TB Strategy calls for scale-up of latent tuberculosis infection (LTBI) services and preventive treatment, little information is available on the human resource requirements to provide such services.
Intervention or response: Our study, on human resource requirements to investigate household contacts, is part of the larger ACT4 pragmatic, cluster randomized trial to evaluate and strengthen the LTBI Cascade of Care in five countries (Benin, Canada, Ghana, Indonesia, and Vietnam). The aim of our study was to quantify the healthcare worker (HCW) time required to perform tasks associated with each step along the LTBI Cascade of Care to inform scale-up efforts. The time and motion (TAM) method was used to directly observe the daily LTBI-related activities of HCW who agreed to participate.
Results and lessons learnt: In the 24 ACT4 health facilities, a total of 82 HCW were followed using TAMs. For all HCW, the average time to perform each step ranged from 6.4 minutes (reading a tuberculin skin test (TST)) to 12.8 minutes (recommending LTBI preventive therapy). When results were stratified by setting (high vs. low or middle income (LMIC)), HCW in facilities in high income settings tended to spend longer on cascade steps relative to those in LMICs (Table 1). An average of 65.4 and 30.1 minutes (high vs. LMICs, respectively) of HCW time is required to complete all steps (excluding follow-up visits) for a contact moving through the LTBI Cascade of Care.
Conclusions and key recommendations: The total time required for a HCW to complete all of the steps in the LTBI cascade is substantial. TB programs considering LTBI program expansion should consider the associated budget implications as human resources are a major driver of cost. Information from this study could be used to help estimate the cost of LTBI program expansion using the annual number of pulmonary TB patients at any health facility.

LTBI Cascade of Care Step	Number of HCW (and patient encounters) observed performing each Step - CANADA	Number of HCW (and patient encounters) observed while performing each Step - LMICs(1)	Mean time (SD) per patient encounter -CANADA	Mean time (SD) per patient encounter -LMICs(1)
1. Identification of contacts	20 (39)	14 (32)	14.0 (11.2)	9.2 (11.7)
2. Place TST(2)	13 (32)	9 (32)	13.1 (7.1)	3.1 (3.4)
3. Read TST(2)	12 (23)	6 (37)	11.4 (7.2)	3.2 (1.6)
4. Conduct medical evaluation	33 (90)	10 (22)	13.0 (7.9)	7.2 (6.6)
5. Recommend and discuss LTBI treatment	32 (92)	7 (19)	13.9 (8.9)	7.4 (5.1)
6. LTBI treatment follow-up visit	40 (188)	11 (47)	11.5 (9.4)	4.8 (5.6)

(1) - LMICs include ACT4 sites in: Benin, Ghana, Indonesia, and Vietnam

(2) Steps 2 & 3 may include HCW time spent on patient education, in addition to placing and reading a TST.

[HCW time required to perform work tasks associated with each step along the LTBI Cascade of Care]

OA-14-408-01 Enhancing the public health impact of latent tuberculosis infection diagnosis and treatment (ACT4): preliminary results from a cluster randomised trial in five countries

O Oxlade,[1] M Adjobimey,[2] TN Buu,[3] V Cook,[4] D Fisher,[5] F Fregonese,[1] P Hadisoemarto,[6] R Long,[7] J Obeng,[8] R Ruslami,[9] ACT,4 Trial Group [1]McGill University Health Centre Research Institute, McGill International TB Centre, Montreal, QC, Canada, [2]Centre National Hospitalier Universitaire de Pneumo-Pthisiologie de Cotonou, PNT, Cotonou, Benin, [3]Woolcock Institute of Medical Research, Ho Chi Minh City, Viet Nam, [4]BC Centre for Disease Control, Faculty of Medicine, Vancouver, BC, Canada, [5]University of Calgary, Calgary Tuberculosis Centre, Calgary, AB, Canada, [6]Universitas Padjadjaran, TB-HIV Research Center and Dept of Public Health, Bandung, Indonesia, [7]University of Alberta, Faculty of Medicine and Dentistry, Edmonton, AB, Canada, [8]Ministry of Health, Komfo Anokye Teaching Hospital, Accra, Ghana, [9]Universitas Padjadjaran, TB-HIV Research Center and Dept of Biomedical Sciences, Bandung, Indonesia. e-mail: olivia.oxlade@mcgill.ca

Background: Treatment of latent tuberculosis infection (LTBI) is essential for global TB control, however, the number of individuals who successfully complete LTBI treatment remains low. Many losses occur throughout the cascade-of-care and the reasons for losses vary by setting. We have conduced a trial of a standardized, but locally driven, public health approach to strengthen the management of household contacts (HHC) of TB patients.

Methods: A cluster randomized trial (NCT 02810678) was conducted in 24 health facilities in Benin, Canada, Ghana, Indonesia and Vietnam. In Phase-1 intervention sites conducted a standard assessment of their LTBI program using pre-existing registries and questionnaires on practices, knowledge and attitudes regarding TB prevention. In a formal decision-making process, local stakeholders used Phase 1 findings to select strengthening activities which were implemented in Phase 2. Activities included contact management registries and regular in-service LTBI management training. Control sites continued their usual LTBI care without evaluation or strengthening activities.

The primary study outcome was the number of HHC initiating LTBI treatment per 100 newly diagnosed TB patient. An intention-to-treat analysis was performed, using Poisson regression.

Results: In intervention sites an increase in the number of HHC initiating treatment was seen following the strengthening activities (49 HHC per 100 index patients), while no significant change was seen in control sites (Table 1). The overall difference in effect between intervention and control sites was 61.2 (95%CI 0.1, 122.4) HHC per 100 Index patients. The effect was stronger in low/middle income sites than in Canadian sites.

Conclusions: Preliminary results suggest that the strengthening approach increased the number of HHC initiating treatment. The success of the approach relies on commitment from key stakeholders and a local data driven decision making process. Cost and sustainability are additional aspects of the intervention that are currently under evaluation and important to inform scale up.

	Control		Intervention	
	Phase 1	Phase 2	Phase 1	Phase 2
Number of TB index patients identified in 6 month period	494	484	494	444
Adjusted rate (95%CI) of HHC initiating treatment per 100 Index TB patient, all sites (N=24)	30 (1,59)	18 (-1, 37)	24 (1, 46)	73 (21, 125)
Adjusted rate difference (difference of differences) (95% CI) of HHC initiating treatment per 100 Index TB patient, all sites (N=24)	61.2 (0.1, 122.4)			
Adjusted rate difference (difference of differences) (95% CI) of HHC initiating treatment per 100 Index TB patient in LMIC sites (N=20)	92 (35, 150)			
Adjusted rate difference (difference of differences) (95% CI) of HHC initiating treatment per 100 Index TB patient in Canadian sites (N=4)	-10 (-141, 122)			

*All rate differences are adjusted for clustering at the health facility level.

[Adjusted difference per arm and rate difference, in household contacts initiating treatment per 100 Index TB patients.]

OA-14-409-01 Voyage to TB elimination: a mass TB treatment and prevention campaign in the Marshall Islands

R Brostrom,[1] A Largen,[2] M Konelios-Langinlur,[3] Z Zachraias,[3] S Yadav,[4] E Ko,[5] G Dugan,[6] J Hill,[6] A Finlay,[7] J Mermin,[8] [1]Centers for Disease Control and Prevention (CDC), Division of TB Elimination, Honolulu, HI, United States of America, [2]State of Hawaii, TB Program, Honolulu, HI, United States of America, [3]Republic of the Marshall Islands, Ministry of Health, Majuro, Marshall Islands, [4]World Health Organisation, Western Pacific Region, Suva, Fiji, [5]World Health Organisation, Western Pacific Region, Pohnpei, Micronesia, [6]Harvard School of Public Health, Zero TB Initiative, Daru, Papua New Guinea, [7]Centers for Disease Control and Prevention (CDC), Division of Global HIV/AIDS and Tuberculosis, Ha Noi, Viet Nam, [8]Centers for Disease Control and Prevention (CDC), National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Atlanta, GA, United States of America. e-mail: hld4@cdc.gov

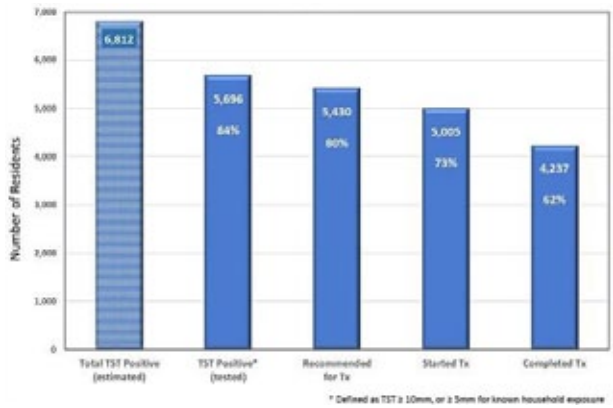
Background: In 2016, the World Health Organization (WHO) estimated TB prevalence in the Republic of the Marshall Islands (RMI) to be 494/100,000. Working

with regional partners, the RMI Ministry of Health implemented mass TB screening in 2018 in Majuro (population 27,649). Campaign goals were to screen ≥80% of residents for TB disease and latent TB infection (LTBI), Hansen's disease (HD), and diabetes, and sustainably improve TB program capacity.

Methods: A multi-agency team completed screening in May-November 2018 using an age-based protocol. For age < 5 years, TB screening was based on examination and prior exposure. Persons age ≥5 received a TST, exposure history, symptom screen, chest x-ray, and Xpert-MTB/RIF® if indicated. TB diagnosis was determined by a committee of experts. For persons without TB disease, treatment for LTBI was offered to those < 5 years with TB exposure and those ≥5 years with a positive TST. All residents were examined for HD. Diabetes testing using HbA1c was done for TB disease, LTBI, and HD referrals.

Results: Of 22,654 (82%) residents who initiated screening, 19,902 completed and 305 active TB cases (1.6%) were identified. Smear, Xpert, and culture positivity were 9%, 16%, and 17% for adult pulmonary cases. LTBI was diagnosed in 5,696 (29%) residents; 5,005 started and 4,237 (85%) completed a WHO-approved LTBI regimen (Figure 1). Additionally, 54 cases of HD were diagnosed. Diabetes was diagnosed in 928 individuals, for whom 44% were new diagnoses. The RMI TB Program capacity expanded to accommodate the increased burden of identified TB.

Conclusions: An integrated screening campaign identified and treated many individuals with TB disease, LTBI, HD, and diabetes. Mass TB prevention was demonstrated with high completion rates using short-course rifampicin-based regimens. With proper engagement of community leaders, careful planning, and adequate resources, a mass TB campaign can be successfully completed.



[Figure 1. LTBI Treatment Cascade for TB and Leprosy Free Majuro, 2018 (Age ≥ 5 y.o.)]

OA-14-410-01 Mathematical modelling of the population impact of bio-marker targeted preventive therapy

T Sumner,[1] T Scriba,[2] M Hatherill,[2] R White,[1] [1]London School of Hygiene & Tropical Medicine, TB Modelling Group, Department of Infectious Disease Epidemiology, London, United Kingdom, [2]University of Cape Town, South African Tuberculosis Vaccine Initiative (SATVI), Division of Immunology, Department of Pathology and Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa. e-mail: tom.sumner@lshtm.ac.uk

Background: Existing tests for Mycobacterium tuberculosis (*M.tb*) infection have poor specificity for predicting progression to tuberculosis (TB) disease. New tests which can predict active disease and allow better targeting of preventive therapy may play a key role in reducing TB burden. However, the impact and efficacy of such tests will be setting specific, depending on the local TB epidemiology.

Methods: Using a simple transmission model we explored the population level impact (percentage reduction in TB incidence) and efficacy (Number Needed to Treat to avert one case of TB (NNT)) of using biomarker based screening to target preventive therapy (3HP). We compared existing tests (Interferon Gamma Release Assays (IGRA)) to a new, more specific, mRNA expression signature (Correlate of Risk (COR)) which is currently being evaluated in a proof-of-concept study in South Africa (CORTIS NCT02735590). We explored how the predicted impact and efficacy depended on current TB incidence and the historical trend in incidence.

Results: Preliminary results show that, over 10 years, the percentage reduction in TB incidence increases with increasing baseline TB incidence while the NNT declines. The impact of screening with IGRA is greater than with COR, since 3HP is provided to more people. However, except at low incidence (below approximately 50/100,000), COR based screening is more efficient, with a lower NNT. The predicted impact and NNT also depend on the trend in TB incidence prior to the introduction of screening.

Conclusions: More specific tests for predicting progression to active tuberculosis may make a significant contribution to reducing TB incidence by allowing more efficient targeting of preventive therapy compared to use of existing tests for *M.tb*. infection. The likely efficacy will depend on both the current TB burden and the trend in recent years.

OA-15-A3 Rapid genetic TB testing: performance and quality

OA-15-411-01 A portable real-time solution for next generation sequencing-based diagnosis of drug-resistant tuberculosis direct from clinical samples

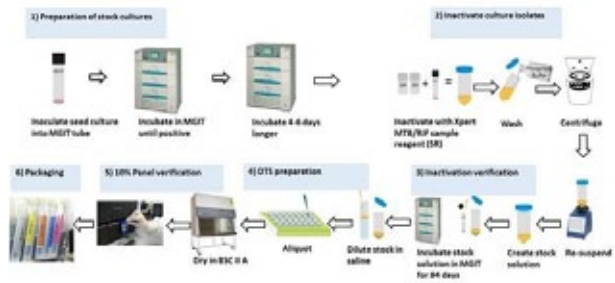
AM Cabibbe,[1] S Battaglia,[1] A Spitaleri,[1,2] A Suresh,[3] R Colman,[3,4] S Uplekar,[3] TC Rodwell,[3,4] DM Cirillo,[1,3]
[1]IRCCS San Raffaele Scientific Institute, Emerging Bacterial Pathogens Unit, Division of Immunology, Transplantation and Infectious Diseases, Milano, Italy, [2]IRCCS San Raffaele Scientific Institute, Center for Translational Genomics and Bioinformatics, Milano, Italy, [3]Foundation for Innovative New Diagnostics (FIND), Campus Biotech, Geneva, Switzerland, [4]University of California, Department of Medicine, San Diego, CA, United States of America.
e-mail: cabibbe.andreamaurizio@hsr.it

Background: Implementation of Whole Genome Sequencing as a comprehensive alternative to conventional rapid molecular tuberculosis (TB) diagnostics is limited by the need for culture as the starting material. Targeted Next Generation Sequencing (tNGS) allows for selective amplification of phylogenetic and drug resistance (DR)-associated regions of *Mycobacterium tuberculosis* directly from clinical samples. The goal of this study was to evaluate the adaptability of the tNGS Deeplex MycTB assay (Genoscreen) for use on the MinION (Oxford Nanopore Technologies), a portable sequencing instrument, to determine if it could be used as simple, rapid clinical solution for comprehensive drug susceptibility testing.
Methods: A collection of 104 DNA samples extracted from smear-positive sputum sediments was amplified using Deeplex, and sequenced on a MinION and Illumina MiniSeq. Sequence quality, mapping statistics and variant analysis of DR genes were evaluated.
Results: The mean MinION read length was 792 bases, reflecting average Deeplex amplicon lengths. The average basecall quality score was 9.1 and 8.6 for two MinION runs (minimum acceptable threshold=7), indicating high quality reads. The mean depth of coverage was 4167x and 4177x on MinION and MiniSeq respectively. We observed 100% concordance for confidence-graded DR mutations between sequencing platforms. False variant calls were initially detected by MinION in the ribosomal region, requiring optimization of analysis thresholds. Two large *pncA* deletions were correctly identified on both platforms, despite a reported high error rate around these regions on MinION.
Conclusions: The Deeplex tNGS assay, run on the MinION sequencer with minimal optimization showed largely equivalent performance to the assay run on a MiniSeq sequencer. The main limitations to the MinION approach are high required DNA input concentrations and high raw error rates. Optimizing the analytics allowed us to overcome the raw error rates. Deeplex tNGS on MinION is a promising clinical solution for intermediate-level TB facilities.

OA-15-412-01 Introducing external quality assurance for Xpert MTB/RIF testing- experiences from India

T Shah,[1] S Chaddha,[1] S Sarin,[1] KS Sachdeva,[2] N Kumar,[2] N Somashekar,[3] V Gumma,[1] K Reddy vc,[4] Z Katz,[5] C Boehme,[6] [1]FIND India, TB, New Delhi, India, [2]Central TB Division, Ministry of Health and Family Welfare GoI, New Delhi, India, [3]National Tuberculosis Institute, Ministry of Health and Family Welfare GoI, Bengaluru, India, [4]FIND India, TB, Bengaluru, India, [5]FIND, TB, Geneva, Switzerland, [6]FIND, *, Geneva, Switzerland.
e-mail: tarak.gshah@finddx.org

Background and challenges to implementation: External quality assessment (EQA) for the Xpert MTB/RIF assay is part of quality system required for clinical and laboratory practice. It ensures reliable and accurate diagnosis, thereby appropriate patient management.
There has been a rapid scale up in deployment of Xpert MTB/RIF in last few years. However, most of the countries are not implementing its EQA due to non-realisation of need and operational challenges.
India has ~1300 Xpert MTB/RIF machines under NTP and private sector and in collaboration with Foundation for Innovative New Diagnostics (FIND), CDC and WHO India piloted EQA in over 200 randomly selected public and private sector sites.
Intervention or response: A total of 209 sites (188 public; 21 private) were included. Proficiency testing (PT) panels were manufactured using CDC's Dried Tube Specimen technology during Feb-May 2018 at National Tuberculosis Institute Bangalore (see figure). Panels were dispatched to the sites in mid-July 2018. The sites tested panels and communicated results. Results were analyzed and shared with the sites in Aug 2018.

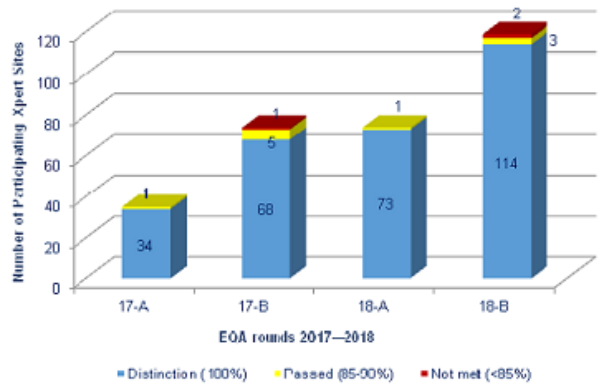


[Manufacturing of PT panels using CDC's DTS technology at NTI-ICELT Lab]

Results and lessons learnt: Of the 209 sites, 10 sites did not participate due to non-functional equipment (n=6) and panel not received (n=4). Average time for receipt of samples by sites was 3.5 days and from sample receipt to results reporting was 1.5 days.

198 out of 199 sites (99.5%) passed PT (>80% concordance). 1 site failed PT due to high error rate in one module. Carry over contamination during sample processing was observed at 2 sites. 24 machines were not calibrated. Cartridge storage condition was a concern at two sites. Quality indicators' review suggested 8 sites with 10% or more uninterpretable results. Corrective actions were carried out.

Conclusions and key recommendations: EQA for Xpert MTB/RIF can be implemented in high burden resource constrained settings. It is critical for monitoring quality and identifying non-conformities related to process, calibration, storage of consumables etc. which can be easily addressed.



[Step-wise Expansion and Participant's performance in the Xpert EQA program in Vietnam 2017-2018]

OA-15-413-01 Establishing a responsive and timely national EQA programme for Xpert MTB/RIF testing in Viet Nam

TH Dinh,[1,2] VH Nguyen,[1,2] NV Gummar,[3] VN Nguyen,[4,5]
[1]National Lung Hospital, Department of Microbiology, Ha Noi, Viet Nam, [2]National TB Control Program, Lab Unit, Ha Noi, Viet Nam, [3]Foundation for Innovative & New Diagnostics, Microbiology, New Deli, India, [4]National Lung Hospital, Board of Directors, Ha Noi, Viet Nam, [5]National TB Control Program, Steering Committee, Ha Noi, Viet Nam.
e-mail: hungmtb75@gmail.com

Background and challenges to implementation: To ensure the quality of Xpert MTB/RIF (Xpert) testing the Vietnam National Tuberculosis Program (VNTP) began participating in the US Centers for Disease Control and Prevention (CDC) Xpert MTB/RIF Performance Evaluation Program in 2013. Apart from benefits of a proficiency testing (PT) program, challenges included long turnaround times, occasional unstable panel quality (degradation of DNA) thought to be because of long transport/customs clearance times and lack of long-term program sustainability.

Intervention or response: Building upon existing TB laboratory infrastructure and quality management systems, and with CDC transfer of Dried Tube Specimen (DTS) panel technology and PT program management training, VNTP established an in-country PT program for Xpert in a step-wise fashion: training, pilot implementation and validation. Staff gained skills in PT panel production and prepared for ISO:IEC 17043 PT provider accreditation.

Results and lessons learnt: VNTP led four rounds of PT, rapidly scaling-up coverage of Xpert sites from 35 in 2017 to 119 in 2018 (Figure).

Over two years, only 16/1510 (1%) were discordant results. Site performance was excellent with 98-100% of sites passing. Panels demonstrated stability, as indicated by an average low false negative result rate of < 0.2% (2/1059 positive PT samples). Turnaround time from panel distribution to final report release dropped from 4 months (external provider) to 5 weeks (VNTP) for immediate root cause analysis. The National TB Reference Laboratory (NTRL) maintained ISO-15189 accreditation and recently achieved ISO:IEC-17043 accreditation in March 2019 for the Xpert PT program. These factors contributed to establishment of a sustainable program, allowing VNTP to expand services regionally, providing external EQA to Myanmar in 2018 (80 sites).

Conclusions and key recommendations: Establishing in-country Xpert PT expertise is feasible, improving timeliness and enabling rapid program response to unexpected results. The Vietnam NTRL has become an accredited regional resource, while dramatically increasing PT services from 35 laboratories to 199 within two years.

OA-15-414-01 Implementation of GeneXpert proficiency testing scheme using dry tube specimen for Xpert MTB/RIF assay in Uganda

J Kabugo,[1] [1]National Tuberculosis Control Program, National Disease Control, Kampala, Uganda.
e-mail: dennismujuni.n@gmail.com

Background: Bacteriological confirmation of TB and Rifampicin Resistance using GeneXpert MTB/RIF assay has rapidly expanded worldwide since 2010 but regular verification assessment through proficiency testing (PT) schemes to monitor technical competency and improve the quality of testing to yield reliable results are often lacking in many settings. Conventional Xpert PT programs use liquid and culture spots which require stringent conditions for storage, transportation and other challenges like cross contamination. A novel, reliable and user friendly method, based on dried tube specimens (DTS), was adopted that can support independent assessment of sites performing Xpert MTB/RIF testing.

Methods: DTS were prepared from standard control isolates inactivated using sample reagent buffer (SR) by drying 100 µl of bacterial dilution inside biosafety cabinet at room temperature for seven days. Panel was validated for the expected results, Cycle Threshold (CT) Mean and standard deviation [SD]). A set of five DTS samples were dispatched to 133 GeneXpert MTB/RIF assay testing sites. Indicators from results' feedback were centrally evaluated and these included Turn Around Time (TAT), return rate, satisfactory performance, non-interpretable results (errors, invalids, no results) reported and participants' consensus CT mean and standard deviation. Results were submitted through mail and couriers.
Results: Result return rate was at 94.74% (126/133) and only 5.26% (7/133) did not return their results. Satisfactory performance (score of ≥80%) was at 95.23% (120/126). Errors and invalids rate was at 1.4%(9/629). Participants' consensus CT mean was within medium range same as the validated results.
All result submission was done within six weeks and majority of the feedback 75.2% (94/125) was submitted through mail and only 24.8% (31/125) used the courier.
Conclusions: Results demonstrate that the DTS is a convenient, user friendly and practical method to use in assessing the proficiency testing of the Xpert MTB/RIF assay across all settings.

OA-15-415-01 Verifying the use of Xpert MTB/RIF Ultra for diagnosing extra-pulmonary tuberculosis in South Africa

P Da Silva,[1,2] A David,[1] P Marokane,[2] N Bosman,[3,4] S Naidoo,[4] C Hayes,[5] T Dolby,[6] W Stevens,[1,2] L Scott,[1] [1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Service, National Priority Programmes, Johannesburg, South Africa, [3]University of the Witwatersrand, Clinical Microbiology and Infectious Diseases, Johannesburg, South Africa, [4]National Health Laboratory Service, Clinical Microbiology, Johannesburg, South Africa, [5]National Health Laboratory Service, Mycobacteriology, Port Elizabeth, South Africa, [6]National Health Laboratory Service, Mycobacteriology, Cape Town, South Africa. e-mail: pedro.dasilva@nhls.ac.za

Background: In 2013, South Africa (SA) extended Xpert MTB/RIF (Xpert) testing to include extra-pulmonary tuberculosis (EPTB) specimen types following World Health Organisation guidance. With endorsement of the more sensitive Xpert MTB/RIF Ultra (Ultra) in 2017, EPTB specimen recommendations remained unchanged except for 'trace' results (lowest detectable amount of M. tuberculosis, Mtb), interpreted as true Mtb positive. At transition from Xpert to Ultra, a verification for Ultra EPTB specimen testing was conducted in the routine diagnostic setting.
Methods: The verification was conducted at three diagnostic laboratories (October 2017-March 2018) as a direct comparison between Xpert and Ultra on the same EPTB specimen. EPTB specimens were processed by addition of sample reagent (SR) buffer in a 2:1 (SR buffer:specimen) ratio, if initial specimen raw volume >1.5ml. Tissue was pre-processed by grinding/homogenising in 2ml Phosphate Buffered Saline and SR buffer added in the same ratio to 1.5ml of tissue homogenate. The final volume of all EPTB specimen types was split, 2ml for Xpert and 2ml for Ultra testing. Mtb detection rate (Mtb detected and 'trace'), rifampicin susceptibility, and error rates between Xpert and Ultra were compared.
Results: 265 EPTB specimens were tested: 148 (50%) cerebrospinal fluids, 50 (19%) fine-needle aspirates, 37 (14%) fluids, 22 (8%) pus, 7 (3%) tissues, and 1 (0.3%) urine. Overall, Mtb detection rate was 3.39% higher with Ultra due to detection of 10 'trace' results. Mtb positivity differences between Ultra and Xpert varied by specimen type with highest increase observed for tissue (13.67%), fluids (8.11%), and pus (4.54%). For 23 specimens with directly comparable rifampicin susceptibility results, 100% concordance was observed between versions. Although Ultra detected three additional errors than Xpert, this was deemed insignificant.
Conclusions: Ultra improves detection of Mtb across EPTB specimen types. Ultra was deemed 'fit-for-purpose' for EPTB specimen testing and implemented in SA's TB program.

OA-15-416-01 Discordant repeat Xpert MTB/RIF results from initially resistant low bacterial load sputa cannot simply be rejected

JCS Ngabonziza,[1,2] W Mulders,[2] B Ushizimpumu,[1] C Merle,[3,4] G Torrea,[2] P Supply,[5] D Affolabi,[6] A Van Deun,[2,7] L Rigouts,[2,8] BC de Jong,[2] [1]Rwanda Biomedical Center, National Reference Laboratory Division, Kigali, Rwanda, [2]Institute of Tropical Medicine, Mycobacteriology Unit, Antwerp, Belgium, [3]UNICEF/UNDP/World Bank/World Health Organisation, Special Programme on Research and Training in Tropical Diseases (TDR), Geneva, Switzerland, [4]London School of Hygiene & Tropical Medicine, Tropical Medicine, London, United Kingdom, [5]Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 - UMR 8204 -CIIL - Center for Infection and Immunity of Lille, Biomedical Sciences, F-Lille, France, [6]Centre Nationale de Pneumo-Phtisiologie (CNHPP), Laboratoire de Référence des Mycobactéries, Cotonou, Benin, [7]International Union Against Tuberculosis and Lung Disease, Biomedical Sciences, Paris, France, [8]University of Antwerp, Biomedical Sciences, Antwerp, Belgium. e-mail: jclaude.ngabonziza@rbc.gov.rw

Background: In Rwanda universal TB drug susceptibility testing (DST) has been achieved with Xpert MTB/RIF assay. A high number of discrepancies were ob-

served between the initial rifampicin resistant (RR) test and a repeat Xpert performed at the National Reference Laboratory (NRL). We aimed to investigate whether these discrepancies are related to false RR associated with a very low bacterial load or heteroresistance. All patients received RR-TB treatment.
Methods: Deeplex-MycTB (Lille, France) target sequencing was used to identify down to 3% mutant subpopulation (heteroresistance). Culture-positive samples were also tested by phenotypic DST (pDST, Löwenstein-Jensen proportion method).
Results: 140 consecutive initial RR had Xpert repeated on a new sputum: 47 (34%) were TB negative, 47 (34%) rifampicin susceptible (RS), 45 (32%) confirmed RR-TB and one was rifampicin indeterminate. Of the repeat negative and RS sputa, 86/94 (91.5%) had a very low bacterial load initially, versus 4/45 (8.9%) of the confirmed RR. Deeplex confirmed 6/6 Xpert concordant RR and detected heteroresistance with 30-35% of *rpoB* 450Leu mutant population in 3/17 (18%) RR/RS by initial/repeat Xpert. Additionally, pDST revealed RR in another 4/35 (11%) Xpert RR/RS or RR/Neg sputa not subjected to Deeplex. On the other hand, pDST missed 6/40 (15%) Xpert RR/RR cases. Among those 2/5 were identified by Deeplex as fixed disputed mutation Asp435Tyr, while three other Asp435Tyr were RR by pDST. Overall, repeat Xpert and pDST failed to confirm 13.5% of true RR detected initially.
Conclusions: Bacterial load and heteroresistance of successive sputa may vary excessively. Accepting the result of a single repeat Xpert result causes excessive loss of true RR. For doubtful RR paucibacillary specimens, heteroresistance will be revealed most often by accepting at least one more RR result among three repeat Xpert tests as conclusive. Repeat false RR are far less likely to occur.

OA-15-417-01 DR-TB or maybe melioidosis, this is the question: importance of adequate laboratory resources, beyond TB detection in the tropics

J Warner,[1] D Pelowa,[2] B Currie,[3,4] [1]James Cook University, Australian Institute of Tropical Health and Medicine, Townsville, QLD, Australia, [2]Balimo District Hospital, Laboratory, Balimo, Papua New Guinea, [3]Menzies School of Health Research, Global and Tropical Health Division, Darwin, NT, Australia, [4]Royal Darwin Hospital, Infectious Diseases, Darwin, NT, Australia. e-mail: jeffrey.warner@jcu.edu.au

Background: Advanced diagnostics (including GeneXpert) have revolutionised TB laboratory diagnostics, increasing the positive and negative predictive value of PTB and EP-TB diagnoses, in a clinically relevant timeframe.
However, there is an imbalance between the diagnostic capacities of TB and the causes of pyrexia of unknown origin in rural communities in the tropics. Melioidosis, caused by *Burkholderia pseudomallei* is endemic in tropical regions and is increasingly reported to mimic TB in its presentation. In TB endemic communities, smear negative TB and treatment failure may be mistakenly attributed to DR-TB rather than melioidosis. Here, we report a program of laboratory strengthening in Papua New Guinea (PNG) that has revealed melioidosis mimicking TB.
Methods: Melioidosis case detection was undertaken at 2 sites as part of PNG laboratory capacity building: (i) in Balimo, Western Province, a rural community with high melioidosis rates and; (ii) at the Central Public Health Laboratory (CPHL) in the national capital, Port Moresby where melioidosis reports are rare. Presenting patients were assessed as per local clinical protocols with samples submitted for bacteriological analysis.
Results: During a 2-year period, 10 cases of melioidosis presented at Balimo Hospital, however 5/10 were initially diagnosed as AFB negative TB and commenced TB treatment. The case fatality rate was 40%, attributable to a delay in melioidosis diagnosis and directed treatment. At CPHL, sputa from 529 suspected TB cases were cultured for *B.pseudomallei* and stained for AFB; 417 were AFB negative with one culture positive for *B.pseudomallei*, representing the predicted proportion of melioidosis cases as 4.6% (95% CI 0.19 - 24.6).
Conclusions: Melioidosis can mimic TB and without adequate diagnostic facilities, which are rare in rural health facilities, it can go undiagnosed resulting in high case fatality rates. In resource poor health systems in the tropics melioidosis should be considered in the differential diagnosis of smear or GeneXpert negative TB.

OA-17-C3 MDR-TB treatment outcomes

OA-17-418-01 Time of culture conversion and risk of subsequent death or treatment failure in multidrug-resistant tuberculosis patients in South Africa

JR Campbell,[1,2] N Ndjeka,[3] Z Lan,[2] D Menzies,[2] [1]McGill University, Department of Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]National Department of Health, Drug-Resistant TB Programme, Pretoria, South Africa. e-mail: jonathon.campbell@mail.mcgill.ca

Background: Multidrug-resistant tuberculosis (MDR-TB) treatment requires timely adjustments based on patient response. A commonly monitored response is time of culture conversion.
However how long after treatment initiation clinical intervention should occur in patients who remain culture-

positive is uncertain. We assessed the association of time of culture conversion with later death or treatment failure.

Methods: We utilized data from individual patients treated with longer (intended duration ≥18 months) MDR-TB regimens in South Africa, who had monthly microbiologic monitoring and were registered in the electronic MDR-TB registry (EDRWeb) as initiating treatment from 2010-2015, inclusive. Further, included patients had pre-treatment fluoroquinolone drug susceptibility testing and known HIV-status as these were markers of adherence to programmatic guidelines. Finally, we excluded patients lost-to-follow-up or with treatment < 2 months. Date of culture conversion was considered the earliest of two-consecutive negative cultures taken more than 4 weeks apart. End-of-treatment outcomes were as reported by clinicians within EDRWeb. We calculated the crude odds ratio and sensitivity and specificity of failure to achieve culture conversion by months 2, 4, 6, and 8, to predict subsequent death or treatment failure.

Results: We included 9113 culture-positive MDR-TB patients treated for an average of 21 months; 7.4% had extensively-drug resistant TB and 63.2% were HIV-positive. In total, 1794 (19.6%) patients died or experienced treatment failure. The majority of patients culture-converted in the first four months of treatment. Compared to those that had converted, odds of death or treatment failure in those who had not converted, consistently increased over treatment. Comparatively, sensitivity and specificity of these measures appeared to be most balanced at month-four, with minimal gains in diagnostic performance after month-six (**Table**).

Time point	Number remaining on treatment	Number still culture-positive (%)	Odds ratio of future death or treatment failure in those not converted (95% confidence interval)	Sensitivity of non-conversion for future death or treatment failure (95% confidence interval)	Specificity of non-conversion for future death or treatment failure (95% confidence interval)
Month 2	9113	5576 (61%)	2.8 (2.4, 3.1)	78% (76%, 80%)	43% (42%, 44%)
Month 4	9109	2189 (24%)	6.2 (5.5, 6.9)	55% (53%, 57%)	84% (83%, 84%)
Month 6	9054	1203 (13%)	13.1 (11.4, 15.0)	45% (42%, 47%)	94% (94%, 95%)
Month 8	8860	789 (9%)	27.0 (22.6, 32.4)	40% (37%, 42%)	98% (97%, 98%)

[Patient Response and Diagnostic Performance of Culture Conversion at Various Time Points During Treatment]

Conclusions: Culture conversion is a useful marker for treatment prognosis. Appropriate clinical action in patients who are culture-positive at four-months appears to balance subsequent risk of death or treatment failure with diagnostic performance.

OA-17-419-01 Final treatment outcomes for the treatment of rifampicin-resistant tuberculosis using delamanid in a high HIV-burden setting in South Africa

E Mohr,[1] A Reuter,[1] V De Azevedo,[2] V Mudaly,[3] Y Kock,[4] L Trivino-Duran,[5] R Acquah,[1] P Isaakidis,[6] G Ferlazzo,[6] [1]Medecins Sans Frontieres, DR-TB, Khayelitsha, South Africa, [2]City of Cape Town Department of Health, Primary Health Care Health Department, Cape Town, South Africa, [3]Provincial Department of Health-Western Cape, Health Programmes, Cape Town, South Africa, [4]National Department of Health, DR-TB Programme, Johannesburg, South Africa, [5]Medecins Sans Frontieres, Coordination Office, Cape Town, South Africa, [6]Medecins Sans Frontieres Southern Africa Medical Unit, HIV/TB/HepC, Cape Town, South Africa.
e-mail: msfocb-khayelitsha-drtb-epi@brussels.msf.org

Background: In the 2018 World Health Organization guidance delamanid (DLM) has been classified as a group C drug for the treatment of rifampicin-resistant tuberculosis (RR-TB). More evidence regarding its use is needed.

Methods: This was an observational cohort of patients who started RR-TB treatment regimens containing DLM from February 2015-March 2018 in Khayelitsha, South Africa. Six-month sputum-culture-conversion (SCC), final treatment outcomes, and serious-adverse-events (SAEs) were described.

Results: Overall, 94 patients initiated RR-TB treatment containing DLM; 58 (62%) were male, the median age was 35 (IQR 29-43), 71 (76%) were HIV-positive (56% HIV-positive had a baseline CD4 count< =200 cells/mm3). Thirty-one (33%) patients had RR-TB with fluoroquinolone-resistance, 16 (17%) had previous RR-TB treatment, and 33 (35%) received regimens including bedaquiline. The main indication for DLM was intolerance to second-line TB drugs (n=50, 53%). Fifty-two (55%) patients had pulmonary TB and were culture positive at DLM initiation; 43 (83%) had SCC within 6-months.

Fifty-one (54%) patients were successfully treated, while 21 (22%), 11 (12%), five (5%), four (4%), and two (2%) were lost to follow-up (LTFU), died, were transferred-out, failed treatment, or were still on treatment and clinically well, respectively. Poor RR-TB treatment outcomes (LTFU, death, and treatment failure) were more common among HIV-positive patients (46% vs 13%, p=0.0058).

There were 62 SAEs in 27 (29%) patients. Twenty one SAEs in 14 (15%) patients were assessed as possibly related to DLM leading to discontinuation of DLM in five patients.

Conclusions: DLM for the treatment of RR-TB appeared to be both a safe and effective treatment option in this cohort of complex patients with high rates of HIV co-infection; however, the rates of death and LTFU in this cohort were high, particularly among those HIV co-infected.

Broader and earlier use of new drugs and innovative psychosocial interventions are needed to increase the chance to cure RR-TB patients.

OA-17-420-01 High dose isoniazid for MDR-TB treatment: is it worth trying?

M Bachir,[1] L Guglielmetti,[1,2] N Veziris,[2,3] F Brossier,[1,2] J Jaffré,[1,2] V Jarlier,[1,2] W Sougakoff,[1,2] J Robert,[1,2] A Aubry,[1,2] [1]Sorbonne Université, Université Pierre et Marie Curie 06, Unité 1135, Team E13 (Bactériologie), CR7 INSERM, Centre d'Immunologie et des Maladies Infectieuses, Paris, France, [2]APHP, Centre National de Référence des Mycobactéries et de la Résistance des Mycobactéries aux Antituberculeux (CNR-MyRMA), Bactériologie-Hygiène, Hôpitaux Universitaires Pitié Salpêtrière-Charles Foix, Paris, France, [3]AP-HP, Hôpitaux Universitaires de l'Est Parisien, Centre National de Référence des Mycobactéries et de la Résistance des Mycobactéries aux Antituberculeux, Département de Bactériologie, Paris, France.
e-mail: marwa.bachir@gmail.com

Background: The WHO recommends the use of high-dose isoniazid (HdH) for the treatment of rifampicin-resistant tuberculosis (RR-TB) 1) as part of the currently recommended standardized short-course regimen (SCR), among those without resistance-conferring mutations for fluoroquinolones and injectables; and 2) as part of the conventional regimen, in the absence of mutations that confer high-level isoniazid resistance (i.e. in *katG*). Our objective was to assess the interest of HdH among RR-TB patients who are eligible to receive it according to WHO recommendations by measuring the prevalence of high-level isoniazid resistance within this population.
Methods: A retrospective analysis of the French National Reference Center for Mycobacteria database was performed. All RR-TB cases diagnosed in France from 01/01/2010 to 31/12/2017 and with available molecular testing results for *katG* (GenoType MTBDRplus), *gyrA* and *rrs* (GenoType MTBDRsl), were included. Eligibility for the SCR was defined as absence of mutations in *gyrA* and *rrs*. Indication for HdH in conventional regimens was defined as absence of *katG* mutation. Phenotypic resistance to isoniazid and high-level isoniazid resistance were defined as resistance to 0.2 mg/L and 1.0 mg/L in Lowenstein-Jensen medium, respectively.
Results: Overall, 604 rifampicin-resistant cases were assessed, including 601 with isoniazid resistance (Table). 443 (73%) cases would receive HdH according to WHO guidelines, 432 as part of SCR and 11 as part of the conventional regimen. According to phenotypic testing, HdH would be effective in only 40 (9%, 95% Confidence Interval: 7%-12%) of these cases.

		Patients eligible for conventional regimen	
Phenotypic Isoniazid Drug Susceptibility Tests Results	Patients eligible for shortcourse regimen, including HdH	Eligible for HdH (no katG mutation)	Not eligible for HdH (katG mutation)
Low-level isoniazid resistance or isoniazid susceptibility	35 (8%)	5 (45%)	1 (1%)
High-level isoniazid resistance	397 (92%)	6 (55%)	160 (99%)
Total	432 (100%)	11 (100%)	161 (100%)

[Table. Isoniazid resistance levels and indications for high-dose isoniazid (HdH) treatment among 604 rifampicin-resistant tuberculosis cases.]

Conclusions: In our cohort, the majority of patients would be prescribed HdH according to latest WHO recommendations based on results of current rapid molecular tests. However, HdH is likely to be effective in less than 10% of those patients based on phenotypic results. Overall, the role of HdH may be limited in our setting.

OA-17-421-01 The addition of linezolid to bedaquiline-containing multidrug-resistant tuberculosis treatment regimens

N Ndjeka,[1] JR Campbell,[2] R Romero,[3] S Katz,[4] D Menzies,[2] [1]National Tuberculosis Control Program, Department of Health, Pretoria, South Africa, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]Northern Cape Department of Health, DCST Namakwa District, Namawaka, South Africa, [4]Northern Cape Department of Health, Provincial Tuberculosis Programme, Kimberley, South Africa. e-mail: ndjeka@esnet.co.za

Background: The World Health Organization recently made a landmark, radical change to the multidrug-resistant tuberculosis (MDR-TB) guidelines. The injectable agents, previously regarded as core drugs, are no longer recommended. Bedaquiline, linezolid, and moxifloxacin/levofloxacin, are now the main drugs recommended in the treatment of MDR-TB with longer (intended duration ≥18 months) regimens. However, there is limited data on use of bedaquiline in combination with linezolid. We analyzed treatment outcomes among patients receiving bedaquiline with or without concomitant use of linezolid in South Africa.
Methods: Patients with end-of-treatment outcomes beginning treatment in 2014-2015 who were registered in the national electronic MDR-TB database (EDRWeb) and treated with an individualized, bedaquiline-containing longer regimen were included. We utilized a case-control approach for patients with and without concomitant linezolid use. Patients were matched exactly, without replacement, on presence of resistance to fluoroquinolones or second-line injectables, HIV, province of treatment, and concomitant treatment with

moxifloxacin/levofloxacin, clofazimine, and/or cycloserine/terizidone. We further used nearest neighbor (caliper = 0.02) based propensity score matching for age, previous treatment, acid fast bacilli smear positivity, and total number of drugs received. We calculated the risk difference and associated 95% confidence interval (95%CI) for the outcome of success (cure or treatment completion) between patients treated with and without linezolid.

Results: Overall, 269 matched pairs were obtained. The median (IQR, interquartile range) age was 35 (28-42) years, the median (IQR) treatment duration was 20.4 (15.4-23.5) months, and 74% were HIV-positive. Treatment success among patients without concomitant linezolid was 54.2%. Comparatively, treatment success was 67.6% among patients receiving concomitant linezolid, for an improvement of 13.4% (95%CI: 5.2% to 21.5%).

Conclusions: The addition of linezolid to bedaquiline-containing MDR-TB regimens was associated with significant improvement in treatment success in South Africa. While our study represents a small sample size, it provides further evidence supporting linezolid as a key component of MDR-TB regimens.

OA-17-422-01 An individual patient data meta-analysis of the effect of concomitant health risks on multidrug-resistant tuberculosis treatment outcomes in HIV-negative patients

JR Campbell,[1,2] ED Chan,[3] D Falzon,[4] A Trajman,[5] ND Goswami,[6] CC Leung,[7] SM Marks,[6] P Viiklepp,[8] DS Rodrigues,[9] D Menzies,[2] The Collaborative Group for the Meta-Analysis of Individual Patient Data in MDR-TB Treatment 2019 [1]McGill University, Department of Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]National Jewish Health / Rocky Mountain Regional Veterans Affairs Medical Center, Department of Medicine, Denver, CO, United States of America, [4]World Health Organization, Global TB Programme, Geneva, Switzerland, [5]Federal University of Rio de Janeiro, Internal Medicine Post-Graduate Program, Rio de Janeiro, RJ, Brazil, [6]US Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, Atlanta, GA, United States of America, [7]Chinese University of Hong Kong, Stanley Ho Center for Emerging Infectious Diseases, Shatin, Hong Kong, [8]National Institute of Health Development, Estonian Tuberculosis Registry, Tallinn, Estonia, [9]Instituto Clemente Ferreira, Secreteria de Estado da Saude, São Paulo, SP, Brazil.
e-mail: jonathon.campbell@mail.mcgill.ca

Background: Tuberculosis that is resistant to isoniazid and rifampicin (multidrug-resistant tuberculosis; MDR-TB) restricts treatment options and is associated with worse outcomes than tuberculosis susceptible to these drugs. Patient factors may also modulate the chance of cure, treatment failure, death, or loss to follow-up (LTFU). We analysed the effect of several modifiable health risks on MDR-TB treatment outcomes in HIV-negative patients receiving individualized longer regimens.

Methods: We compiled individual patient data for 9112 HIV-negative MDR-TB patients from 53 studies in 40 countries. Meta-analyses for effects on outcomes (**Table**) were conducted on patients with complete information on health risks: diabetes mellitus (DM), smoking, alcohol abuse, underweight body mass index (BMI; < 18.5kg/m^2), and overweight/obese BMI (≥25.0kg/m^2). Propensity-score based adjustment was made for country income group, treatment year, age, sex, disease severity, past and present treatment, and drug resistance, with a study-level random effect. Explanatory variables with missing data were imputed. Associations with 95% confidence intervals (95%CI) were expressed as adjusted odds ratios (aOR) referenced to groups without the health risk.

Results: Of 9112 MDR-TB patients, 6553 (72%) had information on at least one health risk. Patients included in this subset were more likely to be from high-income countries and have severe disease. Being underweight was associated with the largest risk for death (aOR 3.3; 95%CI 2.4-4.6) and alcohol abuse had the largest risk for treatment failure/relapse (aOR 1.7; 95%CI 1.2-2.6). No statistically significant association between health risks and LTFU occurred. Notably, DM was not associated with any of the unfavourable outcomes evaluated (**Table**).

			Adjusted odds ratios (95% confidence interval)		
Health Risk	Patients included (Number of studies)	% Patients with Health Risk	Treatment failure or relapse vs. success	Death vs. success	Loss to follow-up vs. all other outcomes
Diabetes Mellitus	5681 (37)	12.7%	1.0 (0.6-1.5)	0.8 (0.5-1.2)	0.9 (0.6-1.2)
Smoking	4349 (25)	38.6%	1.4 (1.04-1.9)	1.1 (0.8-1.4)	1.0 (0.8-1.2)
Alcohol Abuse	4300 (26)	28.2%	1.7 (1.2-2.6)	1.5 (1.1-2.1)	1.3 (0.97-1.6)
BMI <18.5 kg/m^2	4496 (26)	35.9%	1.5 (1.04-2.0)	3.3 (2.4-4.6)	0.9 (0.8-1.2)
BMI ≥25 kg/m^2	3329 (26)	13.4%	1.2 (0.7-2.2)	0.5 (0.2-1.00)	0.9 (0.6-1.3)

[Risk of Unfavourable Outcomes in Patients with Concomitant Health Risks]

Conclusions: Among non-HIV health risks analysed, underweight BMI and alcohol abuse were the most significantly associated with unfavourable outcomes. It remains to be determined if early intervention to control these health risks can improve the efficacy of an optimised MDR-TB regimen. Future analyses should also evaluate the interactions of multiple health risks.

OA-17-423-01 Reduced time to culture conversion in patients with MDR-TB is associated with genotypic susceptibility but not minimum inhibitory concentration of pyrazinamide

J Kuhlin,[1,2] L Davies Forsman,[1,2] M Mansjö,[3] M Jonsson Nordvall,[4] M Wijkander,[3] R Groenheit,[3] J Werngren,[3] T Schön,[4,5] J Bruchfeld,[1,2] [1]Karolinska Institutet, Division of Infectious Diseases, Department of Medicine Solna, Stockholm, Sweden, [2]Karolinska University Hospital, Department of Infectious Diseases, Stockholm, Sweden, [3]Public Health Agency of Sweden, Department of Microbiology, Stockholm, Sweden, [4]Linköping University Hospital, Department of Medical Microbiology, Linköping, Sweden, [5]Kalmar County Hospital, Department of Clinical Microbiology and Infectious Diseases, Kalmar, Sweden.
e-mail: johanna.kuhlin@ki.se

Background: Pyrazinamide (PZA) is important in the treatment of drug-susceptible tuberculosis (TB), however it's role in multidrug-resistant TB (MDR-TB) is less clear. The objective of the study was to assess if minimum inhibitory concentration (MIC) and the absence of established *pncA* resistance mutations was associated with time to sputum culture conversion (SCC) and treatment outcome in patients with MDR-TB treated with PZA.

Methods: We collected demographic, microbiological and clinical data from all consecutive patients with MDR-TB in Sweden between 1992 and 2014. PZA MIC were performed in isolates from patients treated with a PZA-containing MDR-TB regimen based on WHO recommendations using the BACTEC MGIT 960 system (range 8-512 mg/L, N=62). Analysis of established drug resistance mutations in the *pncA* gene was performed by whole genome sequencing. We used a Cox-regression model for statistical analysis.

Results: Of all 158 patients in the cohort, 54.4% (N=86) had a PZA resistant strain and 50.3% (N=79) were treated with PZA. Median PZA treatment length for patients with PZA susceptible strains were 437 days (IQR 94-583). For patients treated with PZA, lower increments of PZA MIC for PZA susceptible isolates was neither associated with time to SCC in adjusted analyses nor final treatment outcome in crude analyses (aHR 0.86 (95% CI 0.63-1.16), p=0.31, N=29 and HR 0.96 (95% CI 0.60-1.55), p=0.88, N=53, respectively). However, genotypic susceptibility in patients treated with PZA showed a predominantly positive association with shortened time to SCC in adjusted analyses (aHR 1.58 (95% CI 0.97-2.56) p=0.07, N=89), compared to patients with genotypic PZA resistant strains or those without PZA treatment.

Conclusions: In patients with MDR-TB who were treated with a PZA-containing regimen, we found that an absence of established resistance mutations in *pncA* may be associated with a shorter time to SCC. However, no association with SCC was detected for MICs of PZA susceptible isolates.

OA-17-424-01 Short treatment regimen as a tool to increase access and improve outcomes of DR-TB care in Afghanistan

A Mesic,[1] J Fernhout,[1] W Hatam Khan,[2] T Billiew,[2] E Hnin Hnin Phyu,[3] S Ishaq,[3] T Ukasha,[3] M Khaled Seddiq,[4] H Khan Amirzada,[5] A Oraegbu,[3] [1]Médecins Sans Frontières, Operational Center Amsterdam, Amsterdam, Netherlands, [2]Médecins Sans Frontières, Operational Center Amsterdam, Kabul, Afghanistan, [3]Médecins Sans Frontières, Operational Center Amsterdam, Kandahar, Afghanistan, [4]Ministry of Public Health (MoPH), National Tuberculosis Programme, Kabul, Afghanistan, [5]Ministry of Health Public Health (MoPH), National Tuberculosis Programme, Kabul, Afghanistan.
e-mail: anita.mesic@amsterdam.msf.org

Background and challenges to implementation: Long DR-TB regimens limit the number of patients that have access to treatment and can remain in care until the treatment ends. The study presents Médecins Sans Frontières' experiences with implementation of DR-TB care, delivered by patient-cantered models in Kandahar, Afghanistan.

Intervention or response: The short treatment regimen (STR) for MDR-TB in Kandahar started in 2016, together with access to individualised long regimens including new anti-tuberculosis drugs, as recommended by the national guideline. Ambulatory care is provided and family-supported self-administered treatment during the oral continuation phase. This retrospective cohort study uses routinely collected programmatic data and includes DR-TB patients registered between June 2016 and April 2019.

Results and lessons learnt: 107 patients with rifampicin resistant TB were registered (61% female, median age 30 years (IQR 5-43)). Half of the cohort originates from outside of Kandahar. 82/107 (77%) patients started on DR-TB treatment. Reasons provided for treatment refusal (17/24) included distance from home, security, and cultural challenges for women. 34/82 was provided STR and 81% (21/26) was cured during the study period; one patient died and 4 were lost to follow up (LFU) during intensive phase. Individualised regimen was given to 48 patients, due to: pre or XDR-TB (n=22; 46%), children (n=10; 21%), kanamycin intolerance (n=10; 21%), pregnancy (n=2; 4%) or previous exposure to DR-TB treatment (n=4; 8%). The long regimen group achieved a 35% success rate; 47% died (n=8) and three were LFU. Most deaths (n=5) occurred among patients who refused to continue the treatment due to distance from home and LFU occurred during the intensive phase.

Conclusions and key recommendations: In order to provide access to effective treatment for all TB patients in contexts similar to Afghanistan, there is need to investigate all-oral, short and better-tolerated regimens for all types of DR-TB and to innovate models of care that empower patients and their communities.

OA-17-425-01 Unfavourable treatment outcomes amongst Vietnamese non-MDR-TB retreatment patients are not driven by low antibiotic exposure

LT Luyen,[1] TVA Nguyen,[2] G Aljayyoussi,[3] C Nguyen,[4] VD Hoa,[5] NV Nhung,[6] BS Nhat,[1] D Sloan,[3,7] S Ward,[3] G Biagini,[3] [1]Vietnam National University, School of Medicine and Pharmacy, Hanoi, Viet Nam, [2]National Institute of Hygiene and Epidemiology, Laboratory of Tuberculosis, Hanoi, Viet Nam, [3]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom, [4]Hanoi Medical University, National Lung Hospital, Hanoi, Viet Nam, [5]Hanoi University of Pharmacy, Dept of Clinical Pharmacy, Hanoi, Viet Nam, [6]National Lung Hospital, Faculty of Tuberculosis and Lung Diseases, Hanoi, Viet Nam, [7]University of St Andrews, School of Medicine, St Andrews, United Kingdom.
e-mail: cuongoc@hmu.edu.vn

Background: Patients with pulmonary tuberculosis (TB) who are not cured by a first course of standard anti-TB therapy are at high risk of failure from re-treatment, even when multi-drug resistant (MDR) disease is not identified on re-presentation. In Vietnam, successful outcomes for non-MDR TB re-treatment patients are only reported in 60-80% of cases. Despite recently revised WHO guidelines, recommended management of such patients is not evidence based.
Methods: New and re-treatment adult Vietnamese patients with non-MDR pulmonary TB were recruited to a longitudinal cohort. MDR-TB cases were excluded by Xpert MTB/RIF and phenotypic drug susceptibility testing at baseline. Treatment was administered using standard WHO antibiotic regimens. Serial sputum samples were collected during the first 8 weeks. Bacteriological response was monitored according to time to culture conversion and rate of change in time-to-positivity of liquid culture.
Clinical outcomes were obtained from national programmatic data. Plasma drug concentrations were measured during week 2. Pharmacokinetic-pharmacodynamic relationships between antibiotic exposure and treatment response were assessed.
Results: 130 (77 "new" and 53 "re-treatment") patients were recruited. Bacterial clearance from sputum was slower in re-treatment patients. Three (5%) "re-treatment" patients failed therapy and four (7.55%) died compared to no failures and one (1.3%) death amongst "new" patients. There was no difference in plasma exposure to first-line antibiotics between groups. Respective median [5^{th} - 95^{th} percentile] 24h-AUC_{ss} for new and re-treatment patients were: rifampicin, 45.1 [30.3-84.4] vs. 55.8 [29.2-82.0] ug/mL.h; isoniazid, 13.9 [6.6-36.6] vs. 16.1 [5.2-38.3] ug/mL.h, pyrazinamide: 436.5 [292.6-686.1] vs. 435.9 [135.3-581.0] ug/mL.h, ethambutol: 21.4 [16.0 - 36.1] vs. 23.2 [11.1-40.2] ug/mL.h).
Conclusions: Bacteriological response and clinical outcomes are worse in re-treatment TB patients, even in the absence of acquired drug resistance. Pharmacokinetic variability does not explain this. Detailed analysis of clinical and microbiological co-variates to identify factors contributing to unfavourable outcomes amongst re-treatment patients is ongoing.

OA-18-C1 TB infection control and prevention across households, hospitals, workplaces and prisons

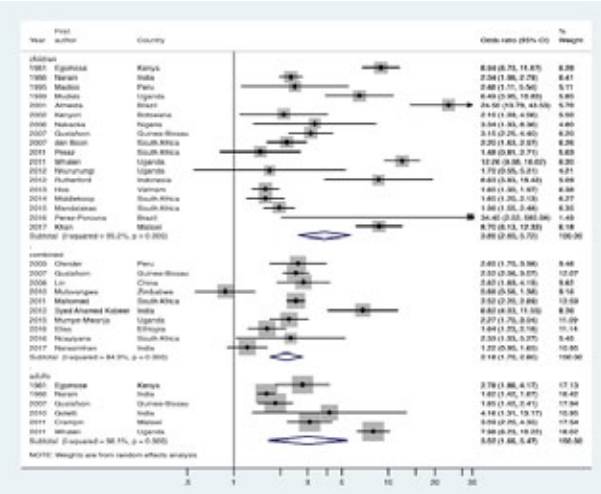
OA-18-426-01 Risk of latent Mtb-infection and tuberculosis disease in children and adults living in TB-affected households: systematic review and meta-analysis of high and low tuberculosis-burden settings

J Ellis,[1,2] R Mansukhani,[2] AS Karat,[2] K Fielding,[2] D Moore,[2] J Falconer,[2] C Bresges,[2] M Wadhwa,[2] E Monk,[2] RC Harris,[2] LSHTM TB Centre Systematic Review Team [1]University College London Hospitals NHS Trust, Hospital for Tropical Diseases, London, United Kingdom, [2]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom.
e-mail: rebecca.harris@lshtm.ac.uk

Background: Paediatric household contacts of tuberculosis cases are known to be at increased risk of *Mycobacterium tuberculosis* (*M.tb*) infection, but risk of tuberculosis disease and *M.tb* infection by age and epidemiological setting has not been quantified. We conducted a systematic review and meta-analysis to evaluate whether individuals living in TB-affected households are at higher risk of latent tuberculosis infection (LTBI) or active tuberculosis disease than the general population.
Methods: Four databases were systematically searched, and records screened for eligibility. Included studies reported on: household contacts of a tuberculosis patient and a non-exposed comparator group; and LTBI or tuberculosis disease incidence/prevalence in both groups. Summary effect estimates were calculated using a random-effects model, overall and stratified by age and epidemiological setting.
Results: 5,236 unique records were assessed; 72 primary research articles and two systematic reviews were included. In high-tuberculosis burden settings, the summary odds ratios (ORs) of TST-measured LTBI prevalence, comparing tuberculosis-affected households with a comparator population, were 3.9 (95% CI 2.6-5.7) in children and 3.0 (95% CI 1.7-5.5) in adults; though between-study heterogeneity was high (I^2 >84%), therefore summary estimates should be interpreted with caution.
In low-tuberculosis burden settings, ORs for TST-measured LTBI prevalence were 4.18 (95% CI 2.59-6.72) for adults and 4.15 (95% CI 3.38-5.10) for children/adults

combined. In high-burden settings, an increased risk of tuberculosis disease prevalence was found for both adults (OR 2.9, 95% CI 2.24-3.77) and children (OR 5.3, 95% CI 2.76-10.18) in tuberculosis-affected households.

Conclusions: Results demonstrate that individuals of all age groups in tuberculosis-affected households are at an increased risk of LTBI and tuberculosis disease, in high- and low-tuberculosis burden settings. This was particularly notable for LTBI in children and low-burden settings. Protective measures are needed within TB-affected households, and may be particularly important for children, and in low burden settings.



[Forest plot for studies in high burden countries based on unadjusted ORs and 95% CIs, using random effects, comparing TB infection prevalence measures by TST among children alone, adults alone, and combined, in TB-affected households versus the general population.]

OA-18-427-01 Risk of Mtb transmission to individuals living in congregate settings: a systematic review and meta-analysis

AS Karat,[1] M Woodman,[2] M Calderon,[3] N Castano-Villegas,[4] H Theodorou,[5] N McCreesh,[1] CJ Calderwood,[6] R Mansukhani,[1] RC Harris,[1] KL Fielding,[1] the LSHTM TB Centre Systematic Review Group [1]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom, [2]Bankstown-Lidcombe Hospital, Medicine, Sydney, NSW, Australia, [3]Universidad Peruana Cayetana Heredia, Medicine, Lima, Peru, [4]University Hospital San Vicente Foundation, Center for Epidemiologic Vigilance and Infection Control, Medellin, Colombia, [5]National Health Service, General Practice, London, United Kingdom, [6]Barking, Havering and Redbridge University Hospitals NHS Trust, Medicine, London, United Kingdom.
e-mail: katherine.fielding@lshtm.ac.uk

Background: Individuals living in institutions are considered at higher risk of tuberculosis (TB). This World Health Organization-commissioned systematic review compared latent TB infection (LTBI) or TB disease outcomes in people in congregate settings versus the general population.

Methods: Four bibliographic databases were searched. A 'congregate setting' was defined as any non-healthcare institution where people reside long-term in close proximity. Two independent reviewers screened titles, abstracts, and full texts and extracted data. Outcomes were incidence or prevalence of LTBI or TB disease.

Results: 5,236 titles/abstracts and 165 full texts were reviewed; 21 articles were included. One study (low TB burden country [LTBC]) reported LTBI prevalence (odds ratios [ORs] 1.87 [95% CI 1.1-3.2; homeless shelter vs. general population] and 0.86 [95% CI 0.5-1.5; care facility vs. general population]). Three studies (LTBCs) reported TB disease prevalence: two in correctional facilities (unadjusted ORs 7.7 and 15.7; prisoners vs. general population) and one in a ′social institution′ (ORs 3.29 [95% CI 2.0-5.4; child residents vs. school-children] and 3.77 [95% CI 1.6-9.0; adult residents vs. general population]).

Eleven studies reported TB disease incidence in prisoners vs. general population: combined rate ratios (RRs) were 6.48 (95% CI 2.7-15.6; two studies; high TB burden countries [HTBCs]; I^2 80.1%) and 7.25 (95% CI 1.9-27.8; three studies; LTBCs; I^2 99.6%; Table). Six studies did not contribute to meta-analysis: RRs were 2.6 and 11.50 (two LTBCs) and ranged from 0.03 to 28 (four HTBCs). Six studies reported TB disease incidence in nursing home residents vs. general population (RR 1.40 [95% CI 0.9-2.2; LTBCs, three studies; I^2 88.8%]); three studies did not contribute to meta-analysis.

Setting	Number of studies	Fixed effects meta-analysis		Random effects meta-analysis		I^2, %
		Unadj. RR	95% CI	Unadj. RR	95% CI	
Correctional facilities - all	5	10.38	9.68-11.13	6.82	2.90-16.03	99.2
Correctional facilities - high burden	2	9.11	7.87-10.54	6.48	2.70-15.60	80.1
Correctional facilities - low burden	3	10.79	9.96-11.68	7.25	1.89-27.82	99.6
Nursing homes - low burden	3	1.67	1.53-1.82	1.40	0.89-2.22	88.8

CI: confidence interval; I^2: percentage of variation across studies that is due to heterogeneity; RR: rate ratio; TB: tuberculosis; Unadj.: unadjusted

[Summary of meta-analyses comparing TB disease incidence in correctional facilities (5 studies) and nursing homes (3 studies) vs the general population]

Conclusions: Individuals in congregate settings are at higher risk of TB than the general population. Between-study heterogeneity was high. Infection prevention measures should be considered in all institutions where people live in close proximity.

OA-18-428-01 Tuberculosis detection and prevention trials in prison settings: a systematic review

IL Haeusler,[1] L Grandjean,[1,2,3] [1]University College London, Institute of Child Health, London, United Kingdom, [2]Imperial College London, Centre for Global Health, London, United Kingdom, [3]Universidad Peruana Cayetano Heredia, Laboratorio de Bioinformatica y Biologia Molecular, Facultad de Ciencias, Lima, Peru. e-mail: ilsa.haeusler@gmail.com

Background: The incidence of tuberculosis in prison communities has been reported as up to 100 times higher than the corresponding civilian population. It remains unclear which control interventions are most effective in prisons. We sought to determine the type of trials that have investigated tuberculosis control in prisons, and the efficacy of these interventions.

Methods: This systematic review followed PRISMA guidelines and included published studies whose aim was to reduce TB incidence or increase the number of people screened for active TB in incarcerated populations. Studies of retrospective data, prevalence studies, and those published pre-1990 were excluded.

Results: 2,429 records were identified, 178 full-text articles screened, and 17 studies included. Trials were published between 1993-2016, with a median trial duration of 23 months (range 5-144). The median prison population was 10,015 (range 300-92,517). Capacity was reported as up to 385%. All but one trial was non-comparative. The most common intervention was the introduction of active case finding but the timing and methods varied. Pre-intervention methods were either not described or were passive case detection. Paired pre- and post-intervention prevalence, incidence, or number of people screened were infrequently reported. Due to the heterogeneity of interventions and trial methodology, it was not possible to quantitate the efficacy of different interventions.

Conclusions: Data from prospective studies of TB control interventions in prisons is limited by lack of reporting of pre-intervention control methods and pre- and post-intervention prevalence and incidence values. Barriers to performing trials in prison populations include safety and ethical concerns, and practical problems resulting from the high turnover of people moving through the prison system. Tuberculosis research in prisons would benefit from ethical and practical guidelines to facilitate overcoming these significant barriers. Prospective comparative trials of adequate duration to determine changes in incidence are necessary to understand which interventions are effective in prison settings.

OA-18-429-01 Effectiveness of BCG vaccination against Mycobacterium tuberculosis infection in adults: a cross-sectional analysis of a UK-based cohort

AL Katelaris,[1] C Jackson,[2] RK Gupta,[2] J Southern,[3] F Drobniewski,[4] A Lalvani,[5] M Lipman,[6] I Abubakar,[2] P Mangtani,[7] [1]London School of Hygiene & Tropical Medicine, Faculty of Public Health and Policy, London, United Kingdom, [2]University College London, Institute for Global Health, London, United Kingdom, [3]Public Health England, National Infection Service, London, United Kingdom, [4]Imperial College London, Department of Medicine, London, United Kingdom, [5]Imperial College London, National Institute for Health Research Health Protection Research Unit in Respiratory Infections, London, United Kingdom, [6]University College London, UCL Respiratory, Division of Medicine, London, United Kingdom, [7]London School of Hygiene & Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom. e-mail: r.gupta@ucl.ac.uk

Background: BCG appears to reduce acquisition of *Mycobacterium tuberculosis* (*Mtb*) infection in children based on interferon-gamma release assays (IGRAs), which allow assessment of *Mtb* infection unaffected by prior BCG. We aimed to determine whether BCG vaccination continues to be associated with decreased prevalence of *Mtb* infection in adults.

Methods: A cross-sectional analysis was conducted of baseline data from adults participating in a large UK cohort study (the PREDICT study) who were contacts of people with TB. Participants were born both in and outside the UK. BCG status was ascertained based on presence of a scar and reported vaccination history and latent TB infection (LTBI) was measured via IGRA. Participants with evidence of active TB at baseline, or who reported a history of TB or prior contact with active TB were excluded.

Multivariable logistic regression was used to estimate odds ratios (ORs) for the association between BCG and LTBI. The effect of infant or older age BCG receipt and time since vaccination on vaccine effectiveness (VE) were also explored.

Results: Of 3453 participants who were contacts of people with TB, 27.5% had LTBI. There was strong evidence of an association between BCG and LTBI (adjusted OR=0.70, 95% CI 0.56-0.87, p=0.0017), yielding a VE of 30%.

Protection against LTBI declined with time since vaccination. Following infant vaccination, versus no vaccination, protection was greater in those vaccinated 11-20 years ago (OR 0.55 [95% CI 0.33-0.90]) than those vaccinated >20 years ago (OR 0.78 [0.60-1.00]).

Conclusions: BCG is associated with lower prevalence of LTBI in adult who are recent TB contacts. These results contribute to growing evidence that suggests BCG may also act by protecting against *Mtb* infection as well as disease.

This has implications for immunisation programmes and TB control efforts worldwide, and supports the potential use of IGRAs as an intermediate endpoint to assess new vaccines.

OA-18-430-01 Evaluating the correlation between rebreathed air exposure using personal CO2 monitoring and the risk of TB infection in a cohort of South African health workers

R Nathavitharana,[1] H Mishra,[2] B Tshigeng,[3] A Sampson,[2] E Nardell,[4] G Theron,[2] [1]Harvard Medical School, Infectious Diseases, Boston, MA, United States of America, [2]Stellenbosch University, Microbiology, Cape Town, South Africa, [3]Stellenbosch University, Medicine, Cape Town, South Africa, [4]Harvard Medical School, Global Health Equity, Boston, MA, United States of America.
e-mail: rnathavi@bidmc.harvard.edu

Background: High rates of tuberculosis (TB) transmission have been reported in hospitals in high-incidence countries like South Africa, yet there is no validated way to evaluate the impact of hospital building and design on airborne infection risk. Unlike low-incidence countries, health workers (HWs) in high-incidence countries are not screened for incident TB infection with tests such as Quantiferon-Plus. We hypothesized that personal carbon dioxide(CO_2) monitoring could be used as a measure of rebreathed air exposure that may correlate with the incidence of TB infection in HWs.
Methods: We analyzed baseline and repeat (12 month) Quantiferon-Plus results in 102 HWs at Tygerberg Hospital, Cape Town, South Africa. The cohort comprised junior and senior doctors and nurses. Quantiferon-Plus results were positive if either TB1 or TB2 values were >=0.35 IU/mL. A random subset of HWs with a baseline negative IGRA underwent personal CO_2 monitoring during a typical work shift.
Results: Of the 102 HWs tested, 55(54%) had a negative baseline IGRA and 47(46%) had a positive IGRA. 22/55 with a baseline negative Quantiferon-Plus result had a positive repeat test at 12 months (40% conversion rate). 5/47 with a baseline positive Quantiferon-Plus result had a negative repeat test at 12 months (11% reversion rate). Of the 38 HWs who underwent CO_2 monitoring, there was no difference in the median CO_2 levels (measured in increments of 500 parts per million, ppm) between converters and non-converters (≥1000ppm, p=0.216, Table).
Conclusions: We detected a high rate of incident TB infection (40%) among HWs at a tertiary referral hospital in South Africa. Our initial analysis suggests that CO_2 levels did not appear to correlate with the risk of TB infection. Unmeasured factors such as the duration of exposure to patients with unsuspected TB, source strength and host susceptibility, may have a higher impact on the likelihood of incident TB in HWs.

	Non-convertors (n=27)	Converters (n=11)
Personal CO_2 (ppm) time spend (min) [Median (IQR)]		
≤500	51 (21-236)	40 (23-76) p=0.129
501-1000	157 (54-254)	152 (113-255) p=0.871
1001-1500	3 (2-25)	19 (4-49) p=0.216
≥1500	0.5 (0-1)	0 (0-2) p=0.973
≥2000	0 (0-0)	0 (0-0) -

[Comparison of personal CO2 levels between HWs with and without Quantiferon-Plus conversion]

OA-18-431-01 Administrative infection control intervention to improve clinical outcomes for pulmonary tuberculosis TB in South African hospitals

M Mphahlele,[1] M Mafeto,[1] P Dhliwayo,[1] A Moran,[2] G Jagwer,[1] [1]University Research Co., LLC (URC), TB South Africa Project, Pretoria, South Africa, [2]University Research Co., LLC (URC), Monitoring, Evaluation, and Learning, Washington DC, WA, United States of America.
e-mail: mphahlelematsie@gmail.com

Background and challenges to implementation: Delays in diagnosing and treating tuberculosis (TB) may result in higher mortality and morbidity due to prolonged disease, as well as increased risk of further transmission of infection. The National Department of Health (NDOH), through USAID Tuberculosis South Africa Project adopted an administrative control intervention named Finding TB cases Actively and Separate Safely (FAST) to address diagnostic and treatment delay.
Intervention or response: The study evaluated the impact of FAST roll-out on time to diagnosis and initiation of treatment in South African hospitals. The FAST Approach has been adopted and implemented in hospitals in all provinces to improve early diagnosis by ensuring that people to be evaluated for TB are separated from the general waiting areas, are tested quickly with molecular diagnostic tools and are initiated on appropriate therapy. Data reporting tools were adapted to enable standardised reporting and monitoring during implementation. Diagnosis and management of TB and DR-TB was in line with national guidelines, with use of GeneXpert MTB/RIF technology as the primary test of diagnosis.
Results and lessons learnt: Total of 1,007,716 patients were screened within eight hospitals in two provinces between October 2017 and December 2018, resulting in the diagnosis of 1,660 people with TB. Average time to diagnosis of TB using GeneXpert reduced from a baseline of two days in October 2017 to 0.3 days by December 2018. Time to treatment of TB cases diagnosed by GeneXpert decreased from a baseline of 4.7 days in October 2017 to 1.6 days in December 2018.

Conclusions and key recommendations: Implementation of the FAST Approach helped in identifying patients who would have otherwise been missed. It also improved time to diagnosis and initiation of treatment, which is critical to ensuring that confirmed TB patients are linked to care and initiated on treatment timeously. However, monitoring of these indicators highlighted gaps in recording of data in case identification registers.

OA-18-432-01 FAST increases tuberculosis drug susceptibility testing and initiation of tuberculosis treatment during hospitalisation

D Tierney,[1] C Mitnick,[2] K Tintaya,[3] E Fuqua,[4] J Barash,[4] T Doctor,[4] K Ali,[4] E Orivis,[4] S Hurwitz,[5] E Nardell,[1]
[1]Brigham and Women's Hospital/Harvard Medical School, Global Health Equity, Boston, MA, United States of America, [2]Harvard Medical School, Global Health and Social Medicine, Boston, MA, United States of America, [3]Socios en Salud, Clinical Research, Lima, Peru, [4]Analysis Group, Consulting, Boston, MA, United States of America, [5]Brigham and Women's Hospital/Harvard Medical School, Biostatistics, Boston, MA, United States of America.
e-mail: dtierney@partners.org

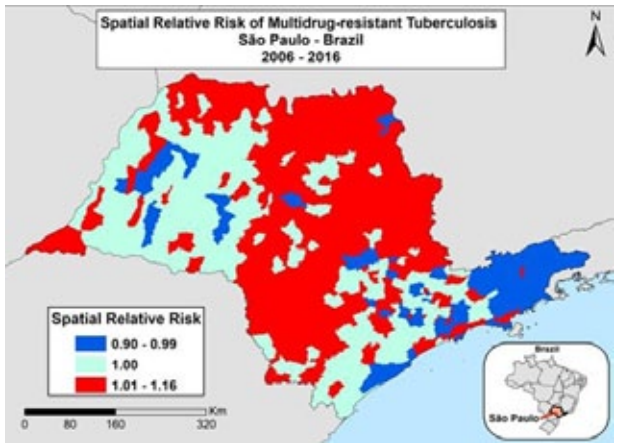
Background: Hospitals are hotspots for the spread of tuberculosis. Using widespread screening, rapid diagnosis with drug susceptibility testing (DST) and expedited treatment based on the DST results, FAST (Find cases Actively, Separate safely, Treat effectively) is designed to reduce hospital transmission of tuberculosis from undiagnosed, untreated cases.
We examined whether patients diagnosed with tuberculosis through FAST experienced decreased times to diagnosis, DST, and treatment compared with historical controls.
Methods: We implemented FAST at a general hospital in Lima, Peru from August 2016 to December 2018. Hospitalized patients underwent symptom-based tuberculosis screening. Those who screened positive were tested with sputum smear microscopy and nucleic acid amplification tests (NAAT). Times to diagnosis, DST, and initiation of treatment were collected prospectively. Similar data were extracted from charts of patients newly diagnosed with smear-positive tuberculosis between December 2015 and July 2016 preceding the initiation of FAST. Statistical analyses included Wilcoxon-Mann-Whitney and chi-square tests.
Results: Sixty-eight newly diagnosed smear-positive historical controls and 48 patients with smear or NAAT-positive pulmonary diagnosed through FAST were included in analyses. The mean time to tuberculosis diagnosis for historical controls was 4.0 ± 11.4 days and 1.2 ± 1.3 days for the FAST cohort. Compared with historical controls, significantly more FAST patients had DST results (57% versus 98%, $p < 0.001$), time to DST was faster (36.8 ± 24.2 days versus 3.6 ± 9.4 days, $p < 0.001$), more patients initiated tuberculosis treatment while hospitalized (41% versus 60%, $p = 0.05$), and more had DST results available prior to treatment initiation (2% versus 46%, $p < 0.001$).
Conclusions: Patients with tuberculosis enrolled in FAST were more likely to have a diagnosis accompanied by DST, treatment initiated while hospitalized, and DST results available at the time of treatment. Accelerated initiation of treatment informed by DST during hospitalization may reduce nosocomial tuberculosis transmission.

OA-18-433-01 Risk factors associated with multidrug-resistant tuberculosis in the state of São Paulo, Brazil

LH Arroyo,[1] LT Campoy,[1] JDA Crispim,[1] DT Santos,[1] M Yamamura,[1] FM Pieri,[2] JD Alves,[1] ET Krainski,[3] VR Bollela,[4] RA Arcêncio,[1] [1]University of São Paulo at Ribeirão Preto College of Nursing, Department of Maternal-Infant and Public Health Nursing, Ribeirão Preto, SP, Brazil, [2]Londrina State University, Department of Nursing, Londrina, PR, Brazil, [3]Federal University of Paraná, Department of Statistics, Curitiba, PR, Brazil, [4]Ribeirão Preto Medical School - University of São Paulo, Department of Clinical Medicine, Ribeirão Preto, SP, Brazil.
e-mail: ricardo@eerp.usp.br

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a serious public health problem worldwide. Identifying predictors for its occurrence may facilitate prevention and care. Accordingly, this study sought to identify individual clinical, social determinants of health and health care performance risk factors for the occurrence of MDR-TB.
Methods: A retrospective cohort of all TB cases diagnosed between 2006 and 2016 in the state of São Paulo, Brazil was analyzed. A Bayesian Spatial Hierarchical Analysis was carried out, in which the occurrence of MDR-TB followed a binomial distribution and the specific effect of the area a BYM model. The variables were structured in a multilevel design, with the first level being composed of individual characteristics of the patients and the second level socioeconomic variables and performance of the health services of the 645 municipalities of São Paulo.
Results: It was identified that the history of previous TB treatment (OR=13.86, 95%CI:12.06-15.93), positive sputum culture test (OR=5.26, 95%CI:4.44-6.23), diabetes mellitus (OR=2.34, 95%CI:1.87-2.91), residing at a standard address (OR=2.62, 95%CI:1.91-3.60), positive sputum smear microscopy (OR=1.74, 95%CI:1.44-2.12), cavitary pulmonary TB (OR=1.35, 95%CI:1.14-1.60) and diagnosis performed due to spontaneous request (OR=1.26; 95%CI:1.10-1.46) were associated with MDR-TB at the individual level. In the second level, municipalities that performed HIV tests in less than 42.65% of patients with TB (OR=1.50, 95%CI:1.25-1.79), that diagnosed TB cases only after death (OR=1.50, 95%CI:1.17-1.93) and that had

more than 20.16% of their population with income between ¼ and ½ of one minimum wage (OR=1.56, 95%CI:1.30-1.87) were related to the occurrence of MDR-TB (Figure 1).
Conclusions: Knowledge of the predictive factors for MDR-TB contributes to the prevention and care of these cases. The study advances knowledge by considering the individual characteristics of the patients, the social determinants and the performance of the health care for the management of cases, being a pioneer in Brazil in relation to its design.



[Spatial Relative Risk of Multidrug-resistant Tuberculosis at São Paulo, Brazil - 2006 to 2016]

OA-20-A2 Drug dosing and the patient achieving a cure

OA-20-434-01 Evaluation of the molecular bacterial load assay and influence of Mycobacterium tuberculosis drug resistance on bacterial load in early treatment with first-line therapy

TH Hoang,[1] NV Dao,[1] DAT Do,[1] TBT Trinh,[1] HP Nguyen,[2] V Srinivasan,[1] G Thwaites,[1,3] TTT Nguyen,[1] [1]Oxford University Clinical Research Unit, Tuberculosis, Ho Chi Minh, Viet Nam, [2]Hospital for Tropical Diseases, Viet-Anh Ward, Ho Chi Minh, Viet Nam, [3]University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom. e-mail: haiht@oucru.org

Background: The molecular bacterial load assay (MBLA) is able to rapidly quantify *Mycobacterium tuberculosis* (*Mtb*), which is important to monitor treatment response and evaluate treatment efficiency.
Methods: We conducted a prospective study in 56 pulmonary tuberculosis patients whose 224 sputum samples were collected before and during the first month of first-line treatment. We aimed to evaluate MBLA for early monitoring of bacterial burden and use MBLA to investigate bactericidal activities of first-line therapy in patients infected with drug resistant isolates.
Results: *Mtb* loads measured by MBLA and MGIT were strongly correlated after one-week (r=0.56) and one-month (r=0.73) of treatment. Meanwhile correlations of MGIT with GeneXpert and microscopy remained much lower during treatment. *Mtb* load by MBLA declined rapidly than GeneXpert after one-week (mean decline by CT/week: 2.73, P< 0.001; 0.95, P=0.297 respectively) and one-month (2.25, P< 0.001; 1.69, P< 0.001). *Mtb* loads in multidrug resistance (MDR) cases were significantly greater than in both sensitive and poly/mono-resistance after one-week (P< 0.02) and one-month treatment (P=0.001). Multiple regression analysis shows early bactericidal activity in MDR was significantly lower than that in sensitive by 0.262 log10 bacteria/ml/day (P=0.026) after one-week and by 0.096 log10 (P=0.013) after one-month of treatment.
Conclusions: MBLA performed better than GeneXpert and microscopy compared to MGIT for quantifying viable *Mtb* during treatment. The effect of first-line regimen is no different for poly/mono-drug resistance; thus combined drugs not only prevent MDR development but also preserve effectiveness of treatment. However, in MDR the effect of first-line regimen significantly reduced leading to treatment failure, indicating an urgent need for early detection and correct treatment of new MDR cases.

OA-20-435-01 Implementation of therapeutic drug monitoring in a high-burden drug-resistant tuberculosis setting in Siberia, Russia

S Zhdanova,[1] O Ogarkov,[1] E Moiseeva,[2] A Belskikh,[1] S Vitko,[3] M Koshcheyev,[2] S Heysell,[3] [1]Scientific Centre of the Family Health and Human Reproduction Problems, Microbiology and Epidemical Infections, Irkutsk, Russian Federation, [2]Irkutsk Regional Clinical TB-Prevention Hospital, Tuberculosis, Irkutsk, Russian Federation, [3]University of Virginia, Infectious Diseases and International Health, Charlottesville, VA, United States of America. e-mail: skh8r@virginia.edu

Background and challenges to implementation: Individual pharmacokinetic variability drives outcomes but implementation of therapeutic drug monitoring (TDM) to measure and correct suboptimal plasma drug exposures has been limited to low burden TB settings with highly specialized centers.
Intervention or response: At Irkutsk Regional TB Hospital where approximately 40% of patients are living with HIV, we aimed to enroll 25 people on representative regimens. TDM took place before the end of the intensive phase in people with HIV and targeted the most commonly prescribed drugs of rifampin, isoniazid (typically given at 10 mg/kg), pyrazinamide and levofloxacin (the latter three also given for rifampin-resistant TB). To

assess the feasibility of a limited sampling strategy, venous blood was collected before the observed dose and then at 1, 2, 6 and 8 hours after. Plasma concentrations were determined at a nearby research center using liquid chromatography-tandem mass spectrometry.

Results and lessons learnt: Twenty-three patients had TDM. Peak concentrations (Cmax) could adequately be assessed from the sampling strategy: (median [interquartile range]) rifampicin 6.53 [5.98-7.67] μg/ml at 1-2 hours; for isoniazid 8.53 [IQR, 7.49-10.19] μg/ml at 2-3 hours; for pyrazinamide 34.03 [22.19-47.26] μg/ml in 1-2 hours; for levofloxacin 3.91 [2.70-4.74] μg/ml in 1-2 hours. Cmax of isoniazid and pyrazinamide were within the expected range. No patients had a Cmax greater than the literature suggested lower limit of 6.6 μg/ml for levofloxacin, or 8.0 μg/ml for rifampicin. Patients tolerated TDM well and laboratory and clinical staff found TDM feasible. Longer term outcomes are being assessed and a protocol created for clinicians to guide routine dose changes based on TDM results that will inform scale-up.

Conclusions and key recommendations: TDM for people with TB-HIV uncovered suboptimal concentrations for rifampin and levofloxacin that were clinically actionable in a high burden TB setting with capability for interventional scale-up.

Acknowledgements: RFBR grant 17-54-30020.

OA-20-436-01 Development and acceptability of a gastric resident drug delivery system for prolonged gram-level dosing of tuberculosis treatment

M Verma,[1,2,3] J Furin,[4] R Langer,[1,2,3] G Traverso,[3,5,6]
[1]Massachusetts Institute of Technology, Biological Engineering, Cambridge, MA, United States of America, [2]Massachusetts Institute of Technology, Koch Institute for Integrative Cancer Research, Cambridge, MA, United States of America, [3]Massachusetts Institute of Technology, Tata Center for Technology and Design, Cambridge, MA, United States of America, [4]Harvard Medical School, Global Health and Social Medicine, Boston, MA, United States of America, [5]Massachusetts Institute of Technology, Mechanical Engineering, Cambridge, MA, United States of America, [6]Brigham and Women's Hospital/Harvard Medical School, Division of Gastroenterology, Hepatology and Endoscopy, Boston, MA, United States of America.
e-mail: mverma@mit.edu

Background: Lack of adherence and interruption of tuberculosis (TB) treatment increases morbidity and mortality as well as the potential for developing drug-resistant strains. Given the dearth in new TB drug development, optimization of current drugs is essential, including novel drug delivery systems.

Methods: Inspired by the capacity of the stomach to hold large objects including bariatric balloons, we reasoned that a gastric resident system (GRS) capable of prolonged dosing could help patients adhere to TB treatment. We describe the development of a GRS for TB treatment and evaluate its safety and efficacy in a swine model. Furthermore, we surveyed 111 TB health care providers and 300 patients with TB at DOTS clinics in India to assess acceptability and feasibility of such a system for use in clinical practice.

Results: The GRS delivered through the nasogastric (NG) route was capable of safely encapsulating and releasing grams of antibiotics for 4 weeks as a proof of concept. The GRS consists of drug pills on a coiled superelastic wire and can be retrieved through the NG route. Initial preclinical safety and drug release of TB antibiotics were demonstrated in a swine model. Extended release of drugs was enabled by formulating drugs in polymers to enable controlled diffusion of the drug from the GRS. Results of the acceptability survey showed that theoretically, a long-term drug delivery device administered through an NG tube was acceptable and feasible in the field.

Conclusions: Our field results indicate that 45% of patients are willing to undergo a NG tube procedure for placement of a GRS compared with swallowing capsules (17%) or drinking drug-fluid mixtures (38%). Promising preclinical data of the GRS in a swine model supports the use multigram drug depots for improving medication adherence. Further work includes studying stability and pharmacokinetic profiles of all TB drugs.

OA-20-437-01 Efficacy of therapeutic dendritic cells vaccine treatment in patients with extensively drug-resistant lung tuberculosis in the follow-up period

A Starshinova,[1] M Nazarenko,[2] M Filatov,[2,3] V Burdakov,[3] I Chernokhaeva,[4] E Beliaeva,[4] P Yablonskiy,[5,6] [1]St. Petersburg State University, Laboratory of Mosaic of Autoimmunity, St. Petersburg, Russian Federation, [2]Research Institute of Phthisiopulmonology, Phthisiopulmonology Department of Children, St. Petersburg, Russian Federation, [3]Leningrad Nuclear Physics Institute, Laboratory, St. Petersburg, Russian Federation, [4]Research Institute of Phthisiopulmonology, Department of Phthisiopulmonology, St. Petersburg, Russian Federation, [5]Research Institute of Phthisiopulmonology, Director, St. Petersburg, Russian Federation, [6]St. Petersburg State University, Medical Faculty, St. Petersburg, Russian Federation. e-mail: starshinova_777@mail.ru

Background: Development of new treatment methods of extensively drug resistant tuberculosis (XDR TB) is an actual challenge. The efficacy of XDR TB treatment is 28% (WHO, 2017).

Methods: 43 patients with XDR TB were treated in 2016-2018. 23 patients - with therapeutic dendritic cells (DC) vaccine (I group) and 20 patients - with standard therapy with drug sensitivity data (II group) (the study was approved by Ethics Committee. The average age was 38.3±10.5 years, the average term of a previous anti-TB

chemotherapy (CHT) - 21.0±3.8 months. Control examination was conducted on the 60th, 120th, 240th, 360 days and 18-24 Months of the main course of CHT. Immunotherapy (IMT) was applied by a suspension with DC, stimulated by the TB recombinant allergen ESAT-6/SFP-10. Statistical analysis was done by Statistica 7.0. Differences were statistically significant at $p < 0.05$.

Results: Symptoms of intoxication decreased after 360 days in 80.0% (I) vs 44.7% (II) of cases. Cessation of bacterial excretion after 360 days was observed in 73.0% (I) vs 40.0% (II) cases. Resorption of focal and infiltrative X-ray changes was noted in 46.7% (I) vs 29.4 (II) cases after 360th days. In the follow period of patients with vaccination in 3 cases we have surgery treatment with positive results; 2 patients - died from TB, 1 - died from other reasons, in 4 case we have efficacy of therapy, in 3 cases we restarted intensive phase of treatment.

Conclusions: Treatment with inclusion of IMT based on DC was efficient in more than 77% cases. This method can be useful in cases with no effect of standard anti-TB CHT.

OA-20-438-01 Sterilising activity of weekly bedaquiline-rifapentine regimens in a murine model of tuberculosis

F Kort,[1] L Fournier Le Ray,[1] A Chauffour,[1] L Guglielmetti,[1] V Jarlier,[1] A Aubry,[1] N Veziris,[1]
[1]Sorbonne Université, Centre d'Immunologie et des Maladies Infectieuses, Paris, France.
e-mail: nicolas.veziris@sorbonne-universite.fr

Background: WHO recommends supervising the treatment of tuberculosis. Intermittent regimens would simplify the supervision and improve compliance. Bedaquiline and Rifapentine, which have a long plasma half-life, are good candidates to develop once-weekly regimens. Our obective was to analyze the sterilizing activity of once-weekly regimens containing bedaquiline and rifapentine, in a murine model of tuberculosis.

Methods: 300 Swiss mice were intravenously infected with 10exp6 Colony Forming Unit (CFU) of *Mycobacterium tuberculosis* H37Rv. Mice were treated once-a-week by regimens containing Bedaquiline, Rifapentine and Pyrazinamide (BPZ), plus Moxifloxacin (BPZM) plus clofazimine (BPZMC), or by the standard daily regimen of tuberculosis, during 4 or 6 months. Bactericidal activity was assessed by lung CFU counts after 2, 4 or 6 months of treatment. Sterilizing activity was assessed by the proportion of relapsing mice, 3 months after the completion of the treatment.

Results: At the beginning of the treatment, the mean lung CFU was 4.60 ± 1.26 log10. After 2 months, the mean lung CFU was 6.03 ± 1,70 log10 in untreated mice, 0.57 ± 0.63 log10 in mice treated by the standard daily regimen, and negative in mice treated by the weekly regimens ($p<0.05$ compared to the daily standard regimen). All mice had negative lung cultures on completion of treatment. The relapse rates in the standard daily regimen were 64% and 13% after 4 and 6 months of treatment respectively. The relapse rates in the weekly test groups were respectively after 4 and 6 months of treatment 5% and 0% in BPZ, 0% and 0% in BPMZ and 0% and 5% in BPMZC ($p < 0.05$ and $p>0.05$ for all weekly groups vs daily control group at 4 months and 6 months respectively).

Conclusions: BPZ-based weekly regimens have higher sterilizing activity than the standard daily regimen and could greatly simplify the supervision and possibly shorten tuberculosis treatment.

OA-20-439-01 Can cART alone deliver in the race between immune reconstitution and TB reactivation?

S Ganatra,[1,2] A Bucsan,[1] X Alvarez-Hernandez,[3] S Mehra,[1] S Khader,[4] J Rengarajan,[5] D Kaushal,[1,2]
[1]Tulane National Primate Research Center, Center for Tuberculosis Research, Covington, LA, United States of America, [2]Texas Biomedical Research Institute, Southwest National Primate Research Center, San Antonio, TX, United States of America, [3]Tulane National Primate Research Center, Department of Microbiology and Immunology, Covington, LA, United States of America, [4]Washington University School of Medicine in St Louis, Department of Molecular Biology, St Louis, MO, United States of America, [5]Emory University, Emory Vaccine Center and Department of Medicine, Atlanta, GA, United States of America.
e-mail: sganatra@txbiomed.org

Background: Mycobacterium tuberculosis (*Mtb*) and Human immunodeficiency virus (HIV) syndemic has resulted in higher incidence of drug resistant tuberculosis leading to poor treatment outcomes and increased mortality in sub-Saharan Africa. The advent of combined antiretroviral therapy (*cART*) has significantly improved survival but tuberculosis still accounts for one third of deaths in HIV infected population, suggesting that immune functions are not completely restored by *cART*.

Methods: To study the immune correlates of TB reactivation following simian immunodeficiency virus (*SIV*) infection, twelve Indian-origin rhesus macaques (*Macaca mulatta*) were infected with aerosolized low dose ~10 CFU of *Mtb* CDC1551. Animals were studied longitudinally for their clinical and immunological responses and upon confirming their latent TB status, they were challenged with intravenous simian immunodeficiency virus $SIVmac_{239}$ 300 $TCID_{50}$ at week 9 post *Mtb* infection. At week 13, animals were randomized to control (n=8) and treatment (n=4) groups and initiated on *cART* consisting of tenofovir, emtricitabine and dolutegravir administered subcutaneously.

Results: *cART* significantly reduced plasma viral load ($p < 0.000001$) and increased CD4+ T cell counts in whole blood ($p=0.0374$) and bronchoalveolar lavage

(p=0.0040) samples collected at necropsy in *cART* treated group compared to *cART-naive* controls. Despite reduced viral load and improved CD4+ T cell counts, there was no intergroup difference in their longitudinally observed clinical parameters viz. temperature, weight, plasma C-reactive protein levels (p=0.9073), and *Mtb* bacterial burden in BAL (p=0.5016) and in lung tissues (p=0.6419).

Conclusions: Early *cART* therapy is indispensable for controlling viral replication, immune reconstitution and in preventing opportunistic infection. But *cART* alone is inadequate in reversing T cell dysfunction induced by HIV, mitigating chronic immune activation and *Mtb* reactivation often seen in TB/HIV co-infection setting. Similar studies involving concurrent administration of *cART* + Isoniazid prophylaxis therapy will help identify the correlates of immunity restored by concurrent reduction in *Mtb* antigen load and *SIV* viral replication.

OA-20-440-01 Isoniazid and rifampicin exposures correlate with early bacillary clearance from sputum, and clinical treatment outcome in drug sensitive pulmonary tuberculosis: a population pharmacokinetic-pharmacodynamic analysis

F Kloprogge,[1] H Mwandumba,[2,3] G Banda,[3] M Kamdolozi,[4] D Shani,[4] E Corbett,[3,4,5] S Ward,[2] S Khoo,[6] G Davies,[2,3,7] D Sloan,[2,3,8] [1]University College London, Institute for Global Health, London, United Kingdom, [2]University of Liverpool, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [3]Malawi Liverpool Wellcome Trust Clinical Research Programme, Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi, [4]University of Malawi, Department of Microbiology, Blantyre, Malawi, [5]London School of Hygiene and Tropical Medicine, Department of Clinical Research, London, United Kingdom, [6]University of Liverpool, Department of Pharmacology, Liverpool, United Kingdom, [7]University of Liverpool, Institute of Global Health, Liverpool, United Kingdom, [8]University of St Andrews, School of Medicine, St Andrews, United Kingdom. e-mail: f.kloprogge@ucl.ac.uk

Background: Improved understanding of relationships between clinical co-variates, systemic antibiotic exposure, serial sputum bacillary load measurements and treatment outcomes will help to facilitate optimisation and/or personalisation of treatment for tuberculosis. This study aimed to characterise these relationships using data from a longitudinal cohort of Malawian adults receiving standard 6-month chemotherapy for a first presentation of drug-susceptible pulmonary tuberculosis.

Methods: Baseline clinical data and steady-state plasma concentrations of isoniazid, rifampicin, pyrazinamide and ethambutol were available from 154 patients. Serial sputum bacillary load measurements over the first 8 weeks, and final outcomes recorded 12 months after completion of treatment, were available from 102 and 87 patients respectively. NONMEM® software was used to develop population pharmacokinetic (PK) and pharmacokinetic-pharmacodynamic (PKPD) models. Non-parametric tests in *R* statistical software were used to study outcomes.

Results: In the PKPD model, higher isoniazid AUC_{0-24} correlated with an increased bacterial killing rate (LAM; exponential 0.0005; $p < 0.01$). The rate of bacterial clearance decreased over time on standard chemotherapy and higher rifampicin AUC_{0-24} correlated with a later onset of decline in bactericidal effect ($t_{1/2}$; exponential 0.0335; $p < 0.01$). Any history of alcohol consumption correlated with decreased bacterial killing rate (LAM; proportional -0.0377; $p < 0.01$). Bacillary clearance from sputum was consequently faster in non-alcohol consuming patients with a higher isoniazid and rifampicin AUC_{0-24}. When PKPD model parameters were related to treatment outcome, slower bacterial killing rate (LAM) and increased loss of bacillary clearance over time (BETA) both correlated with long-term treatment failure. Slower bacillary killing rate (LAM) also correlated with post-treatment relapse.

Conclusions: This study shows that longitudinal bacterial biomarkers of treatment effect are important to predict study outcome. Pooled individual patient data analyses from larger datasets are needed to confirm the factors which are relevant to shortening and/or personalisation of TB treatment.

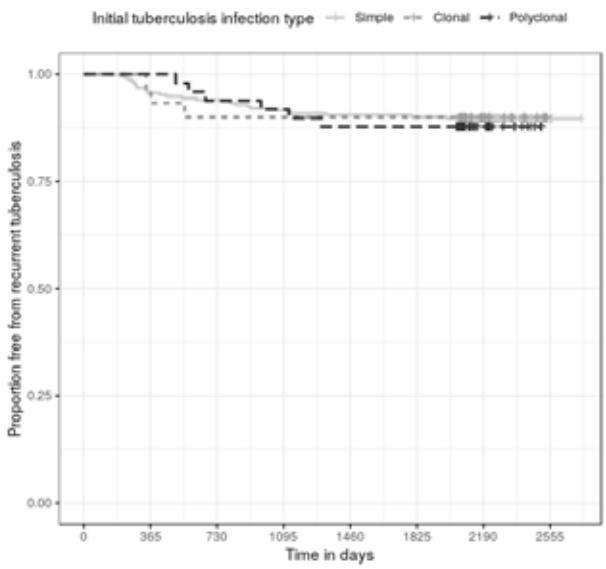
OA-20-441-01 Complex M. tuberculosis infection and recurrence after treatment completion

PGT Cudahy,[1] D Wilson,[2] T Cohen,[3] [1]Yale School of Medicine, Medicine, New Haven, CT, United States of America, [2]Edendale Hospital, Internal Medicine, Pietermaritzburg, South Africa, [3]Yale School of Public Health, Epidemiology (Microbial Diseases), New Haven, CT, United States of America. e-mail: patrick.cudahy@yale.edu

Background: Individuals may be infected with multiple genotypes of *Mycobacterium tuberculosis* (*Mtb*) at one time-point, i.e. "complex *Mtb* infection". This can result from within-host clonal evolution (clonal complexity) or infection with multiple strains of *Mtb* (polyclonal complexity). Complex *Mtb* infection could potentially allow minority drug resistant strains to emerge, leading to treatment failure or disease recurrence.

Methods: We enrolled 500 adults with smear-positive pulmonary tuberculosis from primary health care clinics in KwaZulu-Natal, South Africa. Baseline sputum cultures were genotyped with 24-loci mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) typing. For patients who completed treatment, we searched for secondary episodes of tuberculosis in the district tuberculosis register using gender, date of birth, and fuzzy matching of name by Jaro-Winkler distance.

Results: 435 participants had baseline MIRU-VNTR genotypes. We matched 417 (96%) to the tuberculosis register. 70% were HIV positive. 8% had clonally complex and 14% had polyclonally complex *Mtb* infection. We followed participants for a median of 2217 days (interquartile range (IQR) 2122-2363 days). 35 participants (11%) had a recurrence of bacteriologically proven tuberculosis after a median of 553 days (IQR 342-942 days). Kaplan-Meier curves stratifying by simple, clonal, or polyclonal complex *Mtb* infection were not significantly different by log-rank test. In a Cox proportional hazards model, 3+ AFB sputum smear grade was associated with recurrent tuberculosis with an odds ratio of 2.69 (95% CI 1.15-6.3, p=0.02). The presence of clonal or polyclonal *Mtb* infection at baseline was not significantly associated with recurrent disease.
Conclusions: We did not find a statistically significant association between complex *Mtb* infection and recurrent tuberculosis after a median of 6 years. A higher sputum AFB smear grade during the initial tuberculosis episode was associated with recurrent tuberculosis. This may be due to a higher inoculum of disease and cavitary disease. Recurrence rates were overall high (11% over 6 years).



[Figure 1: Recurrent tuberculosis after treatment completion or cure]

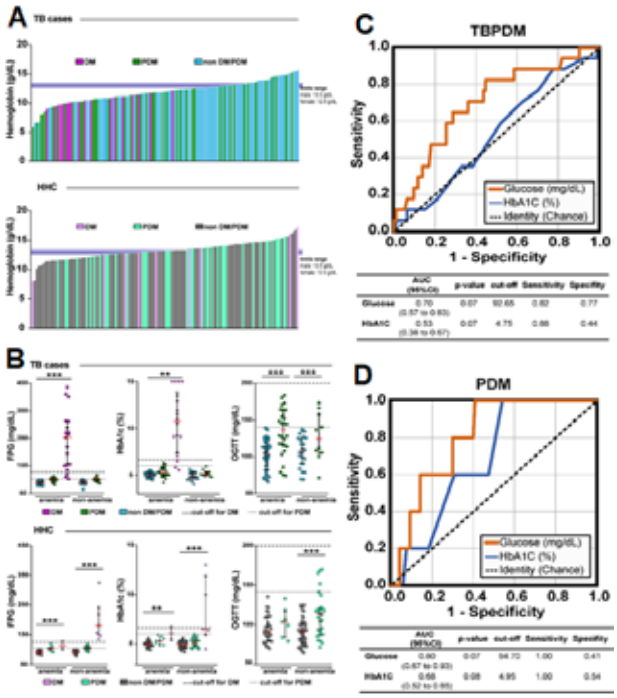
OA-21-D1 Providing quality care for TB patients with comorbidities

OA-21-442-01 Low accuracy of glycated haemoglobin levels for diagnosis of hyperglycaemia in patients with tuberculosis from Peru: a prospective cohort study

R Calderon Espinoza,[1,2] MB Arriaga,[3,4,5] N Barreda Ponce,[1] O Sanabria Salazar,[1] K Lopez Tamara,[1,6] J Neto F.,[7] DN Araújo,[7] L Lecca Garcia,[1] B Andrade B.,[3,5,7] [1]Socios En Salud Sucursal Peru, Laboratorio, Lima, Peru, [2]Universidade Federal de Rio de Janeiro, Faculdade de Medicina, Rio de Janeiro, RJ, Brazil, [3]Universidade Federal da Bahia, Faculdade de Medicina, Salvador, BA, Brazil, [4]Fundacao Jose Silveira, Instituto Brasileiro para Investigacão da Tuberculose, Salvador, BA, Brazil, [5]Fundação Oswaldo Cruz, Instituto Gonçalo Moniz, Salvador, BA, Brazil, [6]Brigham and Women's Hospital, Department of Rheumatology, Immunology, and Allergy, Boston, MA, United States of America, [7]Fundacao Jose Silveira, Multinational Organization Network Sponsoring Translational and Epidemiological Research (MONSTER) Initiative, Salvador, BA, Brazil. e-mail: rcalderon_ses@pih.org

Background: Hyperglycemia conditions as diabetes mellitus (DM) and prediabetes (preDM) increases the risk of tuberculosis (TB) developing, but TB, DM/preDM and anemia associations remains poorly understood. Heterogeneity in performance of HbA1c diagnostics has been studied, but less is known its relationship with anemia and TB in Peru. To examine the association of anemia in TB patients with DM/preDM, we examined systemic levels of hemoglobin in pulmonary TB patients and their household contacts affected with DM or preDM from Lima, Peru.
Methods: We conducted fasting plasma glucose (FPG), HbA1c and oral glucose tolerance testing (OGTT) in 136 TB patients and 138 of their household contacts to diagnose DM and preDM. We assess FPG and HbA1c diagnostic performance vs OGTT. Potential effects of sociodemographic and clinical factors on detection of hyperglycemia were analyzed, including hemoglobin testing.
Results: DM and preDM prevalences were higher than expected in TB patients and contacts. All enrolled TB-DM patients showed anemia and low hemoglobin levels were significantly associated with higher levels of OGTT, FPG and HbA1c. Both FPG and HbA1c showed poor agreement (Kappa < 0.2 in all groups) for hyperglycemia detection (vs OGTT) in TB patients. Among TB-preDM patients, HbA1c showed a lower ROC curve as compared to the FPG test and anemia is associated with this poor accuracy.
Conclusions: FPG and HbA1c are available methods for diagnosing DM or preDM in tuberculosis patients and contacts but anemia interferes raising its levels. In low

income settings, surveillance of DM/preDM among tuberculosis patients and contacts using FPG or HbA1c should be evaluated in order to optimize diagnostic strategies, given the identified limitations. In Peru, TB is widely associated with anemia and the diagnostic utility of HbA1c alone will be affected. New test thresholds should be explored in order to determine the prevalence among TB patients and ultimately improve TB DM/preDM control.



[PFG and HBA1c performance for DM/preDM stratified by anemia in TB cases and contacts in Lima-Peru]

OA-21-443-01 Extending HIV testing to people with TB symptoms to close case detection gaps and find the missing cases

C Banzakadilo,[1] C Kadianda,[1] S Muyano,[1] M Kawen,[1] C Tendo,[1] P Milenge,[1] I Thior,[2] D Canagasabey,[2] J-C Kiluba,[1] [1]PATH, DRC Country Program, Lubumbashi, Congo (Democratic Rep.), [2]PATH, HIV/TB Programs, Washington, DC, United States of America.
e-mail: cbanzakadilo@path.org

Background and challenges to implementation: While significant gains have been made to diagnose and treat people living with HIV (PLHIV) and active tuberculosis (TB), missing cases continue to fuel the dual epidemic, with a 48% TB case detection rate and an estimated 40% of PLHIV diagnosed in the Democratic Republic of the Congo.
Intervention or response: To improve case finding among individuals not currently reached by screening efforts and increase early TB and HIV diagnosis, the USAID-funded Integrated HIV/AIDS Project in Haut Katanga and Lualaba piloted a strategy that expanded the criteria for HIV testing by offering testing services to people with presumptive TB instead of only testing those confirmed with active TB.
We piloted this approach in three referral hospitals (with TB diagnostic centers) in major transit/mining hubs: Kasumbalesa Referral Center, Kolwezi Personnel Hospital, and Lubumbashi University Hospital. We analyzed programmatic data gathered between May 2018 and March 2019 using descriptive statistics.
Results and lessons learnt: All 1,212 people who presented at these facilities with TB symptoms were tested for TB, among whom 160 were diagnosed with active TB (13%). 586 of the 1,212 people with TB symptoms were tested for HIV, and 15% (n = 88; all first-time testers) were identified HIV-positive. 19 PLHIV were coinfected with TB, a 22% coinfection rate among those tested for HIV.
If all 1,212 people with TB symptoms were tested for HIV, we would expect to identify 182 PLHIV, assuming 15% HIV prevalence. If we tested only active TB cases for HIV and assumed a TB/HIV coinfection rate of 22%, we would expect to identify only 36 people with TB/HIV coinfection, thus missing 146 PLHIV.
Conclusions and key recommendations: More PLHIV were identified by testing all people with presumptive TB for HIV. This approach should be rapidly extended to other TB diagnostic centers in TB/HIV hotspots to diagnose hard-to-reach PLHIV and link them to treatment.

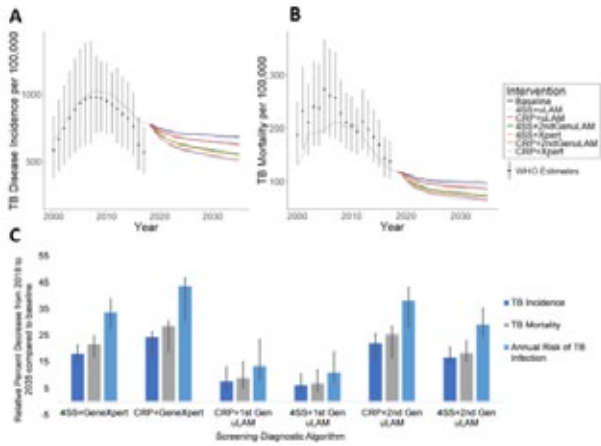
OA-21-444-01 Point-of-care screening-diagnostic algorithms for tuberculosis administered at the time of HIV testing substantially improve TB incidence, mortality, and annual risk of infection in South Africa

H Hannah,[1] B Wagner,[2] S Chang,[2] P Drain,[3] [1]University of Washington, Epidemiology, Seattle, WA, United States of America, [2]Institute for Disease Modeling, Tuberculosis Team, Bellevue, WA, United States of America, [3]University of Washington, Epidemiology, Medicine, and Global Health, Seattle, WA, United States of America.
e-mail: bwagner@idmod.org

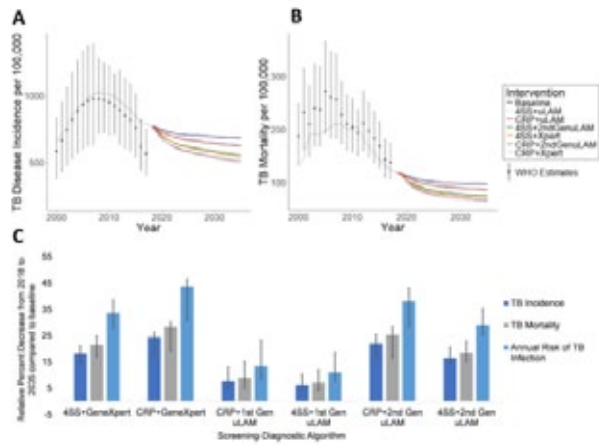
Background: TB deaths are preventable with early diagnosis and treatment. Recommended TB tests rely on laboratory-based diagnostics, which result in treatment delays and loss to follow-up. Nearly 70% of undiagnosed TB cases in South Africa are missed as a result of diagnostic failures. Point-of-care (POC) testing may improve case-detection, thereby reducing TB transmission, incidence, and mortality.
Methods: We used EMOD-TB, an individual-based TB transmission model, to estimate the impact of offering TB testing annually at the time of HIV testing on the TB burden (disease incidence, mortality, and annual risk of

infection (ARI)) in South Africa. Screening-diagnostic algorithms were developed by combining a screening test (Four-symptom screen (4SS) and C-Reactive Protein (CRP)) and confirmatory diagnostic test (1st- and 2nd-Generation urine liparabinomannan (uLAM) and GeneXpert). Test sensitivities and specificities differed by HIV status and CD4 count. The model assumed each algorithm was offered with HIV testing annually, regardless of HIV positivity, beginning in 2018. Reductions in the TB burden were compared between 2018 and 2035 relative to baseline trends.

Results: Administering TB testing at the time of annual HIV testing resulted in reductions in the predicted TB burden under all scenarios. CRP+GeneXpert yielded the greatest overall decline in TB burden with estimated additional reductions of 24% (95% CI: 16-26%) in incidence, 28% (95% CI: 19-30%) in mortality, and 43% (95% CI: 31-47%) in ARI. A 2nd-generation uLAM diagnostic resulted in similar reductions in the TB incidence (22%; range 16-26%) as compared to GeneXpert. The 1st-generation uLAM diagnostic resulted in less reductions in the TB incidence in comparison to 2nd-generation uLAM (8%; 95% CI: 5-13%).



[TB incidence, mortality, and transmission absolute reductions (A,B) and relative to baseline (C)]



[TB incidence, mortality, and transmission absolute reductions (A,B) and relative to baseline (C)]

Conclusions: Incorporating TB testing into annual HIV testing may greatly reduce TB transmission, incidence, and mortality in South Africa. As compared to the current standard of care, CRP and 2nd-generation uLAM are promising POC tests for TB.

OA-21-445-01 Treatment outcomes in adult tuberculous meningitis: a systematic review and meta-analysis

J Ellis,[1,2] A Stadelman,[2,3] E Mutengesa,[2] T Samuels,[2] L Tugume,[2] M Rutakingirwa,[2] J Dobbin,[2] K Ssebambulidde,[2,4] D Boulware,[3] F Cresswell,[2,5]
[1]University College London (UCL), Infection and Immunity, London, United Kingdom, [2]Infectious Diseases Institute, Meningitis, Kampala, Uganda, [3]University of Minnesota, Meningitis, Minneapolis, MN, United States of America, [4]London School of Hygiene & Tropical Medicine, Phd Fellow, London, United Kingdom, [5]London School of Hygiene & Tropical Medicine, PhD Fellow, London, United Kingdom. e-mail: j.ellis@doctors.org.uk

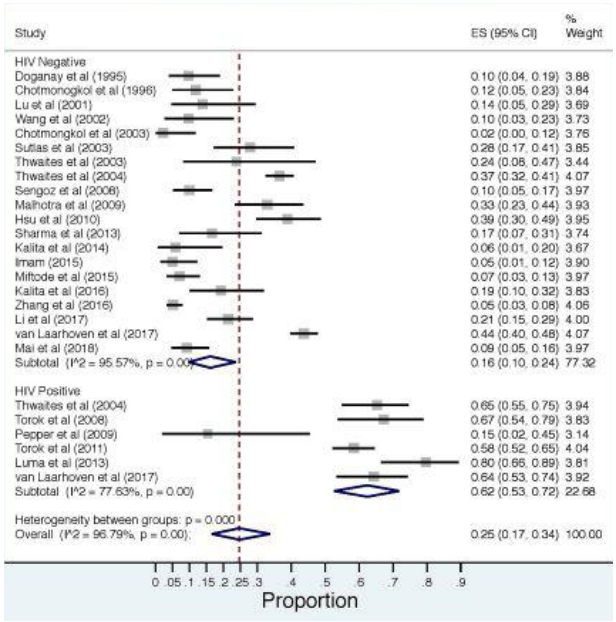
Background: There is substantial heterogeneity in the reported treatment outcomes for adult tuberculous meningitis (TBM) across studies. Treatment outcomes by epidemiological setting and HIV status have not previously been systematically explored.

Methods: We performed a systematic review and meta-analysis to characterize treatment outcomes for adult TBM. Following a systematic literature search (MEDLINE and EMBASE), studies were two-stage screened by two reviewers and were eligible for inclusion if they (i) included adults with suspected TBM (ii) applied a systematic diagnostic criteria (iii) described treatment regimens (iv) reported on treatment outcomes of interest (mortality and neurological sequelae). We employed a random effects model for all meta-analyses; heterogeneity was evaluated by the I^2 statistic.

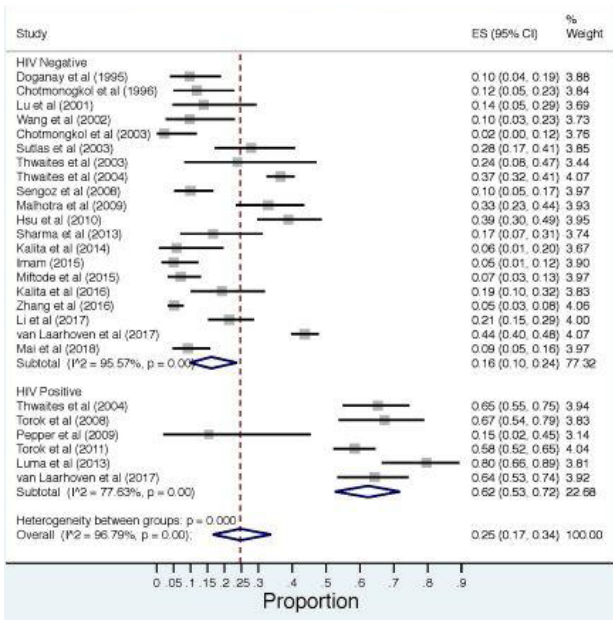
Results: 2,197 records were assessed for eligibility; 41 primary research articles met our inclusion criteria, including a total of 6100 individuals. Of 41 articles, 11 (27%) were case series, 1 (2%) was cross-sectional, 18 (44%) were cohorts, and 11 (27%) were randomized controlled trials. The commonest outcome measure was 6-month mortality. In studies from Asia, 6-month mortality ranged between 12% and 30%. In sub-Saharan Africa, mortality ranged between 17% and 36%. Six studies included HIV-positive adults, overall treatment outcomes in HIV-positive adults were significantly worse with mortality between 53-72%, compared to 10-24% in HIV-negative cohorts. There was considerable heterogeneity across studies with I^2 statistics consistently >50%.

Conclusions: Treatment outcomes in adult TBM are poor and vary considerably by region and HIV-status, with highest mortality amongst HIV-positive adults. The poorer outcomes reported in studies from sub-Saharan Africa may relate to the high prevalence of HIV co-infection but varying quality of supportive care

and severity of disease at presentation need also to be considered. Inconsistent reporting of end-points limits comparison across studies. Standardized reporting of treatment outcomes will be essential to improve data quality, facilitate multi-center TBM research, and improve TBM management.



[Treatment outcomes in tuberculous meningitis by HIV status]



[Treatment outcomes in tuberculous meningitis by HIV status]

OA-21-446-01 Patient awareness and adherence to return instructions increase when laboratory results are delivered in a secure message to their phone: a pilot study

B Jarrett,[1] L DiAndreth,[2] J Elf,[3,4] T Nishath,[3] B Donville,[5] J Moreton,[6] L Lebina,[7] E Variava,[8,9] J Golub,[1,10] N Martinson,[7,9] [1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America, [2]Johns Hopkins University, School of Nursing, Baltimore, MD, United States of America, [3]Johns Hopkins Bloomberg School of Public Health, International Health, Baltimore, MD, United States of America, [4]Colorado State University, Environmental and Radiological Health Sciences, Fort Collins, CO, United States of America, [5]Johns Hopkins School of Arts and Sciences, Biotechnology, Baltimore, MD, United States of America, [6]University of the Witwatersrand, Tshimologong, Johannesburg, South Africa, [7]University of the Witwatersrand, Perinatal HIV Research Unit (PHRU), SA MRC Soweto Matlosana Collaborating Centre for HIV/AIDS and TB, Soweto, South Africa, [8]University of the Witwatersrand, Internal Medicine, Johannesburg, South Africa, [9]Klerksdorp-Tshepong Hospital Complex, Medicine, Klerksdorp, South Africa, [10]Johns Hopkins University, Center for TB Research, Baltimore, MD, United States of America. e-mail: brooke@jhmi.edu

Background: South Africa processes 1.2 million tuberculosis (TB) sputum tests annually, and patients—whether positive or not— must return to clinic for their results. Similarly, patients living with HIV must return regularly for CD4 and viral load (VL) results, even if they indicate no further clinical action. The purpose of this study was to assess an mHealth intervention to deliver laboratory results to patient mobile phones in Klerksdorp, South Africa.

Methods: For this pilot non-randomized trial, we enrolled 400 participants receiving a TB, CD4, and/or VL laboratory test. Participants saw their result either by returning to clinic (control, n=174) or via a secure message to their phone (intervention, n=226). Messages instructed participants in the intervention arm to return if they had a positive GeneXpert TB, CD4< 200, VL≥400, or were not on antiretroviral therapy, per national guidelines. Our outcomes were whether 1) participants saw ≥1 laboratory result within seven days of enrollment and 2) returned to clinic per their treatment arm instructions. We compared proportions using $\chi 2$ tests and estimated adjusted prevalence ratios with Poisson regression using robust variance, controlling for potential confounders. Intervention participants completed a 7-item satisfaction survey.

Results: A greater proportion of participants in the intervention arm (73%, 165/226 vs. 8.6%, 15/174, p< 0.001) saw their results within seven days of enrollment compared to controls (Table 1). Among those instructed to return, more participants in the intervention arm (20%, 14/70) returned to clinic than controls (8.6%, 15/174) in seven days. These results held after stratifi-

cation by test type (TB, CD4, and VL) and adjustment for confounders. Participants reported high satisfaction with the intervention.

	Total (n = 400)	Control arm (n = 174)	Intervention arm (n = 226)	p-value
Viewed ≥ 1 test result within seven days after enrollment	180 (45.0)	15 (8.6)	165 (73.0)	< 0.001
CD4 (n = 236)	126 (53.4)	7 (8.1)	119 (79.9)	< 0.001
Viral Load (n = 238)	103 (43.3)	6 (6.0)	97 (70.3)	< 0.001
Tuberculosis Xpert (MTB / RIF) (n = 114)	45 (39.4)	10 (14.5)	35 (77.8)	< 0.001
Instructed to return to clinic within seven days to retrieve their results	244 (61.0)	174 (100)	70 (31.0)	—
Returned to clinic within seven days, as instructed	29 (11.9)	15 (8.6)	14 (20.0)	0.02
CD4	20 / 148 (13.5)	7 / 87 (8.0)	13 / 61 (21.3)	0.03
Viral Load	9 / 119 (7.6)	6 / 100 (6.0)	3 / 19 (15.8)	0.16
Tuberculosis Xpert (MTB/RIF)	15 / 87 (17.2)	10 / 69 (14.5)	5 / 18 (27.8)	0.30

[Comparison of an mHealth intervention to deliver laboratory test results (n=226) to the standard of care (n=174) in South Africa]

Conclusions: Few participants returned for their laboratory results in this study, however those in the intervention arm returned in greater numbers. A national mHealth program for delivering results may be feasible and acceptable, and can increase patient return rates.

OA-21-447-01 Hepatotoxicity during MDR-TB treatment in a cohort of patients with high baseline prevalence of viral hepatitis receiving bedaquiline or delamanid

M Bastard,[1] C Hewison,[2] O Kirakosyan,[3] N Danielyan,[4] P Nair,[5] Z Avaliani,[6] N Sargsynats,[7] S Zhavoronok,[8] N Melikyan,[9] H Huerga,[9] [1]Epicentre, Research, Geneva, Switzerland, [2]Médecins Sans Frontières (MSF), Medical, Paris, France, [3]Médecins Sans Frontières (MSF), Medical, Yerevan, Armenia, [4]Médecins Sans Frontières (MSF), Medical, Tbilisi, Georgia, [5]Médecins Sans Frontières (MSF), Medical, Minsk, Belarus, [6]Ministry of Health, National Center for Tuberculosis And Lung Diseases, Tbilisi, Georgia, [7]Armenicum Clinical Centre, Infectious Disease, Yerevan, Armenia, [8]Belarusian State Medical University, Infectious Diseases, Minsk, Belarus, [9]Epicentre, Research, Paris, France. e-mail: mathieu.bastard@geneva.msf.org

Background: The endTB multi-center observational study is one of the largest cohort of patients receiving bedaquiline and/or delamanid. The objective of this study is to assess the incidence of clinically relevant hepatotoxicity in the endTB cohort and associated risk factors, including pre-existing viral hepatitis.
Methods: Data was censored on May 1, 2018 and included patients who initiated treatment with bedaquiline and/or delamanid between April 1, 2015 and June 30, 2017 in Armenia, Georgia and Belarus. Laboratory values (liver enzymes aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) were measured monthly and collected in an electronic medical record. Hepatotoxicity of clinical relevance was defined as an AST or ALT result greater than 5 times upper limit of normal. To assess risk factors for hepatotoxicity, we used a competing-risk regression model.
Results: A total of 447 patients were included: 79.6% were male, median age was 38 years [IQR 29-48], 90.4% were previously treated with second-line TB drugs, and 70.3% had strains resistant to fluoroquinolones. At treatment initiation, 7.9% were HIV-positive, 2.9% had positive serology for Hepatitis B and 22.9% had positive serology for Hepatitis C. Clinically relevant hepatotoxicity occurred in 48 (10.7%) of the patients in a median time of 2.8 months [IQR 1.5-7.5] after treatment initiation. The incidence of hepatotoxicity was 0.75/100 person-months in this cohort (95%CI, 0.56-1.00). Patients with positive serology for Hepatitis C at treatment initiation were more likely to develop hepatotoxicity during MDR-TB treatment (aSHR=2.78, 95%CI 1.57-4.91).
Conclusions: We observe a high prevalence of coinfection with Hepatitis C and a high incidence of clinically relevant hepatotoxicity during treatment. Patients with positive serology for hepatitis C were more likely to experience hepatotoxicity and should be particularly well monitored. Attribution of the hepatotoxicity to individual drugs is challenging as most of the drugs in MDR-TB regimens can potentially cause drug-induced liver injury.

OA-21-448-01 Frequency of deep-vein thrombosis among a cohort of drug-resistant TB patients in Lesotho with high rates of HIV co-infection

D Holtzman,[1] M Asfaw,[1] A Leta,[2] L Maama,[3] P Nkundanyirazo,[1] L Oyewusi,[1] [1]Partners in Health, MDR TB Program, Maseru, Lesotho, [2]Partners In Health, Partners In Health, Maseru, Lesotho, [3]Lesotho Ministry of Health, National TB Program, Maseru, Lesotho. e-mail: dholtzman@pih.org

Background: Deep vein thrombosis (DVT) is an important medical condition that can be triggered by diseases that cause systemic inflammation, including tuberculosis. Case series have reported on the occurrence of DVT among TB patients but none have examined DVT among drug-resistant (DR) TB exclusively. We describe the prevalence of DVT among DR TB patients in Lesotho enrolled in a prospective observational cohort.
Methods: DR TB patients initiated on bedaquiline or delamanid were enrolled in an observational cohort after providing informed consent. Participants enrolled between October 2015-June 2018 were included in this analysis. The study database and pharmacy records

were searched for adverse events consistent with venous thromboembolic event (VTE) and prescription of an anticoagulant. Files of identified participants were then reviewed to find confirmed DVT cases (a case was considered confirmed if a Doppler ultrasound visualized the DVT). Univariate analyses were carried out for relevant covariates.
Results: 225 individuals were enrolled during the study period. Sixteen participants with definitive DVT diagnoses were identified (7.1% incidence. No individual experienced more than one DVT episode. 56% of DVT cases were female and the average age was 42.6 years (range 25-76). 94% of DVT cases were HIV positive with 62% having a baseline CD4 count ≤200 cells/mm^3 (the HIV negative patient had breast cancer). 25% of DVT cases died during TB treatment.
Conclusions: DVT was a common co-morbidity among this DR TB cohort with high HIV co-infection. The true incidence of VTEs was likely higher than 7.1% as Doppler ultrasounds were not systematically done and diagnostic modalities were limited for diagnosing pulmonary embolism. Further study is needed to identify the risk factors associated with DVT among DR TB patients in order to mitigate the morbidity and mortality from these events.

OA-21-449-01 Preventive HBV antiviral therapy to reduce liver injury induced by anti-TB treatment for the patients with TB and HBV co-infection: a retrospective cohort study

J Cui,[1] Y Wang,[1] X Cui,[2] B Zhang,[1] J Ma,[1] Y Gao,[1]
[1]First Affiliated Hospital of Xinxiang Medical University, First Department of Tuberculosis, Weihui, China, [2]First Affiliated Hospital of Xinxiang Medical University, Second Department of Tuberculosis, Weihui, China.
e-mail: cjw8693@163.com

Background: Presently, China has high burden of tuberculosis (TB) incidence with high prevalence of hepatitis B virus (HBV) infection. In clinical practice, TB co-infected with HBV is a common phenomenon. In the anti-TB treatment, liver injury usually experiences substantial increased, especially for the patients with TB and HBV co-infection. Liver injury including moderate to severe liver injury or even liver failure may occur and possibly leads to fatality. In the current guideline of hepatitis B antiviral therapy, active TB treatment is not listed as an indication for preventive HBV antiviral therapy. The purpose of this study is to further understand the effect of preventive HBV antiviral therapy on liver injury caused by anti-TB treatment.
Methods: A total of 1098 patients with TB co-infected with HBV diagnosed from 2010 to 2018 were identified. 83 patients were excluded due to the lose follow of the programmed treatments, and the 1015 patients in the study period were divided into "antiviral therapy group (AT-G)" (nucleoside antiviral therapy combined with initial-treated anti-TB treatment, 369 cases) and "no antiviral therapy group (N-AT-G)" (simple initial-treated anti-TB treatment, 636 cases).
Results: After 2 months of treatment, the levels of alanine transaminase (ALT) and total bilirubin (TBIL) in AT-G were significantly lower than those in N-AT-G (ALT: 47.0±30.4 vs.72.4±65.7, TBIL: 20.0±10.3 vs. 24.8±22.7, $P< 0.01$). The incidence of moderate and severe liver injury in AT-G were also substantially reduced compared with that in N-AT-G (4.1% vs. 22.2%, $P< 0.01$).
Conclusions: Antiviral therapy for HBV can effectively reduce the damage rate of liver injury for the patients with TB-HBV co-infection during the anti-TB therapy. Therefore, the anti-HBV treatment is recommended in the process of clinical anti-TB treatment.

OA-22-D8 Vulnerability to TB has many faces

OA-22-450-01 Geospatial clustering and mathematical modelling provide policy guidance to distribute funding for active case finding in Ethiopia

D Shaweno,[1,2] J Trauer,[3,4] T Doan,[2] J Denholm,[5,6] E McBryde,[2,7] [1]The University of Sheffield, ScHARR, Sheffield, United Kingdom, [2]The University of Melbourne, Medicine, Melbourne, VIC, Australia, [3]Monash University, School of Public Health and Preventive Medicine, Melbourne, VIC, Australia, [4]Peter Doherty Institute for Infection and Immunity, Victorian Tuberculosis Program, Melbourne, VIC, Australia, [5]The University of Melbourne, Microbiology and Immunology, Melbourne, VIC, Australia, [6]Peter Doherty Institute, Victorian Tuberculosis Program, Melbourne, VIC, Australia, [7]James Cook University, Australian Institute of Tropical Health and Medicine, Townsville, VIC, Australia.
e-mail: d.shaweno@sheffield.ac.uk

Background: Tuberculosis (TB) exhibits considerable spatial heterogeneity, occurring in clusters that may act as hubs of community transmission. We evaluated the impact of an intervention targeting spatial TB hotspots in a rural region of Ethiopia.
Methods: To evaluate the impact of targeted active case finding (ACF), we used a spatially structured mathematical model. From model equilibrium, we simulated the impact of a hotspot-targeted strategy (HTS) on TB incidence ten years from intervention commencement and the associated cost-effectiveness. HTS was also compared with an untargeted strategy (UTS). We used logistic cost-coverage function to estimate the cost of our intervention strategies.

Results: At a community screening coverage level of 95% in a hotspot region, which corresponds to screening 20% of the total population, HTS would reduce overall TB incidence by 52% compared with baseline. For UTS to achieve an equivalent effect, it would be necessary to screen 80% of the total population. In a scenario in which, case detection rate (CDR) is increased to 70% in each strategy from baseline, the cost per averted case of active TB was estimated at USD1,300 for HTS and USD 4,400 for UTS. Compared with hotspot targeting, the UTS approach would avert 22 new TB cases at an additional total cost of USD 182,300, which translates to USD 8,200 for each additional case averted. Where regional TB program spending was capped at current levels, the intervention impact increased with increased proportional budget allocation to hotspots. Increased regional spending was associated with further incidence reductions, with maximum gains seen when an increased regional budget (five times higher than currently available) was shared between hotspots and non-hotspot regions in the ratio of 60% to 40%.
Conclusions: Our analysis suggests that a spatially-targeted strategy is efficient and cost effective with the potential for significant reduction in overall TB burden.

OA-22-451-01 Exploring the impact of subclinical TB on incidence estimates from prevalence surveys

AS Richards,[1,2] B Sossen,[3] JC Emery,[1,2] H Esmail,[3,4,5] RMGJ Houben,[1,2] [1]London School of Hygiene and Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom, [2]London School of Hygiene and Tropical Medicine, TB Modelling Centre, London, United Kingdom, [3]University College London, Institute for Global Health, London, United Kingdom, [4]University College London, Medical Research Council Clinical Trials Unit, London, United Kingdom, [5]University of Cape Town, Wellcome Centre for Infectious Diseases Research in Africa, Institute of Infectious Diseases and Molecular Medicine, Cape Town, South Africa.
e-mail: alexandra.richards@lshtm.ac.uk

Background: While the concept of a subclinical tuberculosis (TB) disease state (i.e. symptom-screen negative but culture positive and potentially infectious) is generally accepted, its implications are not well understood. If individuals can progress as well as regress from this state, the relationship between prevalence (which measures subclinical TB through radiographic screening, alongside symptomatic, clinical disease) and incidence (which focuses on clinical disease) will be affected. We explore the quantitative consequences using a mathematical model and data from a systematic review of historical literature of outcomes of untreated disease identified through active case finding.
Methods: A cohort model was developed, with a subclinical disease state and the potential to progress and regress between states. Progression and regression from the population found in two prevalence surveys was used to inform the likely number of incident cases under different assumptions and definitions.
Results: Our analysis of the historical literature suggests that between 20% and 40% of individuals regress from or stabilise in the subclinical stage, i.e. do not progress to clinical disease. Incidence estimates from prevalence surveys that do not take stagnation or regression into account could therefore overestimate the true incidence by up to 45% of the true value. The higher the percentage of individuals that do not progress to active disease, the larger the overestimate becomes. We explore this initial impact on its extension to multiple cohorts.
Conclusions: The dynamics of subclinical TB have a direct impact on the translation of prevalent burden to incident TB. Our findings are not limited to just prevalence surveys, but can also inform the estimated long-term impact on incidence from other activities that include radiographic components, such as community-based case finding efforts. We conclude that current burden estimates may set unrealistic case-finding targets for national TB programmes, meaning people are searching for non-existent cases of clinical TB.

OA-22-452-01 The potential impact of reducing the gender gap in TB screening in Viet Nam: a modelling study

KC Horton,[1,2] RG White,[1,2] R Bakker,[2,3] NB Hoa,[4] T Sumner,[2,5] EL Corbett,[1,6] RMGJ Houben,[2,5] [1]London School of Hygiene and Tropical Medicine, Department of Clinical Research, London, United Kingdom, [2]London School of Hygiene and Tropical Medicine, Tuberculosis Modelling Group, London, United Kingdom, [3]Erasmus MC University Medical Centre Rotterdam, Department of Public Health, Rotterdam, Netherlands, [4]National Tuberculosis Program of Vietnam, n/a, Hanoi, Viet Nam, [5]London School of Hygiene and Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom, [6]Malawi-Liverpool-Wellcome Trust Clinical Research Programme, n/a, Blantyre, Malawi.
e-mail: katherine.horton@lshtm.ac.uk

Background: In Viet Nam, pulmonary TB prevalence is over four times higher among men than women, and prevalence-to-notification ratios indicate greater gaps in detection and reporting among men than women. Men are estimated to remain infectious in the community a year longer than women, suggesting TB screening rates are much lower among men than women. We assessed the impact of reducing the gender gap in screening on TB incidence and mortality in men, women, and children.
Methods: We developed a sex-stratified *Mtb* transmission model incorporating sex-specific risks of *Mtb* infection, TB disease, and treatment completion, including social contact patterns, HIV and ART prevalence, tobacco smoking, alcohol consumption, and TB screening rates. The model was calibrated to population estimates

and to overall and sex-, age- and HIV-stratified (each where available) TB prevalence, incidence, case notification rates, and mortality for Viet Nam. We explored the impact of increasing screening rates in men over the next five years to reduce the gender gap in screening by 25%, 50%, and 100% (the latter indicating equal screening rates for men and women).

Results: Results suggest that reducing the gender gap in screening by 25%, 50%, and 100% would avert around a tenth, a quarter, and a third, respectively, of expected incident TB cases and TB deaths between 2020 and 2035. Reducing the gender gap in screening by these levels would lower the expected TB incidence in 2035 by approximately 20%, 40%, and 50%, respectively. Reductions in expected incidence were similar for men, women, and children.

Conclusions: Strategies to reduce the gender gap in TB screening in Vietnam could have a substantial impact on TB incidence and mortality, not only in men, but also in women and children.

OA-22-453-01 Sustainable active case finding in high-burden settings: modelling cost-effective approaches

L Cilloni,[1] N Arinaminpathy,[1] [1]Imperial College London, Infectious Disease Epidemiology, London, United Kingdom. e-mail: lc4215@imperial.ac.uk

Background: India's 2017 National Strategic Plan identifies sustained active case-finding (ACF) amongst vulnerable populations, as a key component of strategies to control TB.

However, while high-performance tests such as Xpert MTB/RIF may be important in accurate TB diagnosis, they will be costly to implement at a large scale. Planning of ACF activities would therefore benefit from diagnostic approaches allowing the selective use of Xpert, without compromising epidemiological impact.

Methods: Using a dynamic model of TB transmission, calibrated to capture conditions typical of an urban slum in India, we simulated an ACF intervention in which half of the slum population is screened per year. We modelled two ACF algorithms:

(i) symptom screening followed by Xpert confirmation, and

(ii) using chest X-ray (CXR) as a second screening tool, amongst those with TB-like symptoms, to narrow eligibility for Xpert.

We compared cost and potential epidemiological impact of both approaches.

Results: In an urban slum of 3 million people, an ACF approach using symptom screening, followed by Xpert confirmation, would cost USD 440 million (95% CrI USD 430-450 million) between 2019 and 2035, and could avert 16% (95% CrI 12%-23%) of TB cases during this time. Employing CXR as an additional screening step would cost USD 320 million (95% CrI USD 315-325 million) and could avert 14% (95% CrI 10%-21%) of TB cases during this time. The reduction in cost arises largely from a 4-fold decrease in the number of Xpert tests being conducted.

Conclusions: For active case-finding to be a sustainable part of future TB control, there is a need to identify the most cost-effective approaches. Chest X-ray may offer a helpful tool for focusing the use of costly diagnostic tests such as Xpert on those most likely to have TB, without sacrificing epidemiological impact. We discuss our findings in the context of new, automated X-ray technologies.

OA-22-454-01 Expected patient impact of the novel BPaMZ regimen depends upon implementation approach and rifampin-resistance epidemiology

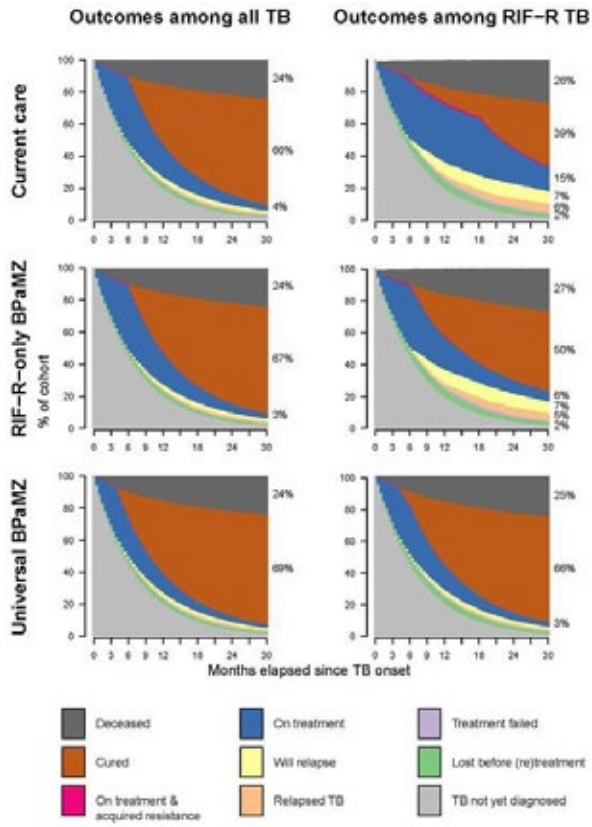
E Kendall,[1] S Malhotra,[2] S Cook-Scalise,[2] C Denkinger,[3,4] D Dowdy,[5] [1]Johns Hopkins School of Medicine, Infectious Diseases, Baltimore, MD, United States of America, [2]Global Alliance for TB Drug Development, Market Access/External Affairs, New York, NY, United States of America, [3]FIND, TB Program, Geneva, Switzerland, [4]University of Heidelberg, Center for Infectious Disease, Heidelberg, Germany, [5]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America. e-mail: ekendal2@jhmi.edu

Background: BPaMZ (bedaquline, pretomanid, moxifloxacin, and pyrazinamide) is a potential treatment-shortening regimen that has shown promise in late-stage clinical trials. If this regimen is approved for use, it will be critical to better understand its likely benefits for patients before implementing it at scale.

Methods: We developed a Markov state-transition model of 100,000 South African adults with rifampin-susceptible (RS) and rifampin-resistant (RR) TB, simulating diagnosis, treatment outcomes including relapse and retreatments, time with active TB, and acquisition of drug resistance. We compared current care to BPaMZ implementation for RR-TB only or for all patients. Sensitivity analyses considered different drug-resistance epidemiology and rifampin drug susceptibility testing (DST) practices.

Results: Using BPaMZ exclusively for RR-TB increased the proportion of patients with RR-TB who were cured by initial treatment from 60±1% to 67±1% (Figure). Expanding use of BPaMZ to all patients increased RR-TB cure further, to 89±1%, and increased cure among all individuals with TB from 87.3±0.1% to 89.5±0.1%). In settings where levels of RR-TB were similar but rifampin DST coverage was lower than in South Africa (10% rather than 70% of new patients, and 38% rather than 75% of retreatment patients), the benefits of BPaMZ were small if restricted to those diagnosed with RR-TB (46±1% of individuals with RR-TB cured, compared to 44±1% with current regimens), but the expected incremental benefit of universal BPaMZ implemen-

tation grew, with RR-TB cure increasing by 40±1% (to 86±1%), versus a 22±1% increase where DST coverage was high. In settings with higher RR-TB prevalence, the benefits of BPaMZ were magnified, both for RR-specific and universal BPaMZ implementation.
Conclusions: Novel regimens such as BPaMZ can play an important role in improving RR-TB cure rates and in shortening treatment for all patients with TB. These findings may aid decision-makers as they weigh early options for implementing such regimens at scale.



[Status over time of simulated South African TB cohort with BPaMZ or current care]

OA-22-455-01 Predictive factors for unfavourable treatment in MDR-TB and XDR-TB patients in Rio de Janeiro State, Brazil, 2000-2016

M Bhering,[1,2] R Duarte,[3] A Kritski,[1,2] [1]Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Rio de Janeiro, RJ, Brazil, [2]Brazilian Tuberculosis Research Network, Rede TB, Rio de Janeiro, RJ, Brazil, [3]University of Porto, Epidemiology, Porto, Portugal.
e-mail: kritskia@gmail.com

Background: The State of Rio de Janeiro stands out as having the second highest incidence and the highest mortality rate due to TB in Brazil. This study aims at identifying the factors associated with the unfavourable treatment of MDR/XDR-TB patients in that State.
Methods: Data on 2269 MDR-TB cases reported in 2000-2016 in Rio de Janeiro State were collected from the Tuberculosis Surveillance System. Bivariate and multivariate logistic regressions were run to estimate the factors associated with unfavourable outcomes (failure, default, and death) and, specifically, default and death.
Results: Among of the total cases 2,129 (93.8%) were MDR-TB and 140 (6.1%) XDR-TB. Susceptibility testing for first-line drugs showed that 69.7% were resistant to pyrazinamide, 39.8% to ethambutol and 43.7% to streptomycin. The proportion of unfavourable outcomes was 41.9% among MDR-TB and 81.5% among XDR-TB. The most frequent reasons for unfavourable treatment were default (19.4%) among MDR-TB, and failure (37.7%) among XDR-TB. Having less than 8 years of schooling, being an Afro-Brazilian, under 40 years old and drug user were associated with unfavourable outcome and default. Bilateral disease, HIV positive, and comorbidities were associated with death. XDR-TB cases had a 4.7-fold higher odds of an unfavourable outcome, with 29.3% of such cases being in the first treatment for multidrug resistance. Despite they had never been treated with second-line drugs, they had strains resistant to second-line injectable drugs, that are not routinely used for any other disease.
Conclusions: The data evaluated in this study suggests that nearly 30% of XDR-TB cases may have occurred by primary transmission. The high rates of failure in this category reflect the limitation of treatment options. This highlights the urgency of Brazil's health system to incorporate new drugs and improve efforts to increase cure and reduce default and implementing public policies that prevent the emergence of new cases of resistance.

OA-22-456-01 TB medicine costs for rifampin-resistant tuberculosis treated with a shorter regimen in a clinical trial setting

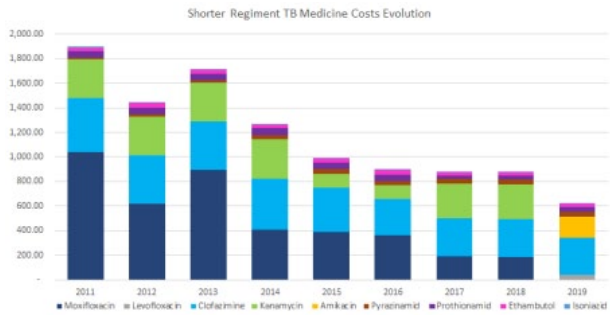
J Komrska,[1] I Qawiy,[1] [1]Vital Strategies, Research Division, New York, NY, United States of America.
e-mail: jkomrska@vitalstrategies.org

Background: The Union/Vital Strategies sponsored STREAM Stage 1 clinical trial confirmed the non-inferiority of a shorter regimen for the treatment of rifampin-resistant tuberculosis. Stage 1 regimen consisted of clofazimine, ethambutol, moxifloxacin, and pyrazinamide administered to patients for 40 weeks supplemented by kanamycin, isoniazid, and prothionamide for the first 16 weeks of treatment. The second stage of the trial comparing three different shorter regimens is ongoing. Access to TB medicines has improved, but remains challenging for certain medicines due to continued high prices.
Methods: TB medicine prices from purchase orders placed by the Sponsor with its suppliers between 2011 and 2019 were collected and used to calculate medicine

costs for the shorter regimen per patient above 50 kg on an annual basis. The prices did not include shipping and customs duties.

Results: The total cost of the study regimen decreased from 1,902.25 USD per patient in 2011 to 880.43 USD in 2018. Clofazimine, kanamycin, and moxifloxacin contributed to 94% of the cost of the regimen in 2011 and although reduced, still contributed to > 80% of the cost in 2018. The decrease in the price of moxifloxacin had the greatest impact on the overall cost reduction; with a price of 1,037.68 USD per patient in 2011 compared to 186.62 USD in 2018. The prices of other medicines evolved too but did not impact overall study regimen costs.

Conclusions: A reduction in costs of the shorter regimen may contribute to its successful roll out by National TB programs (NTPs). Increased competition on the market for clofazimine and other drugs may also contribute to decreased costs. However, additional cost reductions are most likely to be achieved only after replacement of moxifloxacin by levofloxacin and kanamycin by amikacin. When planning the roll out of the shorter regimen, NTPs should also consider other costs like shipping and customs duties.



[Shorter regimen TB medicine costs evolution (for a patient above 50 kg)]

OA-22-457-01 Attainment of target rifampin concentrations in cerebrospinal fluid during treatment of tuberculous meningitis

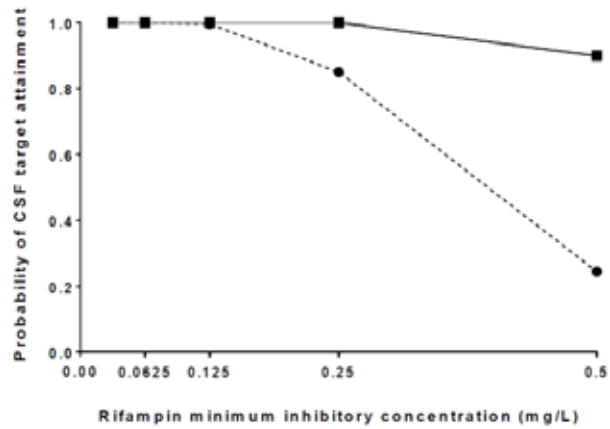
A Mezochow,[1] I Zentner,[2] L Kagan,[3] S Subbian,[2] C Vinnard,[2] [1]University of Pennsylvania, Perelman School of Medicine, Medicine, Philadelphia, PA, United States of America, [2]Rutgers University, Public Health Research Institute, Newark, NJ, United States of America, [3]Rutgers University, Pharmaceutics, Piscataway, NJ, United States of America. e-mail: christopher.vinnard@njms.rutgers.edu

Background: There is considerable uncertainty regarding the optimal use of rifampin for the treatment of tuberculous (TB) meningitis. We performed a pharmacokinetic modeling and simulation study of rifampin concentrations in cerebrospinal fluid during TB meningitis treatment using an intensively sample clinical pharmacokinetic dataset, and evaluated alternative rifampin dosing strategies.

Methods: We estimated parameters for rifampin pharmacokinetics in cerebrospinal fluid using individual-level rifampin pharmacokinetic data, and externally validated the model in three separate patient cohorts. We performed Monte Carlo simulations of rifampin serum and cerebrospinal fluid concentrations. The area under the rifampin cerebrospinal fluid concentration-versus-time curve during 24 hours ($AUC_{0\text{-}24}$) relative to the minimum inhibitory concentration (MIC) served as the pharmacodynamic target, based on the reported rifampin MIC distribution of wild-type (rifampin susceptible) isolates.

Results: Monte Carlo simulation of CSF rifampin target attainment according to rifampin MIC level, comparing standard (10 mg/kg) and intensified (20 mg/kg) dosing strategies, are shown in the Figure. Across all simulated patients on the first treatment day, 85% attained the target $AUC_{0\text{-}24}$/MIC ratio of 30 under a weight-based dosing scheme approximating 10 mg/kg. At the rifampin MIC of 0.5 mg/L, the probability of $AUC_{0\text{-}24}$/MIC target attainment was 26%. With an intensified dosing strategy corresponding to 20 mg/kg, target attainment increased to 99%, including 93% with an MIC of 0.5 mg/L.

Conclusions: Under standard dosing guidelines, few TB meningitis patients would be expected to attain therapeutic rifampin exposures in cerebrospinal fluid when the MIC is 0.5 mg/L or greater. Either downward adjustment of the rifampin MIC breakpoint in the context of TB meningitis, or intensified rifampin dosing upwards of 20 mg/kg/day, would reflect the likelihood of pharmacodynamic target attainment in cerebrospinal fluid.



[Monte Carlo simulation of target attainment. Dashed: 10 mg/kg. Solid line: 20 mg/kg.]

OA-23-E4 Rights-based considerations in TB person-centred care

OA-23-458-01 Coercion in tuberculosis: building a taxonomy of coercive techniques

L Ruhl,[1] B Citro,[2,3] D Silva,[4] [1]Simon Fraser University, Faculty of Sociology and Anthropology, Burnaby, BC, Canada, [2]Northwestern University, Pritzker School of Law, Chicago, IL, United States of America, [3]Northwestern University, Kellogg School of Management, Chicago, IL, United States of America, [4]Simon Fraser University, Faculty of Health Science, Burnaby, BC, Canada.
e-mail: leo_ruhl@sfu.ca

Background: Coercion is frequently used in the tuberculosis (TB) response for many different purposes. This study describes and organizes the different kinds of coercion that are applied in the context of TB to identify who or what uses coercion, on whom, and to what ends. Knowing which actions are coercive is necessary before their rightness and wrongness can be morally evaluated.
Methods: We conducted a literature review using a variety of databases such as Pubmed, JSTOR, and Google to find cases of coercion related to TB. Our study defined coercion as a commissive or omissive act performed on one entity by another with the goal of bringing about some intended end. Our goal was to describe various coercive acts, but not to judge the rightness or wrongness of the coercion.
Results: We created a taxonomy of different coercive techniques using cases found in the literature. The taxonomy includes categories such as coercion using technological tools, physical coercion, legal coercion, social or relational coercion, normative or ethical coercion, financial coercion, professional coercion, and the use of coercive incentives. Remarkable examples of coercion were discovered, including imprisonment of people with TB in Kenya as punishment for treatment non-adherence and the consideration of implanting microchips to track people with drug-resistant TB in India. We also consider factors that create an environment that facilitates or encourages coercion, such as the use of stigmatizing and dehumanizing language to describe people with TB, including TB suspects and defaulters.
Conclusions: This study serves to broaden our understanding of coercion and how it is used in the context of TB. Ethics and human rights research in the future can use this taxonomy to argue when and where the use of coercion is justifiable and legitimate.

OA-23-459-01 Restriction vs. respite: hospitalisation of TB patients who use substances in Cape Town, South Africa

A Versfeld,[1] [1]University of Witwatersrand, WISER, Johannesburg, South Africa.
e-mail: annaversfeld@gmail.com

Background: TB and substance use frequently co-occur, particularly in conditions of poverty. People who use substances are particularly susceptible to poor engagement and retention in care. In Cape Town one consequence of this is that healthcare workers use extended periods of inpatient treatment in TB hospitals as a means of retaining a level of control over patients they think are unlikely to complete their treatment. This runs counter to international calls for decentralised, home-based TB care, which draw on argument of cost effectiveness, reach and human rights.
Methods: This presentation draws on a year of ethnographic fieldwork in Cape Town (in 2014) split across two sites: an inpatient TB hospital and an outpatient treatment center for substance use and on six weeks of in three TB clinics (in 2012). Research methods included participant observation, eleven life history interviews, six focus groups, over 30 interviews with facility staff, and a cross-sectional chart review of patients (N=167) in DP Marais hospital.
Results: Some patients who used substances experienced the restrictions and rules of hospitalisation as uncomfortably close to internment and sought discharge as soon as possible. Other patients actively orchestrated hospital admissions and extended stays, even if they were not extremely ill. In the context of drug use and poverty, centralised, in-patient care can provide stabilisation and respite from the precarity of everyday life. For patients who have experienced or used the hospital in this way, discharge can cause fear and stress.
Conclusions: Extended hospitalisation might not represent a loss of agency, but rather TB-affected people's capacity to use the resources for healing at their disposal. The validity of arguments for decentralised care should not undermine the recognition that TB hospitals can play important, positive, roles in the lives of affected people, especially in contexts of substance use and poverty.

OA-23-460-01 TB Mukt Vahini (TMV) Bihar-A network of TB survivors: working to ensure a rights- based, patient-centric ecosystem

SK Singh,[1,2,3] R Mumtaz,[1] A Kumari,[4,5] A Kumar,[6] KN Sahay,[7] RS Sharma,[8] SN Jha,[9] [1]TB Mukt Vahini, Health, Patna, India, [2]Country Coordination Mechanism(CCM), TB, Patna, India, [3]State TB Forum, Health, Patna, India, [4]National TB Forum, Health, New Delhi, India, [5]District TB Forum, Health, Muzaffarpur, India, [6]TB Mukt Vahini, Health, Vaishali, India, [7]State Health Society, Health, Patna, India, [8]TB Mukta Vahini, Health, Patna, India, [9]TB Mukt Vahini, Health, Samstipur, India.
e-mail: sudeshwar_singh@yahoo.com

Background and challenges to implementation: During the End TB Summit Delhi 2018 the Prime Minister of India listened the story of one of TB survivor from Bihar, he emphasized the role of TB Survivors towards making India TB Free. This led to the prioritization of community engagement through the TB Champions across the country towards TB care & control.
Intervention or response: Build the capacity of TB survivors as TB champions to engage them for TB program and fourteen trained TB survivors cum champions from 7 districts of Bihar formed a state level network of TB survivors called TB Mukt Vahini (TMV) which has grown up to more than 243 members from 18 districts in Bihar. TMV members have started sensitizing the community on stigma reduction, treatment adherence, providing psychosocial support, facilitating early detection and engaging decision makers of the society.
Results and lessons learnt: TMV has been registered under Society Registration Act 1869. The members got recognition in various national and international platforms like as a member at CCM, Moth Storytelling workshop, invited by the US Embassy of India etc. 11 TMV members have been included as members of National, State and District levels forums under RNTCP thereby providing the voice to the thousands of TB patients that they represent. TMV members have provided psychosocial support to 477 TB patients, 483 presumptive TB cases have been examined, notification 82 new TB cases has been done, 28 LFU cases linked to treatment, helped 64 TB patients to get DBT and they have been treatment supporters of 19 TB patients and have sensitized 7178 people.
Conclusions and key recommendations: TMV has demonstrated that coming together of TB survivors in a structured and cohesive manner can lead to the augmentation of the services provided by the government, reaching the hitherto unreached population and advocating for enforcement of existing RNTCP guidelines for effective treatment adherence.

OA-23-461-01 Building the capacity of TB survivors to be empowered champions and advocates: a report from India

A Srinivasan,[1] S Kumar,[2] A Panda,[2] P Mishra,[2] K Majumdar,[2] A Sharma,[2] R Ananthakrishnan,[3] N Krishnan,[3] A Shah,[4] [1]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, Chennai, India, [2]REACH (Resource Group for Education and Advocacy for Community Health), TB Call to Action Project, New Delhi, India, [3]REACH (Resource Group for Education and Advocacy for Community Health), Organisation, Chennai, India, [4]USAID India, Health Office, New Delhi, India.
e-mail: anupamasrinivasan.reach@gmail.com

Background and challenges to implementation: TB survivors remain relatively unengaged, despite having witnessed first-hand TB's impact. Survivors are uniquely positioned to translate their personal TB stories into powerful advocacy narratives. Empowered TB survivors can drive the transition towards person-centred care for people with TB.
Intervention or response: Under the Call to Action project supported by USAID, REACH organized 8 capacity-building workshops in 6 states over a 4-month period. Participants were identified through an open call and in coordination with state government and district TB staff. The 4-day workshops focused on building the capacity of survivors in advocacy and communications, and improving their knowledge of TB and the public health system at various levels. TB Champions work with a three-fold mandate: to provide psycho-social support to people with TB, conduct meetings in their communities and refer those with symptoms, and advocate with key stakeholders for better services.
Results and lessons learnt: Over 225 TB survivors were trained as TB Champions. 21% were women. Of those trained, 180 TB Champions from 112 districts were enrolled in a six-month mentorship program, supported by 42 mentors. Over 50 TB Champions are members of State and District TB Forums and provide real-time feedback to the health system. Over 40 TB Champions were invited to speak at various national, state and district level meetings. Six state-level, survivor-led networks were formed to advocate for the rights of the affected community. Of these, one network is registered as a legal entity.
Conclusions and key recommendations: This intervention has demonstrated a systematic and rigorous process of training TB survivors. Trained TB Champions are highly motivated to work among their communities and must be supported with financial resources and refresher trainings. Involving TB Champions has been included in the NTP's community engagement strategy, and an experimental beginning of empowering TB Champions has paved the way for an intensified community engagement programme.

OA-23-462-01 TB control in humanitarian emergencies in the Middle East: case detection, enrolment and treatment outcomes for refugees, migrants, internally displaced and other vulnerable populations in 2017-2018

MS Qayyum,[1] N Wilson,[1] H Yaacoub,[2] E Mahyoub,[3] A Naser,[4] H Faroun,[5] G Sharkas,[6] [1]IOM-The UN Migration Agency, Migration Health Division (MHD), Amman, Jordan, [2]National TB Program, Ministry of Health, Beirut, Lebanon, [3]National TB Program, Ministry of Health, Sana'a, Yemen, [4]National TB Program, Ministry of Health, Aden, Yemen, [5]National TB Program, Ministry of Health, Damascus, Syrian Arab Republic, [6]National TB Program, Ministry of Health, Amman, Jordan. e-mail: sqayyum@iom.int

Background and challenges to implementation: Complex emergencies in some countries in the Middle-East region has forced millions of people to leave their homes. Political conflicts and civil uprising in Syria and Yemen have resulted in breakdown of existing public and social services. Jordan and Lebanon, as neighbouring countries, are also affected by massive influx of refugees.
IOM has been working with NTPs addressing challenges in TB case detection and treatment through the Middle East Response(MER) initiative—a differentiated approach of the Global Fund to ensure continuity of TB treatment for people affected by conflict in Yemen, Syria, Lebanon and Jordan.
Intervention or response: NTPs were supported with diagnostic equipment(e.g.,Xpert), lab consumables, drugs, staff remuneration and technical capacity development. Activities included awareness raising, active and passive case finding with symptom screening, mobile X-ray and Xpert testing in refugee camps, hard-to-reach and urban areas using CHWs and mobile medical teams, case referrals, diagnosis, treatment follow-up, hospitalization and contact management.
Results and lessons learnt: From January2017-December2018, 24,803 cases from these conflict affected four countries were diagnosed as having drug sensitive TB disease and enrolled on TB treatment—case detection approximates to **67%** of the WHO estimated TB burden (36,502) in the same four countries for 2017-18; among them 12,689 (51%) male and 12,114 (49%) female; 2,935 (12%) pediatric (≤ 14 years). 116 cases were diagnosed as MDR-TB, including 3 with XDR-TB.

Patients	Success	Died	Lost-to-follow-up	Failure
12,336*	11,215(91%)	272(2%)	752(6%)	97(1%)

[Treatment outcome of 2017 cohort of drug sensitive TB patients]

12,477 cases enrolled (*141 were not evaluated) on TB treatment in 2017, among them from Yemen 9,408 (75.5%), Syria 2,845 (23%), Lebanon 151(1%) and Jordan 73 (0.5%).

Continuing TB case finding and good treatment outcome (**>90%**) for refugees, migrants, internally-displaced in humanitarian contexts is possible through differentiated and well-coordinated approaches.
Conclusions and key recommendations: The results of Middle East Response initiative to TB control in humanitarian emergencies indicate that collaborative efforts of the International communities and the NTPs can lead to successfully maintaining continuity of TB services.

OA-23-463-01 Transgender women and TB vulnerability, care access and quality in South Africa: a qualitative study

A Versfeld,[1] K Grant,[2] T Mokganyetji,[3] A Best,[4] T Katlholo,[5] H Hausler,[6] [1]TB HIV Care, NA, Cape Town, South Africa, [2]Independent Consultant, NA, Johannesburg, South Africa, [3]University of Cape Town, School of Public Health, Cape Town, South Africa, [4]TB HIV Care, Communications, Cape Town, South Africa, [5]StopTB Partnership, Country and Community Support for Impact, Geneva, Switzerland, [6]TB HIV Care, Management, Cape Town, South Africa. e-mail: annaversfeld@gmail.com

Background: Gender impacts on TB vulnerability, care access and quality. Gendered analyses of TB vulnerability and care often exclude transgender women, despite the fact that they face numerous rights abuses, struggle to access healthcare, and are 49 times more likely to be living with HIV than the general population. TB HIV Care, supported by the StopTB Partnership, implemented a TB gender assessment in South Africa which incorporated a focus on transgender women.
Methods: Qualitative research conducted in two provinces September - November 2018, included: key informant interviews (4), focus group discussions with TB-affected individuals (5) and with healthcare providers (2), and participatory research activities with 19 TB-affected people. The University of Cape Town provided ethics approval. Participants could use one of three official languages. Data were transcribed, translated if required, and thematically analysed using NVivo. Findings were validated by a multi-stakeholder group and analysed against the local legal and policy framework.
Results: Despite legal protections, transgender women experience stigma and discrimination in all aspects of life. This results in layered vulnerabilities to TB infection and disease: social marginalisation is related to homelessness, joblessness, sex work and drug use. This increases HIV infection risk and incarceration rates, which further exacerbate TB vulnerability. Stigma in-community hampers freedom of movement, undermining care access. Care quality is undermined by healthcare workers' insufficient knowledge of human rights and the requirements of gender-sensitive care.
Conclusions: There has been insufficient focus on transgender women as a potential TB key population. Efforts to take a gender-responsive, human rights approach to TB must ensure that the challenges and needs of trans-

gender women both within and outside of healthcare facilities are considered. This includes gender sensitivity training for healthcare providers, creation of cross-sectoral partnerships and social protection programmes, designed and implemented in partnership with affected people.

OA-23-464-01 Lessons learned from using indigenous methodologies for cocreation of TB policy: preliminary results

N Grewal,[1] K McMullin,[2,3] D Goodridge,[4] M Oddie,[5] J Gordon,[6] LM Puchalski Ritchie,[7,8,9] V Hoeppner,[4] E Rea,[10,11] W Wobeser,[1] [1]Queen's University, Departments of Biomedical and Molecular and Public Health Sciences, Kingston, ON, Canada, [2]University of Saskatchewan, Department of Health Sciences, Saskatoon, SK, Canada, [3]Gabriel Dumont Institute of Native Studies and Applied Research, Saskatchewan Urban Native Teacher Education Program, Prince Albert, SK, Canada, [4]University of Saskatchewan, Department of Medicine, Saskatoon, SK, Canada, [5]Queen's University, Cultural Studies Program, Kingston, ON, Canada, [6]Sioux Lookout First Nations Health Authority, Administration, Sioux Lookout, ON, Canada, [7]Li Ka Shing Knowledge Institute, University Health Network, Toronto, ON, Canada, [8]Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada, [9]University of Toronto, Department of Medicine, Toronto, ON, Canada, [10]Toronto Public Health, Tuberculosis Program, Toronto, ON, Canada, [11]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada. e-mail: n.grewal@queensu.ca

Background and challenges to implementation: In Canada, Indigenous peoples continue to experience higher rates of TB than the Canadian-born, non-Indigenous population. We are working towards quantifying the relative contribution of relapse and reinfection to recurrent TB in four Canadian jurisdictions. By doing so, we aim to better understand the role of reinfection TB in Indigenous communities.

Our initial work in this area includes integrated knowledge translation (iKT) events to identify the main TB themes for Indigenous peoples.

Intervention or response: The iKT work began with a team gathering in September 2018 on the traditional lands of the Haudenosaunee and Anishinaabek in Kingston, Canada. In keeping with North American Indigenous epistemological research approaches, a Sharing Circle was chosen as the method to share knowledge among the research team and community. The Circle was open to the public and guided by an Indigenous Elder and the team's Indigenous Engagement Advisor. The discussion was transcribed, and a thematic analysis was conducted using NVivo 12.

Results and lessons learnt: Participants noted stigma associated with TB may stem from harsh historical TB management approaches, including mandatory transportation to sanatoria; cultural perceptions; the fact that active TB is contagious; and historically was a fatal illness. Challenges, including decreased provider awareness to the continued existence of TB, inconsistent testing leading to missed diagnoses, and loss-to-follow up during screening and treatment, were highlighted. There were discussions regarding patient considerations in TB management. The importance of ensuring patient autonomy and dignity and fostering respect and trust were noted.

Conclusions and key recommendations: The discussion indicated the importance of fostering dialogue about TB amongst community members, researchers, care providers and policy-makers to decrease stigma and work towards achieving elimination of TB in high-burden communities. Subsequent Circles are planned, with an emphasis on engaging individuals with lived experience.

The Circles will inform the team's work by exploring considerations for creating effective knowledge translation products for communities.

OA-23-465-01 Engaging the housing sector to address tuberculosis burden in the slums in Nigeria

R Igbinoba,[1] [1]Cranfield University, Economics and Finance, Milton Keynes, United Kingdom.
e-mail: rigbinoba@gmail.com

Background and challenges to implementation: This intervention was based on the escalating conversations that ending tuberculosis (TB) especially amongst key and vulnerable populations such as people living in slums in Nigeria would not only be successful by the investment in medical interventions but also by actively engaging multisectoral approaches especially as it concerns human rights; in this case - the right to adequate housing. A Legal Environment Assessment (LEA) of Nigeria was recently carried out which identified risks factors for high rates of TB in the slums areas as; overcrowding, inadequate housing and poverty. The LEA argues that when the rights to housing is being violated, it puts people in the risk of getting TB.

Intervention or response: Meaningful engagement of the key and vulnerable population was carried out with thirty-three (33) people affected with TB in Ijora-Badiya slums in Lagos. The dialogue centered on ending TB as it relates to their families/friends from their own perspective. A perceptive analysis was carried out using NVIVO 11. The results were bench-marked against the WHO Health and Housing Guidelines.

Results and lessons learnt: It was evident that the living conditions of the TB patients did not meet any of the WHO guidelines. Worse still was that their income cannot improve their living conditions and they are constantly under the threat of government officials destroying their abode. Also, no remedy has been proffered by health officials as it concerns their living conditions and housing.

Conclusions and key recommendations: The fact that no health official has proffered helping with the living conditions and housing in the slum calls for concern and an urgent implementation for a joint effort between the housing and health ministry. A robust and favourable legal environment is also required to push for this multi-sectoral approach. A strong advocacy for the implementation of the right to housing should be embarked upon especially for this key population

SHORT ORAL ABSTRACT SESSIONS (SOA)

SOA-10-C2 Pharmacokinetics, pharmacovigilance and chain supply in the treatment of TB

SOA-10-1095-01 Health workers perception of the shorter regimen in MDR-TB treatment: qualitative evidence from Ethiopia

L Rosu,[1] M Girma Tefera,[2] I Langley,[1] J Madan,[3] BS Squire,[1] on behalf of the STREAM Collaboration
[1]Liverpool School of Tropical Medicine, Clinical Sciences, Liverpool, United Kingdom, [2]Addis Ababa Science & Technology University, School of Business and Economics, Addis Ababa, Ethiopia, [3]University of Warwick, Clinical Trials Unit, Warwick, United Kingdom.
e-mail: laura.rosu@lstmed.ac.uk

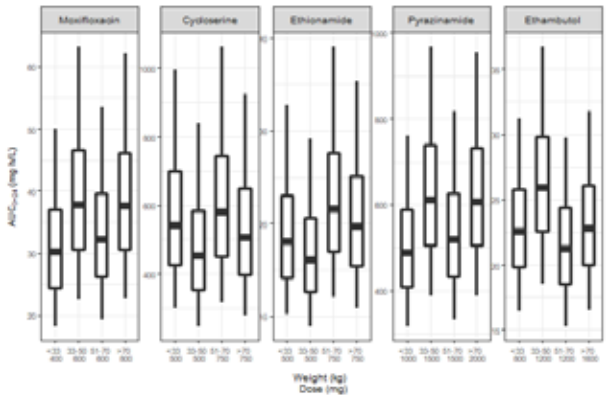
Background: Ethiopia has recently adopted the 9-month Multi-drug resistant tuberculosis (MDR-TB) treatment regimen within its national TB control programme. The aim of this study is to identify and understand country specific gaps between policy and practice. We also identify concerns relating to the shorter regimen (compared to the standard regimen), from a health worker, patient, and health system perspective. Understanding these issues will be useful for programmes implementing shorter TB regimens.
Methods: Fourteen health workers managing patients enrolled into the STREAM randomised clinical trial were selected from St. Peters and AHRI hospitals, Addis Ababa, Ethiopia. A snowball sampling technique was used to recruit key informants from each staff category (study clinicians and ward and community nurses) along the clinical treatment pathway. In-depth interviews were conducted using a semi-structured interview guide. Thematic data analysis was performed using Atlas.ti software.
Results: Health workers in Ethiopia perceived the benefits of the shorter treatment for patients to include returning to work sooner, fewer side effects, reduced pill-burden and fewer health facility visits. The low pill-burden, milder side effects and the shorter duration of the regimen were perceived to reduce patients' psychological distress and increase their adherence to treatment. There were benefits for staff from workload reduction and reduced patient exposure while the health system benefited from resource savings.
Conclusions: Health workers' satisfaction was high due to the decrease in workload, resulting from the shorter nature of the regimen, fewer side effects and better patient compliance. Building strong collaboration between the local government and partners was identified as key to ensuring long-term affordability and sustainability of the new regimen. Ongoing training to strengthen the staff capacity in managing the regimen will be required.

SOA-10-1096-01 A comparison of exposure to drugs used for the treatment of MDR-TB across dosing weight bands

MT Chirehwa,[1] R Court,[1] R Warren,[2] L Wiesner,[1] N de Vries,[3] J Harding,[4] T Gumbo,[5] P Denti,[1] G Maartens,[1] H McIlleron,[1] [1]University of Cape Town, Division of Clinical Pharmacology, Department of Medicine, Cape Town, South Africa, [2]Stellenbosch University, DST/NRF Centre of Excellence in Biomedical Tuberculosis Research, SAMRC Centre for Tuberculosis Research, Cape Town, South Africa, [3]Brooklyn Chest Hospital, Tuberculosis, Cape Town, South Africa, [4]DP Marais Hospital, Tuberculosis, Cape Town, South Africa, [5]Baylor Research Institute, Baylor University Medical Center, Center for Infectious Diseases Research and Experimental Therapeutics, Dallas, TX, United States of America.
e-mail: maxwell.chirehwa@uct.ac.za

Background: To evaluate the exposure to five drugs used for the treatment of multidrug-resistant tuberculosis (MDR-TB) in patients with different body size and propose doses that minimise exposure differences across weight bands.
Methods: Patients with rifampicin-resistant TB (n=133) were recruited into a pharmacokinetic study in Cape Town and underwent pharmacokinetic sampling two to six weeks after initiating TB treatment. The standard MDR-TB treatment regimen consisted of moxifloxacin, kanamycin, cycloserine dosed as terizidone, pyrazinamide, ethambutol, and ethionamide or isoniazid (in high doses for patients with *inhA* mutation). Patients received daily 400 mg of moxifloxacin, regardless of weight and weight-band adjusted doses of all the other drugs. Population pharmacokinetic models were developed separately for moxifloxacin, cycloserine, pyrazinamide, ethambutol, and ethionamide and the effect of body size was included using allometric scaling. Monte Carlo simulations with these models and historical demographic data from 1225 TB patients were used to explore drug exposure under several dosing scenarios based on the recommended weight bands; < 33, 33-50, 51-70, and >70 kg.
Results: Moxifloxacin showed the largest weight-related differences in drug exposure, with patients in the larger weight bands achieving lower exposure. Doses of 400, 600, and 800 mg for patients in the < 33, 33-70, and >70 kg weight bands, respectively, reduced the maximum difference in median exposures between weight bands from 35% to 20%. For all drugs whose dose was weight-adjusted, the current recommendations produced lower exposures for patients in the lower weight bands, who thus required a dose increase. Drug exposures associated with the proposed dose for each weight band are presented in Figure 1.

Conclusions: We propose weight-adjusted doses using population pharmacokinetic models which take into account the effect of body size. Weight-adjusted dosing targeting a constant mg/kg dose underexposes patients with lower weight whereas flat dosing underexposes patients with higher weight.



[Boxplot of simulated 24-hour AUC (based on proposed doses) stratified by weight band]

SOA-10-1097-01 Population pharmacological investigation of first-line anti-tuberculosis drugs, a multicentre prospective study

Y Gao,[1] Y Hu,[1] L Davies Forsman,[2,3] S Hoffner,[4] J Bruchfeld,[2,3] J-W C. Alffenaar,[5] [1]Fudan University, School of Public Health, Department of Epidemiology, Shanghai, China, [2]Karolinska University Hospital, Department of Infectious Disease, Stockholm, Sweden, [3]Karolinska Institutet, Department of Medicine, Stockholm, Sweden, [4]Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden, [5]University of Sydney,School of Pharmacy and Westmead Hospital, Faculty of Medicine and Health, Sydney, NSW, Australia. e-mail: yzgao17@fudan.edu.cn

Background: We aimed to describe the population pharmacokinetic (PPK) of rifampicin (RIF), isoniazid (INH) and pyrazinamide (PZA) in Chinese adult tuberculosis (TB) patients and assess the adequacy of drug exposures in steady-state.

Methods: A multi-centre PPK study of RIF, INH and PZA was prospectively conducted in Jiangsu, Shandong, Sichuan and Fujian Province, China between January 2015 and December 2017. Six blood samples/patient were withdrawn for drug concentration measurement. Nonlinear mixed effect analyses were used to develop PPK models. Maximum drug concentrations (Cmax) and area under concentration-time curve (AUC) were derived from Bayesian forecasting. Multivariate logistic and linear regression analyses were performed to identify factors associated with suboptimal drug exposures.

Results: Blood samples from 217 patients were collected. Compartment analyses were performed and pharmacokinetic profiles of RIF and PZA were best described by one-compartment models, while a two-compartment model was more appropriate for INH. RIF clearance was elevated as body mass index increased and female patients had a lower RIF clearance, independently of BMI. Acetylator status based on NAT2 genotype was associated with INH clearance and INH AUC whereas body weight was associated with PZA clearance and volume of distribution. The estimated median (interquartile range) Cmax for RIF, INH and PZA were 8.37 (7.36-9.67), 3.55 (2.78-4.39) and 31.1 (22.8-39.7) mg/L, respectively. Overweight and inadequate weight-based dosing were significant risk factors for low RIF Cmax. Fast acetylator status was a strong predictor of suboptimal INH Cmax (OR=8.07, $p < 0.001$). Inadequate weight-based dosing was also significant risk factor for low PZA Cmax. Diabetic patients and patients with inadequate weight-based dose had significantly reduced AUC of PZA.

Conclusions: A "one dose fits all" strategy is not able to result in adequate exposure for all drugs in all patients. Information on risk factors for low drug exposure could be used by clinicians to guide dose selection.

Predictors of low drug Cmax (below proposed target)[a]

Characteristics	Odds ratio (95%CI)	*p*-value
Rifampicin		
BMI level		
Normal (18.5-23.9)	Reference	
Overweight (≥24)	3.85 (1.98 to 7.51)	<0.001
Underweight (<18.5)	0.48 (0.14 to 1.63)	0.24
Dose/TBW < 10 mg/kg	3.75 (1.94 to 7.24)	<0.001
Isoniazid		
Fast NAT2 acetylator[b]	8.07 (4.00 to 16.28)	<0.001
Pyrazinamide		
Dose/TBW < 25 mg/kg	4.74 (2.09 to 10.77)	<0.001

Note: Cmax, maximum concentration; BMI, body mass index; TBW, total body weight.
a: Table depicts predictors of low maximum concentrations for rifampicin, isoniazid and pyrazinamide in multivariate logistic analysis. Proposed target was 8 mg/L, 3 mg/L and 20 mg/L for RIF, INH and PZA, respectively. b: No slow acetylators had INH Cmax below reference range, so slow and intermediate acetylators were merged in the analysis.

Multiple linear regression identifying factors associated with drug AUC[a]

Characteristics	Coefficient(95%CI)	*p*-value
Rifampicin		
Female	7.95 (1.98 to 13.92)	0.009
Dose/TBW < 10 mg/kg	-5.76 (-11.37 to -0.16)	0.044
Isoniazid		
NAT2 acetylator		
Slow	Reference	
Intermediate	-17.16 (-22.41 to -11.90)	<0.001
Fast	-27.75 (-32.75 to -22.75)	<0.001
Pyrazinamide		
Diabetes	-95.92 (-187.48 to -4.36)	0.04
Dose/TBW < 25 mg/kg	-157.14 (-234.53 to -79.75)	<0.001

Note: AUC, area under the concentration-time curve; TBW, total body weight.
a: Factors including area, age, BMI level, drug formulation, cigarette use, alcohol consumption, C-reaction protein, fasting blood glucose, 2-hour oral glucose tolerance test, alanine transaminase, aspartate transaminase, alkaline phosphatase, albumin, total bilirubin, serum creatine, urea nitrogen and urine acid turned out to be insignificant in multivariate analysis

[Factors associated with drug exposure]

SOA-10-1098-01 Therapeutic drug monitoring including individual determination of minimum inhibitory concentrations of linezolid during routine MDR-TB treatment

L Davies Forsman,[1,2] J-W Alffenaar,[3] T Schön,[4,5] C Giske,[6] J Jonsson,[7] J Kuhlin,[1,2] R Groenheit,[8] J Bruchfeld,[1,2] [1]Karolinska Institutet, Department of Medicine, Division of Infectious Diseases, Stockholm, Sweden, [2]Karolinska University Hospital, Department of Infectious Diseases, Stockholm, Sweden, [3]University of Sydney and Westmead Hospital, School of Pharmacy, Faculty of Medicine and Health, Sydney, NSW, Australia, [4]Linköping University Hospital, Department of Medical Microbiology, Linköping, Sweden, [5]Kalmar County Hospital, Sweden, Department of Clinical Microbiology and Infectious Diseases, Kalmar, Sweden, [6]Karolinska Institutet, Department of Laboratory Medicine, Stockholm, Sweden, [7]Public Health Agency of Sweden, Unit for Epidemiological Monitoring, Department of Public Health Analysis and Data Management, Stockholm, Sweden, [8]Public Health Agency of Sweden, Department of Microbiology, Public Health Agency of Sweden, Stockholm, Sweden.
e-mail: lina.davies.forsman@ki.se

Background: The repurposed drug linezolid (LZD) is now recommended for all patients treated for multi-drug-resistant tuberculosis (MDR-TB). Long-term LZD treatment is associated with severe adverse events, such as bone marrow depression and polyneuropathy. Therapeutic drug monitoring (TDM) is warranted to avoid toxicity and ensure adequate drug exposure.
However, few settings are able to determine the minimum inhibitory concentrations (MICs) and drug concentrations measurements of LZD.
Therefore, we report the first experiences after the introduction of TDM for LZD in MDR-TB 2015 and onwards.
Methods: In this retrospective cohort study, all patients with MDR-TB in Sweden from 2015-2018 were included. MIC determination for LZD was performed in liquid media using Bactec MGIT 960 including testing at the critical concentration (CC 1 mg/L). Blood samples for LZD concentrations were collected before dose intake and 2 hours post-dose and measured in plasma using liquid-chromatography mass-spectrometry (LC-MS/MS). Target attainment estimating AUC/MIC assessed according to a previously published study (Kamp IJAA 2017 Jun;49(6):688-694).
Results: Out of the 69 patients included, there were 41 (59.4%) male patients. The median MIC was 0.5 mg/L, with a narrow distribution (range: 0.25-1 mg/L). All isolates were susceptible to LZA at the CC. The median dose was 600 mg daily, with a median trough plasma concentration of 2.8 mg/L (0.5-5.5 mg/L) and 12.5 mg/L (2.2-16 mg/L) at 2 h post-dose (n=25).
For the nine patients with complete information regarding individual MIC and drug concentrations, the previously suggested target drug exposure was attained for all patients treated with 600 mg daily, but not in the only patient treated with 300 mg daily.
Conclusions: MICs of LZD are generally low with a narrow distribution. Target attainment was reached if a dose of 600 mg daily was given. TDM may be a useful tool to assess drug exposure of LZD in order to avoid toxicity.

SOA-10-1099-01 Pharmacodynamical parameters and genetic polymorphisms predict risk of systemic drug reaction during weekly rifapentine and isoniazid therapy for latent tuberculosis infection

J-Y Wang,[1] M-R Lee,[2] H-L Huang,[3,4,5] [1]National Taiwan University Hospital, Internal Medicine, Taipei, Taiwan, [2]National Taiwan University Hospital, Hsinchu Branch, Internal Medicine, Hsinchu, Taiwan, [3]Kaohsiung Municipal Ta-Tung Hospital, Internal Medicine, Kaohsiung, Taiwan, [4]Kaohsiung Medical University Hospital, Internal Medicine, Kaohsiung, Taiwan, [5]Kaohsiung Medical University, Graduate Institute of Medicine, College of Medicine, Kaohsiung, Taiwan. e-mail: 990325kmuh@gmail.com

Background: Weekly rifapentine and isoniazid therapy (3HP) for latent tuberculosis (TB) is increasingly used while systemic drug reaction (SDR) remains a major concern. Little, however, was known regarding the potential contributor and predictor of 3HP-related SDR.
Methods: We prospectively recruited two TB close contact cohorts who received 3HP regimen. In single nucleotide polymorphism (SNP) cohort, we collected clinical information of SDR and examined SNPs of *NAT2*, *CYP2E1* and *AADAC*. In pharmacokinetic (PK) cohort, we measured plasma drug and metabolite level 6 hours and 24 hours after 3HP administration. Generalized estimating equation (GEE) model was used to explore factors associated with SDR. Candidate SNPs predicting SDRs were also validated in the PK cohort.
Results: A total of 177 participants in the SNP cohort and 129 participants in the PK cohort were recruited, with 14 (8%) and 13 (10%) of participants developed SDR, respectively. In the SNP cohort, *NAT2* rs1041983 (TT vs CC+CT, OR [95% CI]: 7.38 [2.17-25.1], p=0.001) and *CYP2E1* rs2070673 (AA vs TT+TA, OR [95% CI]: 3.49 [1.02-12.0], p=0.047) were associated with development of SDR. In the PK cohort, INH level 24 hours after 3HP administration (OR [95% CI]: 1.44 [1.02-2.03], p=0.036), but not rifapentine level, was associated with development of SDR. Also, the association between *NAT2* SNP and SDR was validated in the PK cohort (rs1041983 TT vs CC+CT, OR [95% CI]: 3.67 [1.09-12.3], p=0.035).
Conclusions: Intermittent high dose INH played a role in 3HP-related SDR. This could provide insight for further design of more optimal LTBI regimen.

SOA-10-1100-01 A novel pyrimidinetrione amide scaffold disrupting magnesium homeostasis in Mycobacterium tuberculosis to death

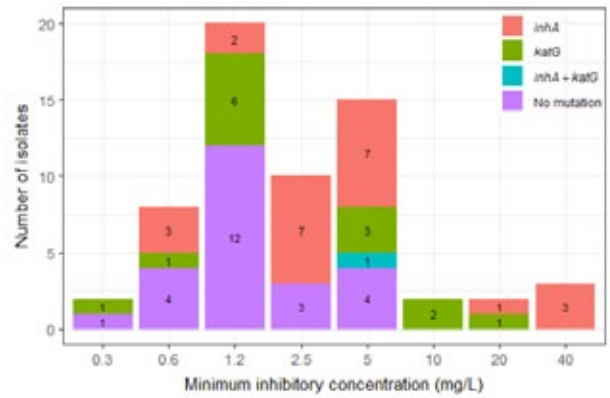
Y Park,[1,2,3] Y-M Ahn,[3] S Jonnala,[3] J Fisher,[3] M Goodwin,[3] L Via,[3] C Barry lll,[3] H Boshoff,[3]
[1]Inje University College of Medicine, Department of Pharmacology and PharmacoGenomics Research Center, Busan, Korea, Republic of, [2]Inje University College of Medicine, Center for Personalized Precision Medicine of TB, Busan, Korea, Republic of, [3]National Institutes of Health/ National Institute of Allergy and Infectious Disease, Tuberculosis Research Section, Bethesda, MD, United States of America. e-mail: happyumi@gmail.com

Background: Magnesium is the essential cation for *Mycobacterium tuberculosis* (*Mtb*) which is deeply and intrinsically woven into cellular metabolism. However, mechanisms of magnesium homeostasis in *Mtb* are poorly understood. Herein we describe the characterization of a pyrimidinetrione amide scaffold that disrupts magnesium homeostasis in the pathogen by direct binding to the CorA Mg^{2+}/Co^{2+} transporter.
Methods: The PA scaffold was selected by whole cell based high throughput screening. To find out mechanism of action, whole-genome sequence of PA resistant mutants were analyzed. We also measured magnesium concentration of PA treated cells and analyzed binding of it to purified *Mtb*CorA. Binding affinity of PA and *Mtb*CorA was measured to verify target of compound. Efficacy of PA was studied *in vitro*, *ex vivo* and *in vivo*.
Results: PA resistant mutants obtained single nucleotide polymorphisms (SNPs) in CorA (E212D and A317S) which is annotated presumable Mg^{2+}/Co^{2+} transporter. We presumed that PA inhibiting magnesium influx via magnesium concentration dependently increased MIC. Furthermore, its resistant mutants required 250-fold higher magnesium concentration in media to grow. We also observed that magnesium bound to PA by UV-VIS spectrum analysis. Next, thermostability test showed evidence of binding between the PA-Mg^{2+} complex and purified *Mtb*CorA. PA analogs were very potent in all conditions *in vitro* and *ex vivo Mtb*. They were also potent to Gram positive strains and *M. smegmatis*. Though, it lacked efficacy *in vivo* since it could not be administered at highest tolerable concentrations due to adverse effects.
Conclusions: Our results indicate that inhibition of Mg^{2+} homeostasis by CorA is an attractive target for tuberculosis drug discovery and the results will aid if the future discovery of improved CorA inhibitors.

SOA-10-1101-01 Ethionamide population pharmacokinetics/pharmacodynamics during treatment of multidrug-resistant tuberculosis

MT Chirehwa,[1] R Court,[1] M De Kock,[2] L Wiesner,[1] N de Vries,[3] J Harding,[4] T Gumbo,[5] P Denti,[1] G Maartens,[1] H McIlleron,[1] [1]University of Cape Town, Division of Clinical Pharmacology, Department of Medicine, Cape Town, South Africa, [2]Stellenbosch University, DST/NRF Centre of Excellence in Biomedical Tuberculosis Research, SAMRC Centre for Tuberculosis Research, Cape Town, South Africa, [3]Brooklyn Chest Hospital, Tuberculosis, Cape Town, South Africa, [4]DP Marais Hospital, Tuberculosis, Cape Town, South Africa, [5]Baylor Research Institute, Baylor University Medical Center, Center for Infectious Diseases Research and Experimental Therapeutics, Dallas, TX, United States of America. e-mail: maxwell.chirehwa@uct.ac.za

Background: To describe the population pharmacokinetics of ethionamide and the distribution of minimum inhibitory concentrations (MIC) in adult multidrug-resistant tuberculosis (MDR-TB) patients.
Methods: We performed a pharmacokinetic study in patients on treatment for MDR-TB in Cape Town. Participants received ethionamide doses of 15-20 mg/kg/day, as part of a multidrug regimen. We measured ethionamide plasma concentrations pre-dose and at 2, 4, 6, 8, and 10 hours post-dose. We interpreted the results with nonlinear mixed-effects modelling and derived individual values of steady-state $AUC_{0\text{-}24}$. Baseline pre-treatment sputum MICs were determined using Sensititre® MYCOTB MIC plates and used to calculate $AUC_{0\text{-}24}$/MIC ratios. An $AUC_{0\text{-}24}$/MIC of 56.2, associated with maximal kill and resistance suppression in the hollow fiber model, was defined as target exposure.
Results: Plasma samples were available from 84 patients of median weight 46 kg (range: 30-81). A one-compartment model described ethionamide pharmacokinetics well and separately estimated the contribution of renal clearance (~31% in a typical patient) from other elimination pathways. Median steady-state $AUC_{0\text{-}24}$ was 17.5 mg·h/L (6.2-49.7). The median MIC (quantified in 63 patients) was 2.5 mg/L (0.3-40) and the resulting median $AUC_{0\text{-}24}$/MIC was 7.81 (0.31-86.3). The target exposure was achieved in 4/63 of the patients, and for MIC≥2.5 mg/L, the median $AUC_{0\text{-}24}$/MIC was 3.77 (1.98-13.5). *inhA* mutation was detected in 37% of the isolates, in whom $AUC_{0\text{-}24}$/MIC was 5.37 (0.31-58.6). *katG* mutation was observed in 22%, in whom $AUC_{0\text{-}24}$/MIC was 7.76 (0.38-85.8). The MIC values for isolates with the *inhA* mutation isolates were higher than those with *katG* mutation only (p=0.008).
Conclusions: Our model estimated a larger contribution of renal clearance than the previously reported value of less than 1%. There was a 75% higher $AUC_{0\text{-}24}$ than in previous reports. In spite of this, ethionamide target exposures were not achieved in most patients, and in 2/38 with *inhA* or *katG* mutations.



[Distribution of MICs in Mycobacterium tuberculosis isolates stratified by genetic mutations]

SOA-10-1102-01 Transforming the supply chain management system for National TB Control Programme, India

K Nair,[1] VS Salhotra,[2] M Kumar,[1] S Sharma,[3] KS Sachdeva,[2] [1]RNTCP WHO Consultant, Central TB Division, New Delhi, India, [2]Ministry of Health and Family Welfare, Central TB Division, New Delhi, India, [3]RNTCP Consultant, Central TB Division, New Delhi, India. e-mail: nairk@rntcp.org

Background and challenges to implementation: With more than 30,000 stocking points, 400,000 drug delivery points and an estimated 2.8 million patients with tuberculosis (TB) every year in India, ensuring access to the best quality drugs at all levels through manual systems is a Herculean task. The continuously changing landscape of management of drug-resistant TB poses additional challenges for management of drugs and diagnostic supplies. To comprehensively support a complicated supply chain management system, a digital technology solution, *Nikshay Aushadi (NA)*, was developed and adopted.

Intervention or response: An interactive software system was developed that effectively enabled real time inventory management in all healthcare facilities across the country for anti-TB drugs. The system provides monitoring and tracking of drugs from periphery, sub-district, district, state and national levels. Through customized dashboards, information and analytics can be processed to monitor stocks and take timely actions. NA also supports quantification, drug request, stock management, online issue and dispatches, quality control, generation of reports, SMS alerts and dashboards for multi-level monitoring. The mobile application facilitates stock management at the most peripheral levels.

Results and lessons learnt: NA connects 6 Regional Medial Stores, 45 State Drug Stores, over 750 District Drug Stores, about 6000 TB unit drug stores, 300 medical colleges, and over 36,000 Peripheral Health Institutions. The software will soon connect with more than 80 anti-retroviral treatment centers and over 250,000 private medical practitioners. With 100 % connectivity at the TB Unit level and 50% implementation at the peripheral level in one year, more than 1.6 million TB patients benefited from NA.

Conclusions and key recommendations: The supply and demand for anti-TB drugs is rapidly met through NA, providing quality support with quick turnaround times and ensuring the availability of drugs even at hard-to-reach places. NA is a game-changer that will help India reach its End TB targets by 2025.

SOA-10-1103-01 Coordinated intervention of TB supply chain improved availability of TB commodities in Tigray region, Ethiopia

G Tsegay,[1] M Abraha,[1] E Michael,[1] A Gebremedhin,[2] A Gebremariam,[3] Z Kidane,[4] D Gemechu,[5] P Suarez,[6] [1]Management Sciences for Health (MSH), Health Programs Group (HPG), Mekelle, Ethiopia, [2]Tigray Regional Health Bureau, Health Promotion, Disease Prevention and Control Cor-Process, Mekelle, Ethiopia, [3]Ethiopia Pharmaceutical Supply Agency (EPSA), EPSA-Mekelle Hub, Mekelle, Ethiopia, [4]Ethiopia Pharmaceutical Supply Agency (EPSA), EPSA- Shire Hub, Shire, Ethiopia, [5]Management Sciences for Health (MSH), Health Programs Group (HPG), Addis Ababa, Ethiopia, [6]Management Sciences for Health (MSH), Health Programs Group (HPG), Arlington, VA, United States of America. e-mail: mabraha@msh.org

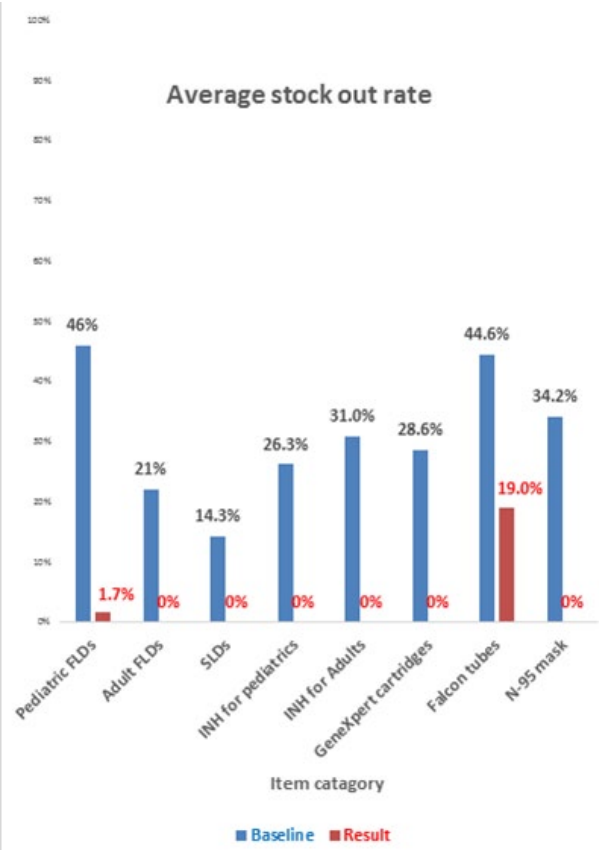
Background and challenges to implementation: Ensuring adequate supply of TB medicines continues to be a challenge, a baseline assessment was conducted by the USAID funded Challenge TB project in 2015 revealed a high rate of stock-outs of essential TB medicines within the Tigray regional TB program.

Intervention or response: The Tigray Regional Health Bureau (TRHB), in collaboration with the CTB project, conducted a training with 505 health professional, including pharmacists and TB program staff, on Integrated Pharmaceutical and Logistics Supply (IPLS), Second Line Drug (SLD) supply management, and TB patient kit use. In addition, routine quarterly joint supportive supervision meetings were instituted between CTB, TRHB, and Woreda TB experts from 16 hospitals and 52 health centers with high TB caseloads. Woreda TB experts then established quarterly supportive supervision meetings to the remaining low load health centers within their respective Woredas to monitor stock-out status and reporting. Lastly, CTB project supported the integration of SLDs and other multidrug-resistant TB (MDR TB) commodities into the main IPLS to easily monitor stock-out status. Monitoring the stock-out status of hospitals and Pharmaceuticals Fund and Supply Agency hubs was completed through telephone updates on a monthly basis after the baseline assessment.

Results and lessons learnt: The baseline assessment found pediatric and adult first line drugs stock out rates to be 46% (22/48) and 21% (10/48) respectively, both

rates decreased at the end line to 1.7% (1/58) and 0% (0/58) respectively. The average stock-out rate of SLDs reduced to zero; similarly isoniazid (INH) drugs for pediatrics and adults also decreased to zero percent to from 26.3% and 31% respectively. The stock-out status of GeneXpert cartridges, Falcon tubes, and N-95 masks and other commodities have also improved (see figure 1 below).

Conclusions and key recommendations: Continuous and coordinated support at all levels of the supply chain contributed to decreased stock-out rates and ultimately improves the availability of TB commodities.



[Stock-out rate of select TB commodities at baseline assessment (April - June 2016)]

SOA-10-1104-01 Access to affordable, quality-assured medicines at risk in high TB burden countries facing regulatory and procurement challenges while shifting from donor-supported to domestically funded procurement

T Masini,[1] C Perrin,[2] C Cepuch,[2] K Akerfeldt,[3]
[1]Independent Consultant at Médecins Sans Frontières, Health Analysis Department, Brussels, Belgium, [2]Médecins Sans Frontières, Access Campaign, Geneva, Switzerland, [3]Médecins Sans Frontières, Operational Centre Brussels, Analysis Department, Brussels, Belgium.
e-mail: christophe.perrin@paris.msf.org

Background and challenges to implementation: Policy changes and constrained funding by the Global Fund (GF) and other donors are contributing to an accelerated shift to national procurement of TB medicines. This shift is taking place before critical challenges with domestic procurement have been addressed. Potential risks to TB patients include stockouts and medicines of unknown quality being used in National Programmes.

Intervention or response: A questionnaire on regulatory environments and procurement practices was implemented in 30 (TB affected) countries where MSF operates. Information was sourced from Medicines Regulatory Authorities, Central Medical Stores, TB Programmes, and policy documents. The overall response rate was 80%.

Results and lessons learnt: 18/30 (60%) of the countries participate in the WHO Collaborative Registration Procedure, but only 10/30 (33%) of them have used this mechanism to register TB medicines. 7/22 (32%) countries have no mechanism for expedited registration. Waivers for importation of non-locally registered medicines are allowable in 23/24 (96%) countries, but these waivers aren't systemically applied for TB medicines. Expedited registration and/or importation waivers for quality-assured TB medicines are key to facilitate sustainable procurement, and in consideration of important new TB medicines emerging from the pipeline. National procurement of TB medicines does not necessarily lead to quality-assured procurement. 6/17 (33%) countries include quality as the priority criterium in national tenders; none of them put it into practice. Other aspects of regulation and procurement assessed include levels of transparency, competition across manufacturers, and presence of restricted tenders.

Conclusions and key recommendations: MSF calls for urgently needed risk assessments, mitigation strategies and flexible timelines to be provided by Global Fund and other donors to ensure sustainable access to TB medicines when countries shift to increased domestic financing. Countries should ensure expedited registration of key TB medicines, and that quality is a priority criterium in procurement.

SOA-11-C8 Active case finding: thinking outside of the box

SOA-11-1105-01 Active case finding of tuberculosis in Nepal: findings from TB REACH Wave-5

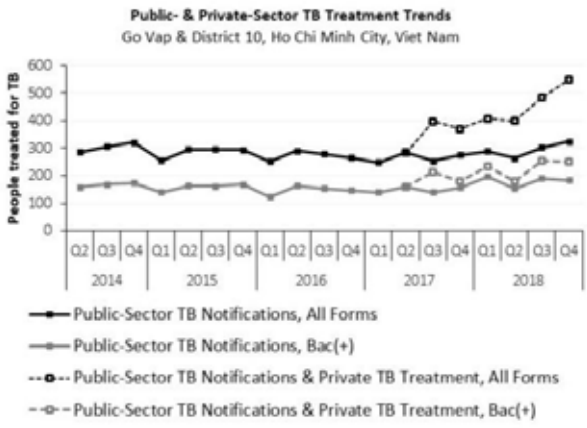
R Dhital,[1] K Dixit,[1] S Gurung,[1] B Rai,[1] S Acharya,[1] G Budhathoki,[1] B Subedi,[2] A Thapa,[3] M Caws,[1] [1]Birat Nepal Medical Trust, Tuberculosis, Kathmandu, Nepal, [2]District Health Office, Tuberculosis, Pyuthan, Nepal, [3]National Tuberculosis Center, Tuberculosis, Bhaktapur, Nepal. e-mail: raghu_dhital@yahoo.com

Background: Tuberculosis (TB) is the seventh leading cause of death in Nepal. The National Tuberculosis Program (NTP) reported 32,474 TB cases in 2018 and estimates that 12,000-13,000 cases are being missed every year. TB diagnosis in Nepal is challenged by dense population and migration in the plains and geographical difficulties in the hills and mountains. Birat Nepal Medical Trust implemented Active Case Finding (ACF) through a TB REACH Wave-5 project to increase case notification.
Methods: The study was conducted from March 2017 to December 2018 in eight districts of Nepal where case notifications were below the national average (all forms 112). Presumptive cases for testing were identified by symptom screening using three strategies of ACF i.e. contact tracing of index patients, screening through TB camps in high burden/remote communities, and at district hospital Out Patient Departments OPD. Symptomatic individuals were tested using smear microscopy or GeneXpertTB/RIF tests. Case notification was compared with eight control districts.
Results: The project screened 54,293 individuals, tested 27,096 and identified 1,092 cases from the three interventions. Through contact tracing, out of 16,038 tests performed, TB was identified in 441 individuals. Camps identified 85 cases from, 7,971 individuals tested. OPD screening through GeneXpert TB/RIF tested 3,087 samples and identified 566 cases. The yield from microscopy testing and GeneXpert was 1.4% and 13.2% respectively. There was a14% additionally in the NTP data of the districts in current fiscal year 2017/18 as compared to the previous fiscal year 2016/17 (3,056 cases vs. 2,681 cases).
Conclusions: The project demonstrated successful implementation of active case finding in eight districts of Nepal and showed particularly high yield of GeneXpert testing. Analysis of the data by strategy and district identifies approaches for further refinement and optimisation of case finding models in Nepal which should be applied during scale-up.

SOA-11-1106-01 Finding the missing cases through a public-private engagement initiative in Ho Chi Minh City, Viet Nam

HB Huynh,[1] RJ Forse,[1] AJ Codlin,[2] LNQ Vo,[3,4] LH Nguyen,[5] HV Le,[6] HB Nguyen,[6] TN Vu,[7] GT Le,[7] NV Nguyen,[6] [1]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [3]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [4]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [5]Pham Ngoc Thach Lung Hospital, Provincial TB Program, Ho Chi Minh City, Viet Nam, [6]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [7]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam. e-mail: huy.huynh@tbhelp.org

Background and challenges to implementation: The National TB Control Program of Viet Nam (VNTP) reported 105,733 TB treatment notifications country-wide in 2017. 8% of these came from PPM activities: 6% from public-public and 2% from public-private engagement. Despite having a mandatory TB notification law and several established PPM models, a recent inventory study indicated that about half of the people with TB who are 'missed' by public-sector TB services are seeking care in the private sector.
Intervention or response: We piloted a TB REACH-funded private provider engagement initiative in two districts of Ho Chi Minh City. Strategy 1 built a diagnostic referral system using one of the VNTP's existing PPM models. It provided access to subsidized chest X-rays (CXRs) and free Xpert MTB/RIF testing. People diagnosed with TB were encouraged to take their TB treatment in the public sector, but could also take treatment from their private provider. Strategy 2 piloted a public-private interface agency model for documenting and reporting private-sector TB treatment.
Results and lessons learnt: Over six quarters, we engaged 522 private providers, resulting in over 5,200 CXRs being performed and the detection of 133 people with Bac(+) TB. Just 57% of patients opted to take treatment in the public sector. We also collected data from 897 people being treated for TB by private providers. If these people had been recognized by the VNTP as official TB notifications, notification rates in our two intervention districts would have increased by +46% for Bac(+) TB and +61% for all form TB at a cost of $251 per person with TB notified.
Conclusions and key recommendations: Private providers are interested in improving diagnostic quality, through use of the Xpert assay. Integration of private-sector TB treatment into official notifications could greatly increase the national notification rate and reduce the proportion of 'missed' TB in Viet Nam, but may require policy reform or changes to the policy implementation process.



[Quarterly notification trends and theoretical additionality from private sector notifications]

SOA-11-1107-01 Improving TB case finding among women through gender-focused programming

F Qureshi,[1] SM Sadat,[1] A Omid,[1] A Sanaie,[1] MK Seddiq,[2] N Ahmadzada,[2] [1]ACREOD, TB, Kabul, Afghanistan, [2]NTP, TB, Kabul, Afghanistan.
e-mail: acreod@gmail.com

Background and challenges to implementation: Women carry higher (57%) burden of TB then men in Afghanistan whilst socio-cultural norms, stigma and lack of economic autonomy have been restricted their access to TB care. Additionally, families prefer that females to be seen in RH centers, where the health staff are solely female whilst TB is yet to be integrated there. The TB REACH initiatives funded a project that focused on engaging 4 gyne obstertric hospitals in TB care services in Kabul city.
Intervention or response: The project trained 120 doctors, nurses and midwives in four hospitals and initiatied TB laborotory services there. Moreover, the project supplied X-ray films to the hospitals that enabled women/girls have thier chext X-ray free of charge. Monthly review of the interventions′ outcomes were carried out by the leading team of the hospitals to further strenghten the services in their rescpective hospitals. Sputum samples collected in the hospitals were tested by GeneXpert. Furthermore, the female doctors also provided samples, through lavage of genito-urinary tract, among women who suferred from infertality.
Results and lessons learnt: During a year, 85,166 women screened. 2,566 (3% of screened) identified with presumptive TB. 1,336 of them tested by chest X-ray and 1,339 by GenXpert that resulted in diagnosis of 79 bacteriologically confirmed including 14 geneto-urinary B+ TB, 106 clinically confirmed and in total 185 all forms TB. The data shows large number of women who accessed hospitals were missed from diagnosed due to lack of TB care services.
Conclusions and key recommendations: In Afghanistan, women are one of TB key affected population. Women gender specific interventions prevent missing of TB cases among wormen. Women with TB do access RH centers, but are mostly missed due to lack of diagnostics and insufficiently trained and motivated health staff. Holistic coverage of RH centre is highly requried.

SOA-11-1108-01 Reaching the unreached - innovative way of crossing the barriers to diagnosis

S Pandurangan,[1] AK Pandey,[1] S Mohanty,[1]
[1]International Union Against Tuberculosis and Lung Disease, TB Care and Control, New Delhi, India.
e-mail: sripriya14@gmail.com

Background and challenges to implementation: India has approximately 27% of the total global burden of TB cases, and 33% of global deaths from TB. In order to move towards the target of TB elimination by 2025, we need to have multi-pronged active case finding strategies for TB detection and notification. To address the challenge of TB detection it is essential to ensure universal access to TB services for timely diagnosis and treatment. However, low awareness about TB, poor accessibility and affordability of health services result in delayed diagnosis, with resultant morbidity and mortality.
Intervention or response: Project Axshya is being implemented by The Union in 128 districts with the objective of enhancing access of vulnerable and marginalized populations to TB services. A cadre of trained community volunteers make home visits to identify presumptive TB patients (PTBP) and link them with diagnostic services. The community volunteers collect the sputum sample from the PTBPs and transports them to the nearest diagnostic centre. Also, for smear negative patients, project facilitated chest X-ray examination.
Results and lessons learnt: : A total of 1.7 million households were visited by the community volunteers during the year 2018. About 109842 presumptive TB cases were identified. Of these 77387 persons sputa were collected and transported and the remaining 30% were referred to the nearest microscopy centres. A total of 79510 (73%) cases were examined at DMCs and 5689 (7%) were found to be positive. In addition, 1111 were diagnosed with other forms of TB using X-ray and clinical evaluation giving a total of 6800 TB patients.
Conclusions and key recommendations: The results of the intervention clearly show that in the key affected population areas, effective active case finding strategies combined with sputum collection and transportation services and free X-ray services leads to additional yield of TB patients. This has also contributed in identifying the missing TB cases.

SOA-11-1109-01 Results-based financing (RBF) as behavioural incentives to improve tuberculosis case finding in Nyanga district, Zimbabwe

MM Gombe,[1] C Sandy,[2] P Mafaune,[3] J Jokwiro,[4] C Chimhundu,[1] T Mapuranga,[2] N Siziba,[2] K Ndlovu,[2] S Mashizha,[2] A Svoren,[1] [1]Clinton Health Access Initiative, TB Access, Harare, Zimbabwe, [2]Ministry of Health and Child Care, National Tuberculosis Program, AIDS and TB, Harare, Zimbabwe, [3]Ministry of Health and Child Care, Manicaland Provincial Medical Directorate, Mutare, Zimbabwe, [4]Clinton Health Access Initiative, Program Officer, Harare, Zimbabwe.
e-mail: mgombe@clintonhealthaccess.org

Background and challenges to implementation: Zimbabwe's National Tuberculosis Program (NTP) aims to increase the Treatment Coverage Rate (TCR) from 71% in 2017 to 90% in 2020. Site assessments in the poorest performing district, Nyanga (21% TCR) identified poor motivation among health care workers (HCWs) and community health care workers (CHWs) as a key driver of low TCR. The NTP investigated the effectiveness of Results Based Financing (RBF) on motivation and therefore TCR.
Intervention or response: Two community TB indicators were added to the RBF framework and one existing facility indicator was updated. A second facility indicator of pediatric notifications (additional incentive for notification of Under 15s) was also added (*Table 1*).

Indicator	Incentive per case
1. Number of TB cases notified	US $8 (increased from US $0.31)
2. Number of Pediatric TB cases notified	US $8 (additional)
3. Number of new TB presumptive cases identified by CHW, sent to the facility for diagnosis	US $3
4. Number of TB presumptive cases identified by CHW who were TB positive	US $1

[Table 1: TB RBF Indicators and incentives]

In addition, TB case management trainings conducted by NTP officers in December 2018, reached 234 CHWs, 7 health managers and 34 HCWs. Implementation began in January 2019. Job aides and tools were updated and distributed. In April 2019, facility-level data was collected from all 27 intervention sites in Nyanga district. 50 qualitative interviews with HCWs and 30 focus group discussions with CHWs were also conducted.
Results and lessons learnt: Community TB screening figures increased four-fold from 487 (Q4, 2018) to 2,247 (Q1, 2019). However there were health system challenges of poor sample transportation experienced and economic challenges hindered community presumptive cases from accessing the health facility for TB diagnosis. This provided evidence that strengthening sample transportation and addressing out-of-pocket patient costs is critical, before national scale up is implemented. CHWs also advocated for non-monetary enablers such as bicycles to improve access to the community and t-shirts and bags that would communicate the TB screening messages to the community.
Conclusions and key recommendations: RBF was effective at increasing community TB screening, operational barriers limited impact on case notification. RBF is recommended as a strategy for sustainable community participation but it is not sufficient as a standalone case finding intervention.

SOA-11-1110-01 Active screening for tuberculosis (TB) during seasonal malaria chemoprophylaxis campaigns (SMC): experience of the National Tuberculosis Control Program (NTP) of Guinea

AM Bangoura,[1] AS Magassouba,[2] MP Baldé,[3] S Camara,[4] S Camara,[5] [1]National Tuberculosis Control Program, Coordination, Conakry, Guinea, [2]National Tuberculosis Control Program, Research and Training, Conakry, Guinea, [3]National Tuberculosis Control Program, M&E, Conakry, Guinea, [4]National Tuberculosis Control Program, Management, Conakry, Guinea, [5]WHO, NPO, Conakry, Guinea. e-mail: magasbakary01@gmail.com

Background and challenges to implementation: Despite ongoing efforts, TB case detection is estimated to be around 60% in sub-Saharan Africa. Intensified case finding (ICF) is necessary to control the epidemic better and to achieve the milestones for TB cases reduction set by the End-TB strategy. In the general population, ICF strategies based on the TB-reach model or targeting "at-risk" populations have been piloted, but are sometimes too expensive to be sustainable in the long-term when implemented by vertical NTPs.
Integrating health activities should increase cost-effectiveness and favor sustainability, but it implies service integration and collaboration across vertical, independent programs.
Intervention or response: The study was conducted in the district of Labé and aimed to assess the feasibility, acceptability, efficacy, and cost of ICF among children by integrating systematic clinical TB screening within door-to-door SMC activities. All suspected children identified in the household by community workers were referred to the microscopy / GeneXpert and X-ray sites and put in treatment if these tests or if they clinically confirm TB. Screening through an examination of the arm (MUAC) was carried out to screen malnourished children.
Results and lessons learnt: This approach allowed us to diagnose 7 cases of TB in 10 days , 72 cases of severe uncomplicated malnutrition and 10 cases of severe malnutrition with complications were diagnosed in 10 days (141,264 children screened). With few resources, we have had to boost the number of diagnostic children in an area that treats fewer than three cases of childhood TB a year.

Conclusions and key recommendations: At the national level, opportunities for integrating NTP activities exist but efforts to bring them into fruition are rarely undertaken. The integration of SMC, TB and malnutrition screening, as piloted in Guinea, is an example of successfully integrated activities. The political willingness of the NTP to collaborate is needed for defining and scaling-up cost-effective, integrated strategies that would benefit populations and programs.

SOA-11-1111-01 TB village approach, a new concept to finding missing TB cases by removing users fees and stigma

MK Kaswa,[1,2] MF Mukunda,[1] P Tshey,[1] A Bele,[1] P Lubamba,[1] KG Koura,[3,4] PY Norval,[5] [1]Ministère de la Santé, Programme National de lutte Antituberculeuse, Kinshasa, Congo (Democratic Rep.), [2]Université de Kinshasa, Faculté de Médecine, Département de Biologie Médicale, Kinshasa, Congo (Democratic Rep.), [3]Union Internationale contre la Tuberculose et les Maladies Respiratoires, Tuberculose et VIH, Paris, France, [4]MERIT IRD, Université Paris 5, Sorbonne Paris Cité, Paris, France, [5]TeAM Technical Assistance for Management, TB, HIV and Malaria, Paris, France. e-mail: michelkaswa@gmail.com

Background and challenges to implementation: In the context of World Day against Tuberculosis 2019, the National TB Program (NTP) in the Democratic Republic of Congo (DRC) held a 4-day intensified case-finding intervention to find missing people with TB.
Intervention or response: From 21st to 24th March, a "TB Village" was set up in Kinshasa, in a site called Place Saint-Thérèse with 3 mobile clinics equipped with digital X ray and GeneXpert MTB/RIF. A tuberculosis active case finding strategy started with symptomatic screening followed by Chest X Ray (CXR) in presence of cough, and GeneXpert for abnormal CXR.
Results and lessons learnt: During the 4 days of activities 1 352 were registered and 1240 (92%) were screened. Fifty-three percent (654/1240) were presumed TB and CXR was performed. Among the 246 with abnormal CXR, GeneXpert was performed for 196 (80%). Eighty patients were diagnosed with TB, out of which 68 have been reported to date to have started treatment. Two cases of Rifampicin-resistant TB were detected and put also on treatment. This represents a yield of additional TB cases 10 times higher than the usual notification rate.
Conclusions and key recommendations: The "TB Village", as an advanced health post, provides care to people within walking distance of their houses, which eliminates transportation fees that the inhabitants of the area cannot afford. Likewise, all TB services including screening, testing and treatment are offered for free to eliminate the financial barrier. The setting of the "TB Village" has helped to ease people to get tested without experiencing the social and cultural stigma linked to this disease.

SOA-11-1112-01 Doubling efforts for doubled results: increased coverage of tuberculosis findings using active approaches

M Chry,[1] SC Choub,[2] K Mom,[3] TE Mao,[4] [1]Cambodia Anti-Tuberculosis Association, Program Lead, Phnom Penh, Cambodia, [2]KHANA, Management, Phnom Penh, Cambodia, [3]Cambodia Anti-Tuberculosis Association, Management, Phnom Penh, Cambodia, [4]National Center of Tuberculosis and Leprosy, CENAT, Phnom Penh, Cambodia. e-mail: rath@thecata.org.kh

Background: Tuberculosis health services have become an important priority for many NGOs in Cambodia where the TB burden is still relatively high. The Cambodian Anti-Tuberculosis Association (CATA) conducted an active approach using mobile mass screenings to sustain and control TB. An active approach aims to increase TB case findings by sending staff and technology to the sourced problem compared to a passive approach which relies on individuals to seek diagnosis and treatment using their own initiative.
Methods: The project was conducted during 2014 to 2018 in eight rural districts in Cambodia. The equipment was actively taken to Village Health Support Groups (VHSG) and Health Centres (HC) in the relevant districts. VHSG recruited people using TB symptom questionnaires to screening people at their houses. Chest X-rays and GeneXpert using a standard and/or ultra-cartridge were used to screen patients.
Results: From June 2017 to May 2018, CXR screened 53,098 patients and Xpert screened 9,705 patients with a total of 777 Bac+ and 2801 AF cases of TB. This was compared to the results of 2014 where CXR screened 11,805 patients, Xpert screened 2466 patients with 454 cases of Bac+ and 1150 cases of AF. A significant increase in TB cases can be observed from the three-year difference. This indicates a change of 450% for CXR, 394% for Xpert, 171% for Bac+ and 243% for AF. In terms of machinery, 18.1% would have remained undetected if Ultra cartridges were not used, and compared to Xpert, CXR exhibited higher percentages found for normal, active, suspected, healed and other TB forms.
Conclusions: This project supports the use of active approaches to find undiagnosed and untreated cases of TB. It has provided an insight into what can be accomplished by using an active method compared to a method that relies on waiting for patients to take action.

SOA-11-1113-01 Economic evaluation of using sputum smear microscopy or GeneXpert testing for active tuberculosis case finding in Nepal

N Siqueira,[1] K Dixit,[2] B Rai,[2] R Dhital,[2] G Mishra,[2] S Gurung,[2] A Thapa,[3] K Lönnroth,[4] B Squire,[1] M Caws,[1] [1]Liverpool School of Tropical Medicine, Clinical Sciences, Liverpool, United Kingdom, [2]Birat Nepal Medical Trust, Research, Kathmandu, Nepal, [3]National TB Control Program (NTP), Statistics, Kathmandu, Nepal, [4]Karolinska Institutet, Public Health Sciences, Stockholm, Sweden.
e-mail: noemia.teixeira.siqueira@gmail.com

Background: The economic evaluation of active case finding (ACF) models can improve resource allocation in low-income countries. This study aimed to compare costs of two ACF models in Nepal, testing by sputum smear (SS) or GeneXpert test (GX).
Methods: The cost analysis was conducted in four districts of Nepal from 2017 to 2018. Costs were calculated from the health system perspective using a bottom-up approach. Recurrent and capital costs were included: training, equipment, laboratory supplies and renovations, personnel, ACF activities and overheads. Total cost, cost per case screened and case diagnosed were reported. One-way sensitivity analyse was performed varying costs of GeneXpert cartridges, discount rates and staff salary.
Results: 9,958 and 11,752 individuals were screened by symptom questionnaire in the SS and GX model, respectively. The yield of diagnosis was 2.3% (227/9,958) for SS model and 3.6% (418/11,752) for GX model. The main cost driver was personnel (47%) for SS and laboratory supply (38%) for GX. The total cost of the SS and GX model was USD 144,795 and USD 381,302, respectively. The cost per case screened was USD 15 and USD 32 for SS and GX models, respectively. The cost per case diagnosed was USD 638 and USD 912 for SS and GX models, respectively. A reduction in 35% in the GeneXpert cartridges is required to make the strategies equivalent in cost (USD 767 *vs* USD 638 for GX and SS, respectively). Variation in staff salary and discount rates did not show significant impact on costs.
Conclusions: This novel study shows that the GX model was more efficient to detect TB cases. A reduction in the costs of GeneXpert cartridges is necessary to make the intervention more affordable to the public health system in Nepal.

SOA-12-C12 Enduring the power of MPOWER

SOA-12-1114-01 Compliance of designated smoking rooms (DSRs) in restaurants, lounges and hotels in eight Indian cities

RD Kennedy,[1] JE Cohen,[1] S Saraf,[1] VG Munish,[2] PK Sinha,[2] V Shah,[3] [1]Johns Hopkins Bloomberg School of Public Health, Institute of Global Tobacco Control, Baltimore, MD, United States of America, [2]World Health Organization, Country Office (India), New Delhi, India, [3]Campaign for Tobacco Free Kids, Global Programs, Washington, DC, United States of America.
e-mail: ssaraf3@jhu.edu

Background: In India, the Cigarettes and Other Tobacco Products Act (COTPA) permits designated smoking rooms (DSRs) in hospitality settings if these venues meet a minimum size requirement (30 seats or rooms). To be compliant, DSRs must meet certain physical criteria and venues cannot provide service(s) to patrons inside a DSR. This study assessed prevalence and compliance of DRSs in hospitality venues in the cities of Bangalore, Chennai, Guwahati, Jaipur, Kolkata, Lucknow, Mumbai, & New Delhi.
Methods: Trained data collectors visited venues that reported in a telephone survey to have a DSR. Data collectors assessed (1) the presence of a DSR, and (2) compliance with COTPA based on the location of the DSR, having floor-to-ceiling walls, having a closed/self-closing door, and having signage indicating the DSR was a "smoking area". Further, the data collectors noted if the venue staff served patrons in DSRs during their visit.
Results: Data collectors visited N=829 venues including bars (n=352), restaurants (n=288), and hotels (n=189). DRSs were identified in 18% (n=126) of venues, of which, most (90%, n=120) were observed by the data collectors to assess compliance. Approximately 45% (n=67) of DSRs observed were not compliant based on their location, 1% lacked full walls (n=1), 32% were not compliant because the door to their DSR was ajar (n=38), 56% of venues lacked 'smoking area' signage (n=67), and 36% of venues were observed providing table service to patrons in the DSR (n=43). Overall, 3% (n=3) of venues were compliant with these COTPA requirements.
Conclusions: Although hundreds of venues reported in a phone survey that they had a DSR, this study found few venues actually had a separate smoking room. Of the DSRs identified, very few were compliant with the requirements under the Indian law. The Framework Convention on Tobacco Control recommends 100% smoke-free public/work places.

SOA-12-1115-01 Interdepartmental convergence is key to accelerating the elimination of tobacco from Indian society

GK Tripathi,[1] [1]International Union Against Tuberculosis and Lung Disease, Tobacco Control, New Delhi, India. e-mail: gtripathi@theunion.org

Background and challenges to implementation: There are many programmes of development run by federal and provincial governments but most of the programmes are being run in segregating manner. Its observed that same data collected by two departments but it differs.

As elimination of Tobacco control needs intra and interdepartmental convergence, Hence, this is important to highlight the important issues by proposed presentation.

Intervention or response: An observation has been made for the programmes are being run by National Health Mission, programmes under Ministry of Rural Development, programmes under School education, programme under Women and Child development, programmes under Ministry of Tourism, Railways, Transport, Welfare programmes of Central and provincial governments, Youth centric programmes, Bodies of local self governments, Agriculture department, sanitation department, Department of Land Reforms.

Results and lessons learnt: The results are very surprising as 95% programmes are being run in segregating manner. Only 5% programmes are being run by establishing convergence.

Conclusions and key recommendations: Indian society is diverse but complex in nature. A system has to work in holistic manner, hence this is important to accelerate the convergence if we need to eliminate the Tobacco from our society. This is to be discussed by the house that this issue should get attention of the global audience to get more clarity and proper mechanism towards elimination of Tobacco.

SOA-12-1116-01 "As long as everyone doess it": retailers' views on tobacco advertising and retailing regulation in four Indonesian cities

PAS Astuti,[1,2,3] NMD Kurniasari,[1,3] NM Kurniati,[3] [1]Udayana University, Public Health and Preventive Medicine, Bali, Indonesia, [2]University of Sydney, School of Public Health, Sydney, NSW, Australia, [3]Udayana University, Udayana Center for NCDs, Tobacco Control and Lung Health, Denpasar, Indonesia. e-mail: ayu.swandewi@unud.ac.id

Background: The physical presence of cigarette outlets enhance perceived availability and foster exposure to tobacco promotion. Indonesia is the second largest cigarette markets with no regulation in place for cigarette retailing. However, there is an ongoing advocacy to introduce tobacco advertising including cigarette display ban at the retailers at sub-national level. Our study aims to describe cigarette retailers' perspective on advertising, display ban and other retailing regulation.

Methods: We conducted in-depth interviews with a total of 40 cigarettes retailers in four cities of Indonesia: Denpasar, Semarapura, Depok and Jogjakarta in January-February 2019. Cigarettes retailers were selected based on its location within 250 m radius of a school; we varied the type of retailer, and the schools' level. The interview questions included retailer perception on the importance of cigarette advertising and display, their views on tobacco advertising ban, display ban and retailing regulation. The interviews were recorded, then transcribed verbatim and analyzed with thematic analysis.

Results: We found that most of the retailers perceived the advertising as not so necessary but the opposite for the cigarette displays. Retailers view the displays as a vital sign of selling cigarette. With the licensing and zoning of no cigarette selling around schools, there was mixed response between following the government's regulation, losing income and the concern of being unfairly treated between the smalls and the bigger retailers. Most of the retailers also argue that even though their store is close to schools, but it was not their intention to sell cigarette to young people and that they mainly served adult smokers.

Conclusions: Cigarette retailers perceived regulation will hamper their business but remain positive if the governments require it and if all retailers are doing it equally. The governments should see this as an opportunity to educate the retailers and to introduce a stronger regulation.

SOA-12-1117-01 Impact on tobacco smoking due to absence of incremental cigarette price increases: analysis of trends data in Sri Lanka

NS Gamage,[1] PR Vithanage,[1] [1]Alcohol and Drug Information Centre, Research and Evaluation Programme, Colombo, Sri Lanka. e-mail: mail2nalaka@gmail.com

Background: In 2016 November, cigarette prices of most sold cigarette brands were increased by 43% due to a considerable tax increase by the government. However, no tax changes were made in subsequent 20 months. WHO recommends incremental tax increases on tobacco to mitigate the effect of inflation on price. This study analyses the impact on smoking amid absence of a price increase on cigarettes. Other confounding factors affecting smoking during this period were minimum since no other policy measures were implemented by the government to control tobacco due to resistance by Ministry of Finance and pro-industry voices. For the null hypothesis, it was assumed there are no difference current smoking percentage in 2017 and 2018. Since female smoking is very small (< 1%) in SL, study has been limited to male smokers.

Methods: ADIC conducts an annual trend survey in July each year in districts representing each province of the country. In total, 2999 (2017) and 2769 (2018) male participants above 15years were included in the study.
Statistical comparison was done with Chi-square independence test in SPSS on current smoking proportions to evaluate the significance of differences in smoking during these two years.
Results: In 2017, current male smoking percentage was 23.6% (n=675) while in 2018 it has become 27.0% (n=724). Chi-Square test produced chi-square value of 8.841 (df=1 and p< 0.01). Therefore the null hypothesis can be rejected. There is an increase of smoking in 2018 and this increase is statistically significant.
Conclusions: This results provides further evidence on how absence of incremental price increases on cigarettes contributes to increase in tobacco smoking. Therefore it is recommended to enforce periodic incremental tax increases on tobacco products as recommended by WHO to discourage smoking initiation and continuation.

Year	n	Current Smoker %	95% CI
2017	2865	23.6%	22.0%-25.1%
2018	2751	27.0%	25.3%-28.7%

[Percentage of current smokers (smoked within last 30 days)]

SOA-12-1118-01 CigControl: an innovative approach to monitor compliance of tobacco control policies

N Maldonado,[1] B Llorente,[2] [1]Jorge Tadeo Lozano University, Economics, Trade and Social Policy, Bogota, Colombia, [2]Fundación Anaas, Tobacco Control, Bogota, Colombia. e-mail: normanmva@gmail.com

Background: Monitoring compliance of Tobacco Control Policies (TCP) is crucial for successful implementation of the Framework Convention for Tobacco Control (FCTC), especially in low and middle income countries where weakness of enforcement institutions is frequently a structural deficiency. At the same time, centralized monitoring by the corresponding government agencies is expensive, because it relies on budget allocation, changes of public servants' functions and centralized primary collection of data by the department of statistics, which by definition is expensive to collect. In addition, the current mechanisms might not collect information in the appropriate way, misleading the design of public policies.
This paper develops a decentralized mechanism to monitor compliance of tobacco control policies, in particular, to monitor cigarette prices, compliance of health warnings and sales of loose cigarettes (banned in Colombia).
Methods: We use crowdsourcing as the central method to collect information, computer science to design an app, and statistical inference based on sampling methods to use the information at the population level.
Results: The mechanism developed consists of (i) an app called CigControl designed to capture data and images on compliance of TCP, (ii) a set of guidelines to arrange the network of people reporting such data, (iii) a dataset containing all the information collected through the app, and (iv) a set of indicators on TCP. The app, named CigControl, has been already developed and it is available at the Apple Store and the Play Store.
Conclusions: Citizens' engagement is a central component of successful TCP. Decentralized mechanisms that allow active participation of citizens is an alternative to overcome the limitations of changing the existing centralized mechanisms of monitoring. They are also a more flexible source of data that can complement official sources, leading to a more comprehensive monitoring of TCPs.

SOA-12-1119-01 Tactics of the tobacco industry interfering in implementation of tobacco control laws in Sri Lanka by public sector field officers

D Periyannan,[1,2] P Chinthika,[1] S Lakmal,[1] I Fernando,[1,3] H Wijesooriya,[1] S Kandeepan,[1] M Perera,[1,4] M Rajasuriya,[1,5] [1]Faculty of Medicine, University of Colombo, Centre for Combating Tobacco, Colombo, Sri Lanka, [2]Alcohol and Drug Information Center, North and East Provincial Programme, Colombo, Sri Lanka, [3]Alcohol and Drug Information Center, Strategic Intervention, Colombo, Sri Lanka, [4]Faculty of Medicine, University of Kelaniya, Department of Public Health, Ragama, Sri Lanka, [5]Faculty of Medicine, University of Colombo, Department of Psychiatry, Colombo, Sri Lanka.
e-mail: dinesh198604@yahoo.com

Background: National Authority on Tobacco and Alcohol (NATA) Act is the legislation on tobacco control in Sri Lanka from 2006. Public Health Inspectors (PHI), Food and Drug Inspectors, Police officers and Excise officers are the authorised officers responsible for its implementation.
Ceylon Tobacco Company (CTC), subsidiary of the British American Tobacco, holds the monopoly to manufacture and sell cigarettes in Sri Lanka. This study aimed to explore the tactics used by CTC to influence NATA's authorised officers.
Methods: An investigative research was implemented. Data including photographic evidence obtained from media reports (print and electronic), annual reports of CTC, social media posts and other web content, and key informants, was analysed using thematic analysis to explore the type of activity, its potential impact and the publicity it received.
Results: Between 2006 and 2019, CTC has conducted training programmes for PHIs through the PHIs' Union. CTC was also involved in training Police and Excise Officers through their professional development programmes. Construction of three police stations has been funded by the CTC. Donation for the construction of

one was handed over to the then Secretary of Defence, and opening of another was by the then Prime Minster of Sri Lanka. Sponsorships for construction of police stations were published in national newspapers (print and electronic) and on the web. An area-distribution agency of CTC sponsored a PHIs' cricket tournament via its affiliated pharmaceutical partners, Gamma Pharmaceuticals and Interpharm (Pvt) Ltd. The banners at the event displayed their logos, while the event received publicity in social media with photographs. CTC is also accused of employing ex-NATA authorised officers to influence their current counterparts in interfering in field level tobacco control actions.

Conclusions: CTC used diverse strategies to connect with and influence all categories of NATA authorised officers, while some activities received wide positive media coverage.

SOA-12-1120-01 Tobacco-related promotions in Sri Lankan newspapers: content analysis

SR Abeysundara,[1] AD Fonseka,[1] S Thilakarathna,[1]
[1]Alcohol and Drug Information Centre, Library, Colombo, Sri Lanka. e-mail: salani.ruwanthika@gmail.com

Background: According to the Article 35.1 of the National Authority on Tobacco and Alcohol (NATA) Act, the major legal framework on tobacco and alcohol in Sri Lanka, direct and indirect advertisements related to tobacco are prohibited. Framework Convention on Tobacco Control (FCTC) Article 13 also recommends complete ban of tobacco advertisements. Aim of this analysis was to explore the tobacco related promotions reported in Sri Lankan newspapers. Results of this newspaper analysis is used by Alcohol and Drug Information Centre (ADIC) for media advocacy purposes.

Methods: We analyzed Sinhala (n=12) and English (n=11) Monday to Saturday and weekend Sunday Newspapers published in Sri Lanka from 1st of January 2018 to 1st of January 2019. Promotions were identified by the characteristic of "glamorizing the substance, industry image building, surrogate advertising, social beliefs, unfair privileges, promotion through prevention and promotion through policy".

Results: During the concerned period 3120 newspapers were traced and out of that 908 Tobacco (Sinhala n=551, 60.7%, English n=357, 39.3 %) Promotions were reported. They were mainly under glamorization (n=339, 37.3%), Image Building (n=132, 14.5%), Surrogate Advertising (n=97 10.6 %), Social Beliefs (n=108, 11.8%), Unfair Privilege (n=33, 3.6%), Promotion through prevention (n=35, 3.8%), Promotion through Policy (n=164, 18%). "Mawbima" (Sinhala, Monday to Saturday; n=112 12.3%), "Daily Mirror" (English, Monday to Saturday; n=83 9.1%), "Diwaina"(Sinahala, Sunday; n=40 4.4%) and Sunday Observer (English, Sunday n=16 1.7%)were the news papers with the highest number of tobacco promotions.

Conclusions: Despite the prohibition still a large number of tobacco promotions are published in Sri Lankan newspapers violating the legal frameworks.

SOA-12-1121-01 Tobacco industry interference in implementation of pictorial health warnings on cigarette packs in Sri Lanka

H Wijesuriya,[1] KMN Perera,[1,2] CS Perera,[1] P Dineshkumar,[1,3] SC Lakmal,[1,4] IB Fernando,[1,4] S Kandeepan,[1] M Rajasuriya,[1,5] Alcohol and Drug Information Centre(ADIC) [1]Faculty of Medicine, University of Colombo, Centre for Combating Tobacco, Colombo, Sri Lanka, [2]Faculty of Medicine, University of Kelaniya, Department of Public Health, Ragama, Sri Lanka, [3]Alcohol and Drug Information Centre, North and Eastern, Colombo, Sri Lanka, [4]Alcohol and Drug Information Centre, SI, Colombo, Sri Lanka, [5]Faculty of Medicine, University of Colombo, Department of Psychiatry, Colombo, Sri Lanka.
e-mail: hiruniwijesooriya88@gmail.com

Background: Ceylon Tobacco Company (CTC) is the British American Tobacco (BAT) subsidiary holding monopoly in cigarette manufacturing and sales in Sri Lanka. CTC challenged legally the government's initiative to impose pictorial health warnings (PHW) on 80% of the surface of cigarette packs. After several rounds of Appeal and Supreme Court hearings, the verdict given was to implement PHWs, but reducing its size to 60%.

However, as the then Minister of Health was later elected the President, the 80% PHWs got implemented through a parliamentary decision, over-riding the court order. Our study aims to describe the industry interference during this process.

Methods: Investigative research techniques were used to identify the documentary evidence and the stakeholders for key-informant interviews. Media reports, court reports, web content and research articles collected through snow-ball sampling were reviewed using content analysis to explore the strategies, front groups and arguments used.

Results: Strategies recognised were: alleged bribery by CTC and BAT; alleged interference in the legal and policy process through high-ranking politicians including the Head of State; influencing stakeholders and public via industry favourable academic publications and media reports; and influencing business community via industry favourable discussion forums. Main arguments used were: Minister of Health not possessing the legal power to enforce such a law; PHWs violating the company's intellectual property rights related to trade names and branding; unproven effectiveness of PHWs; and inadequate time availability for implementation. The only front group visible was the media in general, which repeatedly published arguments against PHWs favouring tobacco industry. The industry ultimately man-

aged to delay the PHW implementation by 23 months and to reduce its extent to 60%. They managed to delay the original 80%-PHW implementation by 29 months.
Conclusions: The tobacco industry interference misled the policy makers and the public delaying implementation of PHWs for more than two years.

SOA-12-1122-01 What factors are effective in provoking a quit response?: results from the study conducted among bidi smokers in four Indian states

MB Aghi,[1] A Pandey,[2] [1]Healis-Sekhsaria Institute for Public Health, Tobacco Control, New Delhi, India, [2]International Union against Tuberculosis and Lung Disease, Tobacco Control, Delhi, India. e-mail: apandey@theunion.org

Background and challenges to implementation: A World Bank- WHO study from 2006 confirms that if the retail price of cigarettes is increased by 10% roughly 4% and 6% current smokers quit smoking in a developed and developing countries, respectively. *Bidi* (Indian leaf-rolled cigarillo) are the dominant form of smoked products in India. The manufacturing cost of *bidi* is very low and tax on *bidi* is also very low compared to the cigarette. Nearly seven *bidi* sell for every cigarette and at price which is at a fraction compared to a cigarette. This makes *bidi* very affordable for a smoker. This study analysed key price and non-price factors which determine current smoking of *bidi* and initiation into *bidi* smoking.
Intervention or response: We interview current and former *bidi* smokers to understand motivations for persistence or quitting *bidi* smoking. Using a pre-tested semi-structured questionnaire, the investigators interviewed 400 bidi current smokers during their purchase at a point of sale for the duration of any entire day of business. The study was conducted in five major cities of India i.e. Lucknow (Uttar Pradesh), Paschim Medinipur (West Bengal), Patna (Bihar), and Bengaluru (Karnataka).
Results and lessons learnt: Preliminary data analysis shows that most *bidi* smokers (78%) started smoking at early age (16.8 years) and are predominantly from lower socio-economic group (incomes less than USD 150 per month). They also have limited understanding on harms of smoking and harms to others. *Bidi* smokers have shown willingness to quit with large pictorial health warning.
Conclusions and key recommendations: This study presents evidence that is necessary for shaping tobacco control policies and programmes in India especially related to tax and smokefree policies. This study also advocates to opt for additional strategies that will encourage *bidi* smokers to quit.

SOA-12-1123-01 Smoking cessation intervention in a rural healthcare setting in south-India: a pilot feasibility trial

A Srinivasaiyer,[1,2] K Bissell,[1] S Mysore,[2] C Prasad,[2] C Bullen,[1] [1]The University of Auckland, National Institute for Health Innovation, Auckland, New Zealand, [2]Swami Vivekananda Youth Movement, Medical Specialties, Saragur, India. e-mail: ananthkumarsriyer@gmail.com

Background: Smoking cessation is key to reducing tobacco-related harms yet support for smokers to quit is limited, especially in low and middle-income countries where around 80% of smokers live. Many live in remote rural settings, as in India. We aimed to evaluate the feasibility and effectiveness of a smoking cessation intervention in a rural healthcare setting in South India.
Methods: The study involved a randomised, two arm pilot trial in rural Karnataka State, India: one arm involved 'ABC' (Ask-Brief advice-Cessation support) with rural hospital out-patient clinic-based, physician-led identification of smokers and brief advice and lay counsellor-led cessation support. The 'ABC-Plus' arm added home-based follow-up to ABC. Feasibility was assessed for reach, adherence to ABC and documentation. Effectiveness was evaluated through biochemically-validated 14 day point prevalence smoking abstinence at 6 months.
Results: One hundred and forty-six individuals were randomised between January and March 2018. Over this period, the hospital attended to an average of 16 male adults daily, of whom a sixth were identified as smokers. Being asked about smoking increased from 29.3% in the first week to 97.8% in the last week of recruitment. Provision of brief advice and cessation support increased from 33.6% to 87.5% and 80% to 100% respectively. Full documentation of ABC increased from 9.5% to 84.4%. Home visits to smokers were 73.6% (53/72) in the second week follow up and 70.8% (51/72) in the third week follow up. Smokers who received ABC Plus were three times (adjusted RR 3.0 95% CI: 1.2 - 7.6) times more likely to have quit smoking at six months compared to smokers who received ABC alone (25% versus 10.8%).
Conclusions: In this rural Indian setting, implementing the ABC approach was feasible; combining ABC with community-based cessation support was also feasible and more effective than hospital-based intervention alone.

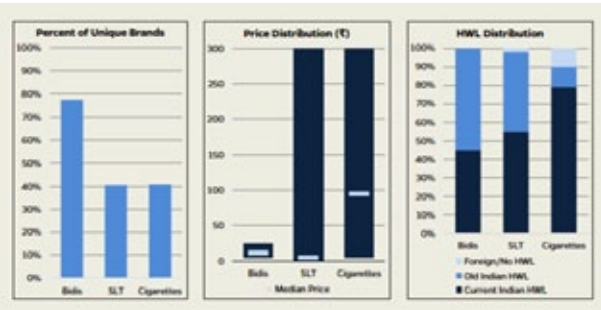
SOA-12-1124-01 The market for bidis and smokeless tobacco in India: evidence from towns in five states

K Welding,[1] M Iacobelli,[1] S Saraf,[1] KC Smith,[1] N Puntambekar,[2] PC Gupta,[2] JE Cohen,[1] [1]Johns Hopkins Bloomberg School of Public Health, Institute for Global Tobacco Control, Baltimore, MD, United States of America, [2]Healis-Sekhsaria Institute for Public Health, Department of Epidemiology, Mumbai, India. e-mail: ssaraf3@jhmi.edu

Background: Bidis and smokeless tobacco (SLT) account for 81% of tobacco consumption in India. Almost 200 million Indians use SLT products and over 70 million use bidis. The products are particularly popular outside of urban areas. This study examines the brand variability, price, and presence of an Indian health warning label (HWL) of bidi and SLT packs in semi-urban and rural towns.

Methods: The Tobacco Pack Surveillance System (TPackSS) systematically collects unique tobacco packs sold in low- and middle-income countries with high tobacco use. From October 26 to November 23, 2017, bidis and SLT products were collected in five states (Maharashtra, Uttar Pradesh, Assam, Rajasthan, and Karnataka). Within each state, five towns were selected across population tiers 3-5, one semi-urban and four rural. Cigarettes collected at the same time act as a comparison.

Results: Across the five states we collected 71 state-unique bidi packs and 240 state-unique SLT packages. The bidis had a higher percent of unique brand families (77% vs. 40%), while SLT products have a wider variety (97 vs. 55 brand families). The median price for a pack of bidis was 12 rupees (₹) with a range from ₹5 to ₹25. The median price for SLT products was ₹5 with a range from ₹1 to ₹300. All bidi packs had an Indian HWL (55% older). Four SLT packs (2%) had no/foreign HWL while 43% had an older Indian HWL.



[Select results, by product type]

Conclusions: Compared to cigarettes (71 packs), bidis and SLT products were less likely to have a current Indian HWL, had more brand variability, and were more affordable products. Very few bidi and SLT products were found without an Indian HWL, but many were older, therefore non-compliant. This may be indicative of localized production and distribution, but poorer implementation. The observed pricing and brand variability of bidis provides the appearance of many small producers.

SOA-13-C2 Quality TB care along the cascade

SOA-13-1125-01 TB implementation cascades to inform retention in care efforts in South Africa

S Pascoe,[1] MP Fox,[2] AN Huber,[1] M Phokojoe,[3] M Gorgens,[4] Y Pillay,[5] D Wilson,[4] N Fraser-Hurt,[4] [1]Health Economics and Epidemiology Research Office, Epidemiology, Johannesburg, South Africa, [2]Boston University School of Public Health, Department of Global Health, Boston, MA, United States of America, [3]National Department of Health, Directorate Care and Support, Pretoria, South Africa, [4]World Bank, Health, Nutrition and Population Global Practice, Washington, DC, United States of America, [5]National Department of Health, HIV & AIDS, TB and Maternal, Child and Women's Health, Pretoria, South Africa. e-mail: nfraserhurt@worldbank.org

Background: South Africa's National Department of Health has introduced 'National Adherence Guidelines for Chronic Diseases', which also target tuberculosis (TB) care. We analysed the drug-susceptible (DS)-TB implementation cascade to identify gaps which need closing to maximize treatment success.

Methods: Patients aged ≥18 and eligible for TB screening at the visit prior to file review (June 2016-January 2017) were enrolled into the screening cohort, using quality-enhanced routine data at 24 clinics in 4 provinces. Patients diagnosed with DS-TB in 2016 were enrolled into the diagnosed cohort from the TB registers. Indicators on screening and diagnostic procedures, follow-up visits, treatments and outcomes were analysed by patient characteristics including HIV status, using proportions and mean time intervals.

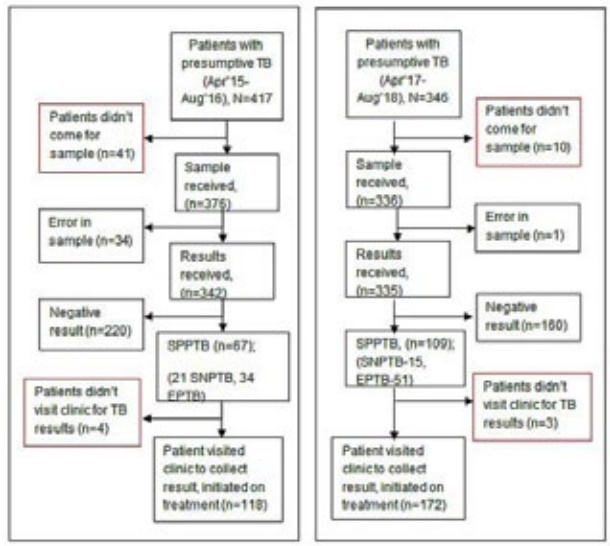
Results: TB screening was implemented for 46% of 3,600 clinic clients. Coverage was much higher for HIV+ (83%) than HIV- clients (23%). Screen-positivity was 7.5% but over 5 times higher in HIV- (17.7%) than HIV+ (3.2%). Of 741 diagnosed cases, 44.2% were HIV+. In the 3 months after diagnosis, 94% had at least 1 visit (median 6), 5% had no visit, and 9 patient files were not traceable. 98% had evidence of intensive phase treatment (86% of initiations in week post-diagnosis), and 81% had evidence of continuation treatment. Treatment success at 6 months was documented for 31% (28% completion, 3% cure), 38% had no microscopy data and 29% lacked visit data. Using all follow-up microscopy, 71% had completion/cure. Retention in care at 6 months was 71%.

Conclusions: Implementation cascades reveal differentials in TB screening effort and screen-positivity rates by HIV status, and points of attrition in the TB care continuum especially during the first 2 months of treatment. They also highlight weaknesses in routine data leading to uncertain patient outcomes. Improvement in DS-TB care requires judicious documentation of client contacts and targeted Adherence Guideline interventions.

SOA-13-1127-01 GeneXpert and CHW supported patient tracing for TB diagnosis in "conflict affected" border areas of Chhattisgarh, India

M Das,[1] D Pasupuleti,[2] S Rao,[3] J Jumayeva,[2] H Mansoor,[1] S Kalon,[1] G Ferlazzo,[4] P Isaakidis,[4]
[1]Médecins Sans Frontières (MSF) / Doctors without Borders, Medical, Mumbai, India, [2]Médecins Sans Frontières (MSF) / Doctors without Borders, Medical, Bhadrachalam, India, [3]Revised National Tuberculosis Control Programme, Bhadrachalam District Hospital, Bhadrachalam, India, [4]Médecins Sans Frontières (MSF) Southern Africa Medical Unit, Medical, Cape Town, South Africa.
e-mail: msfocb-delhi-epi@brussels.msf.org

Background: Access to early and accurate diagnosis for tuberculosis (TB) is challenging for 'conflict-affected hard to reach' population. Médecins Sans Frontières (MSF) have been providing diagnosis and treatment for patients with TB via mobile-clinics in conflict-affected border areas of Chhattisgarh, India since 2009. The study aims to document TB diagnostic model of care used in MSF TB programme including GeneXpert and Community health workers(CHW) for TB diagnosis.
Methods: It is a descriptive study including patients with presumptive-TB attending MSF TB Programme during Apr2015-Aug2018. GeneXpert in district hospital (Bhadrachalam) was used for TB diagnosis from January2017. Trained CHW from same community supported in patient-tracing, in case patient missed appointments for 2weeks.
The study compares the proportion of bacteriological confirmation and pre-treatment lost to follow up for two time-periods: 1) Apr2015- Aug2016 (Before utilization of GeneXpert upfront for TB-diagnosis), 2) Apr2017-Aug2018 (GeneXpert used for TB-diagnosis). Bacteriological confirmation was defined as presence of MTB+ in GeneXpert/Smear results. Error=failure to test for diagnosis of TB, which included poor-quality of sputum or technical error of equipment. Pre-treatment lost to follow up was defined as patients with presumptive-TB, after first-consultation who did not visit clinic for diagnosis/receipt of results within 1 month of consultation-date.
Results: A total of 1042 patients with presumptive TB were enrolled during Apr 2015-August 2018, of whom 376(36%) had TB. On comparing two time-periods, the bacteriological confirmation rate increased from 20%(67/342) to 33%(109/335) and error in TB diagnosis decreased from 9%(34/376) to 0.1%(1/336). The pre-treatment lost to follow up decreased from 11%(45/417) to 4%(13/346).
Conclusions: TB diagnosis with GeneXpert upfront and CHW supported patient tracing reduced the pretreatment lost to follow up by two-thirds. The mobile-clinic model of care for TB shows feasibility for replication in similar 'conflict-affected hard to reach' areas for improved access to quality TB diagnosis and care.



SPPTB- Smear-positive pulmonary tuberculosis, SNPTB- Smear negative pulmonary tuberculosis, EPTB- Extra-pulmonary tuberculosis

[Figure. Bacteriological confirmation & Pre-treatment lost to followup during Apr'15-Aug'16 and Apr'17-Aug'18 (GeneXpert used for TB-diagnosis)]

SOA-13-1129-01 Risk factors for hospitalisation or death in individuals with advanced HIV in South Africa

CJ Calderwood,[1] M Tlali,[2] AS Karat,[1] S Charalambous,[2] S Johnson,[3] AD Grant,[1] KL Fielding,[1] [1]London School of Hygiene and Tropical Medicine, TB Centre, London, United Kingdom, [2]The Aurum Institute, Science Office, Johannesburg, South Africa, [3]Foundation for Professional Development, Technical Assistance Cluster, Pretoria, South Africa. e-mail: clairejcalderwood@gmail.com

Background: Individuals with advanced HIV disease experience high mortality, particularly due to tuberculosis (TB). We aimed to identify factors associated with poor outcomes among individuals with advanced HIV at linkage-to-care in resource-limited settings.
Methods: Secondary analysis of data from the TB Fast Track trial, which enrolled adults attending primary healthcare clinics in South Africa, not on antiretroviral therapy, and with CD4 ≤150 cells/μL. We included all individuals in nine standard-of-care arm clinics where haemoglobin was routinely assessed. The outcome was death or hospitalisation within six months. Multivariable Cox regression was used to estimate associations

between baseline exposures and the composite outcome.
Results: Among 1099 individuals (58% female, median age 36 years, median CD4 70 cells/μl)), 89% started antiretroviral therapy (ART) and 13% started TB treatment over six months follow-up. 155 outcomes occurred over 489 person-years of observation (43 deaths and 112 hospitalisations). The overall outcome rate was 31.7/100 person-years; 66.2 and 24.3/100 person-years prior to and on ART respectively. Among 982 individuals with non-missing data, lower baseline CD4 count (adjusted hazard ratio (aHR) 1.17 per 25 cell/μL decrease), presence of anaemia (aHR 1.56 per WHO category increase in severity), positive WHO TB symptom screen (aHR 1.73 compared to negative) and positive urine lipoarabinomannan (LAM; aHR 1.40 compared to negative) were strong independent risk factors for the outcome (table). Increasing grades of LAM positivity appeared to be associated with even higher rate of outcome. Positive TB symptom screen at baseline was associated with the outcome during the early period, but not beyond four months from enrollment.

		HR (95% CI)	aHR (95% CI)	p			HR (95% CI)	aHR (95% CI)	p
Gender Ref: Women	Men	1.09 (0.78-1.52)	1.18 (0.81-1.71)	0.4	CD4 count	Per 25cell/μL decrease	1.23 (1.11-1.36)	1.17 (1.06-1.29)	0.002*
Age / years Ref: 18-29	30-39	1.24 (0.77-1.98)	1.19 (0.73-1.92)	0.6	LAM Ref: Negative	1+	1.45 (0.87-2.43)	1.40 (0.84-2.34)	<0.001**
	40-49	1.18 (0.70-1.99)	1.27 (0.74-2.17)			2+	4.51 (2.41-8.43)	3.78 (2.00-7.15)	
	50+	1.20 (0.65-2.20)	1.53 (0.82-2.86)			3-4+	6.71 (3.48-12.94)	4.15 (2.11-8.19)	
BMI / kg/m²	Per category decrease	1.35 (1.14-0.88)	1.18 (1.00-1.59)	0.05*	TB symptom screen Ref: Negative	Positive	2.12 (1.38-3.26)	1.73 (1.12-2.68)	0.01
					Anaemia	Per category increase in severity	1.57 (1.32-1.88)	1.56 (1.28-1.90)	<0.001*

Abbreviations: HR = crude hazard ratio, adjusted for fixed effect of clinic district to account for clustering; aHR = hazard ratio adjusted for all other variables in table and fixed effect for district; CI = confidence interval; p = p-value from likelihood ratio test (LRT) for association in adjusted model or LRT for trend where indicated (*); Ref = reference category; LAM = urine lipoarabinomannan; BMI = body-mass index; TB = tuberculosis; n = number individuals included in analysis.

Categories for BMI and anaemia as per WHO (BMI: <17, 17-18.4, 18.5-24.9, 25-29.9, 30+ kg/m²; anaemia severe = <80, moderate = 80-109, mild = 110-129 (men) or 119 (women), normal ≥130 (men) or ≥120 (women) g/dL)

* p-value for trend shown; no evidence for departure from linear trend (p>0.25 for each); ** p-value for linear trend from LRT <0.001 and >0.3 for departure from linearity.

[Unadjusted and adjusted hazard ratios for hospitalisation/death by baseline exposures (n = 982; 143 events/435 person-years)]

Conclusions: Simple measures that can be routinely assessed in primary care in resource-limited settings identify individuals with advanced HIV at high risk of poor early outcomes. Incorporated into a multi-component score, these factors may be useful to inform differentiated care of individuals in similar settings.

SOA-13-1130-01 Hospital clinicians' "mindlines" in prescribing non-standardised drugs for uncomplicated TB patients in designated hospitals in an Eastern China province

G Zou,[1] K Kielmann,[2] [1]Guangzhou University of Chinese Medicine, School of Economics and Management, Guangzhou, China, [2]Queen Margaret University, Institute for Global Health and Development, Edinburgh, United Kingdom. e-mail: zgy1021@hotmail.com

Background: In the context of integration of tuberculosis (TB) care into 'designated' public hospitals in China, there is increasing concern regarding non-standardised prescribing behaviour of hospital-based TB clinicians treating uncomplicated TB. We use the concept of 'mindlines' (Gabbay and le May 2004) to elucidate the tacit and collectively shared rules that underpin TB clinicians' prescriptions in this context.
Methods: This study was conducted in two separate TB clinics set up within designated hospitals in an Eastern Chinese province. We reviewed 340 medical records of uncomplicated TB patients and conducted 43 in-depth interviews with health providers related to TB control. Qualitative data was analysed using a thematic approach.
Results: Non-standardised prescription of drugs for uncomplicated TB was common. Overall, 53%, 51% and 16% of the patients were prescribed with non-free liver protection drugs, immune-boosting drugs, and first-line individual anti-TB drugs versus recommended free fixed-dose combination (FDC) respectively. Clinicians reinforced their professional identity and autonomy through recourse to tacit local knowledge on TB drug regimens, rather than international guidelines that were perceived to have limited applicability in the Chinese context. Following practices common at higher level hospitals, they emphasised adaptive prescription practice based on the medical and financial conditions of the individual patients. Non-free, individualised TB drugs were perceived to be of better quality and efficacy than FDC. Liver protection drugs were commonly prescribed to prevent perceived liver damage caused by the anti-TB drugs. However, there were inconsistent views regarding the efficacy of immune-boosting drugs.
Conclusions: Hospital-based TB clinicians' 'mindlines' around TB drug prescriptions were based on shared assumptions about what is appropriate, acceptable and efficacious in the southern Chinese context. It is important for the TB programme to understand local rationales and 'communities of practice' for non-standardised TB drug regimens in order to review and improve the evidence base for TB control.

SOA-13-1131-01 Adverse drug reactions (ADR) during intensive phase of first line anti-tuberculous treatment (ATT): a prospective cohort study from rural central India

G Phutke,[1] S Patil,[1] Y Jain,[1] [1]Jan Swasthya Sahyog, Ganiyari, Family Medicine, Bilaspur, India.
e-mail: gajananphutke@gmail.com

Background: Scant literature focusses on adverse drug reaction(ADR) incidence and profile with most studies as either cross-sectional or retrospective design and none with prospective design in indian tuberculosis patients. This prospective study was done to measure the incidence of common ADRs in intensive phase of treatment in rural indian population with high under-nutrition, low HIV prevalence.
Methods: 405 newly diagnosed TB patients were prospectively enrolled with baseline demographic and clinical details and face to face follow up at days 15, 30, 45,60 and 90 of treatment for new symptoms ,common ADR, and lab tests for serum alanine transferase(ALT) ,serum creatinine. ADRs were documented using a predefined format with standard definitions, by active enquiry by physicians at each visit and by active enquiry by trained paramedic staff telephonically in between two visits. ADRs were managed as per ATS guidelines.

Type of ADR	BM I>18.5 kg/m2 Number (%)	BMI 17 - 18.49 kg/m2 Number (%)	BMI 16 - 16.9 kg/m2 Number (%)	BMI <16 kg/m2 Number (%)	Total Number (%)
JOINT PAIN	11(2.7)	16(4)	14(3.5)	48(12)	89(22)
ABDOMINAL PAIN	8(2)	11(2.7)	5(1.25)	34(8.5)	58(14.5)
FATIGUE	8(2)	4(1)	4(1)	31(7.7)	47(11.7)
VOMITING	1(0.25)	2(0.5)	5(1.25)	14(3.5)	22(5.5)
DRUG RASH	1(0.25)	4(1)	3(0.75)	8(2)	16(4)
ITCHING	3(0.75)	2(0.5)	2(0.5)	7(1.75)	14(3.5)
SYMPTOMATIC HEPATITIS	2(0.5)	3(0.75)	2(0.5)	6(1.5)	13(3.2)
ASYMPTOMATIC HEPATITIS	0(0)	1(0.25)	1(0.25)	3(0.75)	5(1.3)

[Major Adverse Drug Reaction Profile in Intensive phase of First Line ATT]

Type of ADR	BMI>18.5 kg/m2 Number(%)	BMI 17-18.49 kg/m2 Number(%)	BMI 16-16.9 kg/m2 Number(%)	BMI <16 kg/m2 Number(%)	Total Number (%)
JOINT PAIN	11(2.7)	16(4)	14(3.5)	48(12)	89(22)
ABDOMINAL PAIN	8(2)	11(2.7)	5(1.25)	34(8.5)	58(14.5)
FATIGUE	8(2)	4(1)	4(1)	31(7.7)	47(11.7)
VOMITING	1(0.25)	2(0.5)	5(1.25)	14(3.5)	22(5.5)
DRUG RASH	1(0.25)	4(1)	3(0.75)	8(2)	16(4)
ITCHING	3(0.75)	2(0.5)	2(0.5)	7(1.75)	14(3.5)
SYMPTOMATIC HEPATITIS	2(0.5)	3(0.75)	2(0.5)	6(1.5)	13(3.2)
ASYMPTOMATIC HEPATITIS	0(0)	1(0.25)	1(0.25)	3(0.75)	5(1.3)

[Major Adverse Drug Reaction Profile in Intensive phase of First Line ATT]

Results: Total 276 ADRs were noted in 169 (42%) patients. 96(24%) patients had single ADR, 45(11%) experienced 2 ADRs, 21(5%) experienced 3 ADRs, 4(1%) experienced 4 ADRs and maximum 5 ADRs were reported by 2 (0.5%) patients. Profile of different ADRs observed are as shown in table 1.
Incidence (per 100 patients) of ADRs as joint pain 22 (per 100 patients), abdominal pain 14, fatigue 12, vomiting 5, drug rash 4, itching 3, symptomatic hepatitis 3, asymptomatic hepatitis 1,drug induced edema 1, pyrazinamide induced hyperuricemia 1, and others like psychosis, altered sensorium, visual problems and giddiness each in 0.4.
We found no significant difference of incidence ADRs across different grades of nutrition. Unfavourable treatment outcomes (death, default) were observed 4.9 times more among patients with ADRs compared with those without ADR.
Conclusions: ADRs contribute significantly to unfavorable treatment outcomes. More prospective studies at multiple sites with larger sample size are required for correct estimation of incidence of ADRs among rural indian patients on first line ATT.

SOA-13-1132-01 Updated findings from an evaluation of the accuracy of 99DOTS, a digital technology for monitoring tuberculosis medication adherence in HIV co-infected and uninfected patients

B Thomas,[1] V Kumar,[1] M Chiranjeevi,[1] G Ramachandran,[2] M Periyasamy,[1] AS Khandelwale,[1] D Shah,[3] R Subbaraman,[4] [1]National Institute of Research in Tuberculosis, Social and Behavioural Research, Chennai, India, [2]National Institute of Research in Tuberculosis, Biochemistry and Clinical Pharmcology, Chennai, India, [3]Municipal Corporation of Greater Mumbai, Public Health Department, Mumbai, India, [4]Tufts University School of Medicine, Public Health and Community Medicine, Boston, MA, United States of America.
e-mail: beenaelli09@gmail.com

Background: Digital technology for monitoring TB medication adherence is gaining importance. 99DOTS is one such cellphone-based strategy which has been rolled out to >200000 TB patients in India. At the 2018 Union conference, we presented preliminary findings on 99DOTS' accuracy.
We now present updated findings and sub-group comparisons from a recently completed cohort study evaluating 99DOTS' accuracy for measuring TB medication adherence in HIV co-infected (ART) and un-infected Indian patients (RNTCP).
Methods: TB patients using 99DOTS at ART centres in Chennai and in RNTCP centres in Mumbai were enrolled. To evaluate 99DOTS' accuracy, we compared patients' 99DOTS medication adherence records against urine isoniazid samples collected via unannounced home visits.

Results: We enrolled 862 patients and collected 650 urine samples via unannounced home visits, of which 597 (287 from ART and 310 from RNTCP) were analysed. The positive predictive value (PPV) of 99DOTS for true medication adherence (by urine test) was 92.9% (CI: 90.7% - 94.6%) and negative predictive value (NPV) was 21.3% (CI: 17.7%—25.4%). The sensitivity and specificity for true medication adherence were 69.8% (CI: 65.6%—73.7%) and 60.6% (CI: 48.3%—72.0%), respectively. We compared differences in adherence between ART vs. RNTCP patients and found PPV to be 90.1% vs. 95.1% and NPV to be 28.4% vs. 11.6%, respectively. The sensitivity and specificity for true medication adherence for ART vs. RNTCP patients were 65.0% vs 73.7% and 66.0% vs 47.6%, respectively.
Conclusions: Although 99DOTS is a promising strategy for real-time monitoring of TB medication adherence, its low NPV suggests many patients are taking TB medications without reporting these doses, which could lead to unnecessary intervention by healthcare providers. In addition, its suboptimal specificity suggests that 99DOTS is missing some non-adherent TB patients who require timely intervention, especially among HIV uninfected individuals, who constitute the vast majority of TB patients in India's government program.

SOA-13-1133-01 An outcome evaluation of an intervention to improve transitions in care for TB patients discharged from hospital in the Western Cape, South Africa

L Dudley,[1] R Dyers,[1,2] F Mukinda,[3] F Marais,[2]
[1]Stellenbosch University, Global Health, Cape Town, South Africa, [2]Western Cape Government, Health, Cape Town, South Africa, [3]University of Western Cape, Public Health, Cape Town, South Africa. e-mail: ldudley@sun.ac.za

Background: South African acute hospitals admitted high numbers of patients with TB, while facing significant health system challenges. Acute hospitals were not integrated in National TB Control Programmes, and TB patients experienced poor continuity of care after discharge. A multifaceted intervention to improve TB patient discharge management and communication between levels of care was implemented at a referral hospital in the Western Cape, South Africa. This study aimed to evaluate the effects of the intervention on continuity of care for TB patients discharged from hospital.
Methods: The study used a before after control 'quasi experimental' design. We compared continuity of care for adult TB patients discharged from intervention and control wards; and for all adult TB patients discharged post intervention to pre-intervention at the same hospital. All adult admissions with a primary or secondary TB diagnosis during the pre and post periods were included. Patient data from routine health information systems were analysed in STATA 15.0. We compared before-after and intervention-control groups using bivariate analysis and Chi2 tests; and conducted a logistic regression to assess associations and control confounding.
Results: The increase in discharged adult TB patients who continued TB treatment from the before (256/636, 40.3%) to the after (548/595, 92.1%) period was highly significant (OR 17.3, $p < 0.001$). In the logistic regression comparing intervention to control wards, and controlling for all other independent variables, the intervention was significantly associated with continuity of TB care (OR 2.03, CI 1.01-4.05, p=0.045).
Conclusions: The intervention improved continuity of care for discharged TB patients. Concurrent changes within the hospital and broader environment may have further improved continuity of TB care. Implementation research should explore contextual factors to understand the what, how and why this intervention worked, and if it can be replicated in similar settings.

SOA-13-1134-01 "Care after TB Cure" in routine programme setting: experiences from a pilot intervention in Kerala, India

MS Manu,[1] M Sunil Kumar,[2] A Kalliyath,[1] M J Valamparampil,[2] MP Sindhu,[3] S Balakrishnan,[4] PS Rakesh,[4] A Raj,[5] [1]State Tuberculosis Training and Demonstration Centre, Kerala Health Services, Thiruvananthapuram, India, [2]State TB Cell, Directorate of Health Services, Govt. of Kerala, Kerala Health Services, Thiruvananthapuram, India, [3]District TB Centre, Kerala Health Services, Thiruvananthapuram, India, [4]World Health Organization, RNTCP Technical Assistant Project, Thiruvananthapuram, India, [5]State Tuberculosis Training and Demonstration Centre, Research Wing, Thiruvananthapuram, India.
e-mail: drmsmanu@yahoo.co.in

Background and challenges to implementation: The National TB Program (NTP), India recommended following up of all patients who completed anti TB treatment till 24 months.
Intervention or response: Thiruvananthapuram district, Kerala, India has piloted the tuberculosis patient follow up program - 'Care after Cure' in which patient follow up is attempted through camp approach. Patients who completed six months after successful declaration of anti TB treatment were requested to attend one of the several camps as per their convenience. Clinical evaluation, random blood sugar testing, tobacco cessation services and spirometry evaluation were provided in the camp. Sputum testing, chest x ray and culture services were made available for those who were symptomatic.
Results and lessons learnt: 202 out of 450 eligible individuals attended the camps till date. Of them, 16 (7.9%) were identified as presumptive TB and underwent complete testing for TB.Four (1.9%)were diagnosed to have recurrent TB.Of the 24 patients who were found to have diabetes at the beginning of anti TB treatment, 18 had poorly controlled blood sugars (RBS >200mg/dl) on follow up after cure. Additionally, 21 (10%) were found to

have high blood sugar values on follow up (RBS >200mg/dl). Of them, 64 out of 79 users quit tobacco during anti TB treatment. Four of them restarted using tobacco. Out of 29 well performed spirometry, 15 restrictive, 5 mixed and 2 obstructive patterns were seen. Co-morbidity especially diabetes among TB patients needs to be screened more frequently and managed more efficiently.
Conclusions and key recommendations: Post treatment follow up of TB patients as a national policy is important to be complied with, since recurrence otherwise could have been missed or diagnosed late were picked up. Post treatment follow up is feasible in program setting. Care after cure provides opportunity to pick up co-morbidity that are risk factors for recurrence and control them which may help to avert recurrence among them

SOA-13-1135-01 Assessing how men's resources influence their TB treatment outcomes in Buffalo City Metro, South Africa: an application of the Network-Individual-Resource model

J Daniels,[1] K Glockner,[2] E Drew,[3] D Olivier,[2] C Bezuidenhout,[2] N Ngcelwane,[4] A Kipp,[5] A Medina-Marino,[2] [1]Charles R. Drew University of Medicine and Science, Psychiatry and Human Behavior, Los Angeles, CA, United States of America, [2]Foundation for Professional Development, Research, East London, South Africa, [3]Northeastern University, Public Health, Boston, MA, United States of America, [4]Buffalo City Metro Department of Health, Eastern Cape Province, East London, South Africa, [5]Vanderbilt University Medical Center, Epidemiology, Nashville, TN, United States of America. e-mail: josephdaniels@cdrewu.edu

Background: Globally, men have worse TB treatment outcomes compared to women. In South Africa, TB is a primary driver of men's lower life expectancy. Research demonstrates that men's health behaviors are influenced by the availability and exchange of resources within their networks.
Therefore, we applied the Network-Individual Resource (NIR) model to outline how men's mental and tangible resources influence their TB treatment behaviors and outcomes.
Methods: In-depth interviews were conducted with men at different points along the TB care cascade in Buffalo City Metro Health District, South Africa. Interview protocol domains included: TB testing; treatment support; clinical care experiences; disclosure to and support from family/friends; stigma; and treatment support preferences. Interviews were conducted in Xhosa, and transcribed/translated into English. Transcripts were analyzed using a constant comparison approach guided by the NIR model.
Results: Thirty-one men were interviewed to outline resources needed or accessed during their TB treatment. Individual-level resources included: employment stability and food security (tangible); and perceived connectedness with peers, abstinence from alcohol, and TB knowledge (mental). Resources received from men's support networks included: money for taxis to attend clinic and meals (tangible); and emotional support during illness and treatment from mothers, partners and sisters (mental).
These resources are explained by men's motivation to access resources from their networks in order to replace individual resources lost, or not present. Men ultimately sought these resources in order to complete treatment and re-build their health in order to work and provide for their family and household.
Conclusions: Men's TB treatment behaviors are influenced by 1) their mental and tangible resources, and 2) how these resources function together. Future studies will outline how and when these resources are engaged across the TB care cascade, especially for men that are lost-to-care. Subsequent male-centered TB interventions should consider the importance and interaction of men's mental and tangible resources.

SOA-14-C10 Improving laboratory diagnostics

SOA-14-1136-01 The role of Stop TB partnership´s GDF in facilitating access to diagnostics: meeting country needs in a changing landscape

W van Gemert,[1] B Angarita,[1] M Babaley,[1] B Waning,[1] [1]Stop TB Partnership, Global Drug Facility, Geneva, Switzerland. e-mail: waynev@stoptb.org

Background and challenges to implementation: Procurement of all of the supplies required to equip and maintain a national TB laboratory network is challenging, given the logistics of sourcing from multiple suppliers and the market presence of products that are not quality-assured. Smaller countries also often have inadequate bargaining power in negotiating with manufacturers. Furthermore in an era of increasing country self-financing, domestic procurement poses significant challenges.
Intervention or response: Stop TB's Global Drug Facility (GDF) started procurement of diagnostics for countries in 2007. Today GDF sources over 500 quality-assured diagnostic products, including the supplies required to run all WHO-recommended TB tests and ensure biosafety. Given changes in the global funding landscape, GDF is positioning itself to supply to countries using domestic funding, including use of its Flexible Procurement Fund to place orders for countries with national regulations that require payment only upon delivery.

Results and lessons learnt: In 2018 the number of countries buying diagnostics through GDF reached 69. Of 122 countries that bought GeneXpert cartridges globally in 2017, 53 (43%) bought them through GDF. The number of countries buying through GDF with domestic funding is growing: 42 countries used domestic funding to buy medicines and/or diagnostics in 2018. Ordering diagnostics through national distributors has been found to cost countries up to 8 times more than ordering through GDF. GDF also provides guidance to countries on forecasting and order planning of key diagnostics to facilitate their introduction. GDF has also played a leading role in aligning partners around improvements to GeneXpert service and maintenance and securing improved access terms for new diagnostic products, including BACTEC MGIT, Omnigene·Sputum and IGRAs.
Conclusions and key recommendations: As the largest global supplier of TB diagnostics, GDF has positioned itself as the market steward. GDF will continue to play a key role in the future as a source of affordable, quality-assured diagnostics, including for countries using domestic funding.

SOA-14-1137-01 A 10-year TB genotyping overview at the National TB Laboratory in Canada

M Sharma,[1,2] H Soualhine,[1] CTLTN MIRU Partners
[1]Public Health Agency of Canada, National Reference Centre for Mycobacteriology, Winnipeg, MB, Canada, [2]University of Manitoba, Medical Microbiology and Infectious Diseases, Winnipeg, MB, Canada.
e-mail: meenu.sharma@canada.ca

Background: Tuberculosis(TB) is a global and Canadian public health priority. The methods used for genotyping of Mycobacterium tuberculosis(MTB) are primarily culture-based including MIRU-VNTR. TB Investigations are challenging due to its long-term persistence in infected individuals (new/relapse). In Canadian subpopulations, there is a need for routine genotyping surveillance due to several issues surrounding population mobility and low genetic diversity of persistently circulating TB strains implicated in ongoing outbreaks.
Methods: Between January 1, 2008 to December 31, 2017, 6755 MTB cultures were tested for TB genotyping using 24 loci MIRU-VNTR at the National Reference Centre for Mycobacteriology(NRCM), Canada. A retrospective epidemiological cluster analysis was performed. A cluster was defined as a group of 2 or more isolates with an identical MIRU pattern. Cluster numbers were generated using BioNumerics software v7.6.2 and the numbers assigned were arbitrary. A 'cluster alert' was based on a formula calculated using number of isolates in a 3 year period.
Results: A ten year data compilation at the NRCM showed that a total of 6755 TB isolates were genotyped. A total of 3040 MIRU clusters were seen: 2424 isolates were associated with unique MIRU patterns while 4331 isolates were associated with 616 MIRU patterns. Cluster 1, is the most predominant cluster in our database, comprising of 354 isolates. It is primarily seen in province A with 3 isolates from neighboring provinces B and C. Cluster 2 is comprised of 191 isolates: 159 isolates are from H, 8 from I, 7 from C, 6 from A, and 6 from E, 3 from D, and 1 each from F and G provinces.
Conclusions: The determination of genetic relatedness generated can help identify transmission chains in potential outbreak scenarios and can have direct patient benefits, resulting in early detection of an index case(transmitter), thus helping break the chain of TB transmission.

SOA-14-1138-01 Building capacity in Mtb whole-genome sequencing and bioinformatics at universities and national reference laboratories in low-income, high TB-burden countries: experience from Ethiopia

E Rivière,[1] C Meehan,[2] G Abebe,[3] T Heupink,[1] R Warren,[4] A Van Rie,[1] [1]University of Antwerp, Medicine and Health Science, Antwerp, Belgium, [2]Institute of Tropical Medicine Antwerp, Biomedical Sciences, Antwerp, Belgium, [3]Jimma University, Mycobacteriology Research Center, Jimma, Ethiopia, [4]Stellenbosch University, Division of Molecular Biology and Human Genetics, Cape Town, South Africa.
e-mail: annelies.vanrie@uantwerpen.be

Background and challenges to implementation: Whole genome sequencing (WGS) is becoming the state-of-the-art tool for TB outbreak investigation and drug resistance detection. High TB burden countries often face human resource, financial and infrastructural challenges in implementing WGS in research, surveillance and clinical settings.
Intervention or response: We organized two 3-week courses followed by long-term mentoring for scientists active in academic TB research and TB reference laboratories in Ethiopia. Our training focussed on WGS theory and practice, bioinformatics, and the public health relevance of WGS in high TB burden settings. While the trainees were introduced to the complete workflow of WGS, practical training focussed on DNA extraction as DNA library preparation and sequencing can be outsourced. The bioinformatics sessions focussed on use of Linux, assembly pipelines (PhyResSE, MTBseq) and phylogeny. To apply the acquired knowledge, trainees were mentored in the development of a WGS-based TB research project that addresses important questions in their setting. Mentoring included development of research questions, writing of the protocol, and application for external funding.
Results and lessons learnt: We faced several challenges. Because of insufficient memory on trainees' laptops, we used a server running the MTBseq pipeline through a

virtual-machine. Absence of a fume hood in the labs of residence forced us to switch from traditional extraction protocols with volatile compounds to commercial kits. Purchase of a photospectrometer (not planned) was essential to assess extracted DNA quality prior to shipment. The concepts of a software pipeline and Linux proved difficult for the trainees, requiring us to allocate more time to these topics. Communication through conference calls proved unstable, forcing us to abort plans for online journal clubs and peer support for research projects.

Conclusions and key recommendations: Training for implementation of WGS in high TB burden countries was more challenging than anticipated. Careful attention to the local circumstance is important for the successful transfer of skills.

SOA-14-1139-01 Reduction of TB culture contamination: lesson learnt from PanACEA TB studies at NIMR-MMRC, Mbeya, Tanzania

E Sichone,[1] D Mapamba,[1] J John,[1] F Njeleka,[1] A Shoo,[1] I Sabi,[1] C Manyama,[1] B Mtafya,[1] N Heinrich,[2] NE Ntinginya,[1] [1]National Institute for Medical Research - Mbeya Medical Research Centre, TB & Emerging Disease, Mbeya, Tanzania, United Rep., [2]Division of Infectious and Tropical Medicine, Medical Centre of the University of Munich, LMU, Munich, Germany.
e-mail: esichone@nimr-mmrc.org

Background: Sputum is the most used diagnostic specimen for detection of pulmonary tuberculosis (TB). It is not sterile and therefore must undergo a chemical decontamination before culture to eliminate contaminants. We evaluated the trend and factors associated with reduction of TB culture contamination rate in PanACEA TB studies.

Methods: We analysed the contamination rate of the REMOX and MAMS TB trial obtained between 2009-2015 and compared with the rate obtained after renovation of the TB laboratory in December 2016. Presence of growth in BA after 48 hours of incubation was scored as contaminated culture. Monthly and annual percentage of contaminated MGIT culture were analysed using Microsoft excel and GraphPad prism 7.04.

Results: In REMOX study, monthly contamination rate was 17.2 ± 8.2% and the annual rate was 20.98 ± 12.37%, 19.16 ± 7.18%, 13.74 ± 3.85% and 13.28 ± 3.85% in 2009, 2010, 2011 and 2012 respectively while in MAMS TB trial, monthly contamination rate was 11.7 ± 8.9% and annual contamination rate was 14.62 ± 8.94% and 10.26 ± 5.54% in 2013 and 2014 respectively. We observed a reduction of contamination rate by 5.5% in MAMS trial compared to the initial REMOX TB trial (P=0.011).

Furthermore, comparing the contamination rate of the REMOX, MAMS TB trial and rates after renovation of the TB laboratory, we observed an improvement of contamination rate, dropping up to an acceptable contamination rate of 3.83 ± 1.68% in 2018 (P< 0.0001). This reduction was the outcome of re re-training of the staff, re-novation and installation of the ventilation system in the TB laboratory in December 2016.

Conclusions: Our in-house assessment of the TB laboratory highlights the importance of ventilation, training and negative pressure systems on reduction of TB culture contamination rate. Finally have quality results with accurate TTP for clinical decision making of the patient treatment.

SOA-14-1140-01 Drug-resistant TB among patients seeking care in private sector of Dhaka: a missed opportunity?

S Saba,[1] KK Paul,[1] S Ahmed,[1] S Alam,[1] S Sultana,[1] MS Bashar,[2] NA Saki,[2] PK Modak,[2] AH Khan,[2] S Banu,[1] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh, [2]Directorate General of Health Services, National Tuberculosis Control Programme, Dhaka, Bangladesh.
e-mail: shahriar.ahmed@icddrb.org

Background: Dhaka, capital of Bangladesh, is the fourth most densely populated city in the world. Like any urban setting, majority population primarily seeks care from private health care sector. Drug susceptibility testing (DST) is not readily accessible from this sector. Being one of the high priority countries for multidrug resistant (MDR) tuberculosis (TB) with 1.6% and 29% MDR in primary and retreatment cases, this is an alarming situation.

Methods: Under operational research framework, icddr,b established TB screening and treatment centers providing digital X-ray and Xpert MTB/RIF to patients, mostly referred from the network of private providers developed under the project.

All presumptive patients referred to and tested at these centers between June'14 and March'19 are included in this analysis. Parametric tests of significance were used for analysis.

Results: A total of 1,46,661 presumptive cases were screened and 1,02,071 were tested by Xpert. MTB was detected in 13,195 (12%) cases. Of these, 520 (4%) patients were found to have rifampicin resistant (RR) TB. Around 70% of the identified TB cases were male. However, no significant difference in distribution of rifampicin resistance according to gender (p=0.110) was observed. Age distribution of TB cases shows that rifampicin resistance was more common among young patients. The odds of RR case to belong to age group of 15-59 was 1.9 (95% CI 1.4, 2.5) times higher compared to RR cases of >60 years age. Rifampicin Resistance was 3% and 12 % respectively in primary and retreatment cases.

The RR Patients were 1.7 (95% CI 1.3, 2.3) times more likely to have features highly suggestive of TB in chest X-ray.

Conclusions: This high proportion of MDR TB among primary cases would remain undetected if not tested by Xpert. Universal access to DST should be ensured and to the very least, every identified TB patient should be tested by Xpert.

SOA-14-1141-01 Phenotypic susceptibility to fluoroquinolone among gyrA/B mutant strains of Mycobacterium tuberculosis

PK Singh,[1] VK Raikwar,[1] U Singh,[1] P Dixit,[1] V Kumar,[1] A Jain,[1] [1]King George Medical University, Microbiology, Lucknow, India. e-mail: amita602002@yahoo.com

Background: *Mycobacterium tuberculosis* develops resistance to fluoroquinolones (FQs) mainly through mutations in *gyr*A/B genes. Recently, concentration of FQ for culture based drug susceptibility testing (DST) is revised by World Health Organization to improve sensitivity of phenotypic DST in detecting clinically relevant *gyr*A/B mutant strains. Here, we studied the frequency of *gyr*A/B mutations and also estimated the proportion of additional cases who would be considered FQ resistant, if tested at revised drug concentration.
Methods: A total of 141 isolates having *gyr*A/B mutation/s (as determined by Genotype MTBDR*sl* assay) were included consecutively during Jan-Feb 2019. Levfloxacin susceptibility testing was performed for all isolates in MGIT media at currently used concentration (1.5ug/ml). Isolates found susceptible to levofloxacin were re-tested at revised drug concentration (1.0ug/ml). Phenotypic resistance pattern was analyzed and were correlated with *gyr*A/B mutations.
Results: Out of 141 mutant strains, 121 (85.8%) were found resistant and rest 20 (14.2%) were as susceptible to levofloxacin at currently used concentration. D94G mutation in *gyr*A gene was most frequent (55.3%); and it was distributed among resistant strains only. A90V was another common mutation (19.9%) which was displayed significantly ($P < 0.001$) by susceptible strains. Of 20 susceptible strains, only 14 turned as resistant when tested at revised concentration.
Conclusions: Susceptibility testing of levofloxacin at revised concentration would increase the proportion of resistant cases by about 10%. Study also suggests that D94G mutation is associated strongly with high level FQ resistance, whereas presence of A90V mutation indicates higher likelihood of low/moderate level FQ resistance.

SOA-14-1142-01 Fluoroquinolones and pyrazinamide resistance among multidrug-resistant tuberculosis patients in Myanmar

WW Aung,[1] PW Ei,[1] JS Lee,[2] WW Nyunt,[3] MM Htwe,[1] AS Mon,[1] SM Win,[1] ST Aung,[4] CL Chang,[5] [1]Advanced Molecular Research Centre, Department of Medical Research, Yangon, Myanmar, [2]Microbiology Section, International TB Research Center, Masan, Korea, Republic of, [3]National TB Reference Laboratory, National TB Program, Yangon, Myanmar, [4]Disease Control Division, Department of Public Health, Naypyitaw, Myanmar, [5]Pusan National University, Department of Laboratory Medicine, Busan, Korea, Republic of.
e-mail: drwahwahaung@gmail.com

Background: Fluoroquinolones (FQ) are the key drugs for the treatment of multidrug-resistant tuberculosis (MDR-TB). Pyrazinamide (PZA) is a standard drug of first-line anti-TB treatment regimen and also of second-line regimen for MDR-TB and extensively drug-resistant TB (XDR-TB).The combination of PZA plus a fourth-generation FQ (moxifloxacin or gatifloxacin) is considered essential in novel rifampicin-sparing TB treatment regimens and in shorter MDR-TB treatment regimens.
Methods: A cross-sectional study was carried out on patients enrolled for MDR-TB treatment during 2015-17 in Myanmar. Phenotypic drug susceptibility testing for first-line and second-line anti-TB drugs including three FQ (ofloxacin, levofloxacin, moxifloxacin) was performed by Lowenstein-Jensen media-based M-KIT plates. Pyrazinamide susceptibility testing was carried out by Mycobacterial Growth Indicator Tube (MGIT) method. Sanger DNA sequencing was used to detect mutations in quinolone resistance-determining region (QRDR) of *gyrA* and *gyrB* genes, and those in *pncA* genes and its promoter region.
Results: Of 71 MDR-TB patients, phenotypic FQ resistance were found in 26.8% (19/71); comprising 16 FQ only resistance (pre-XDR) and 3 both FQ and second-line injectables resistance (XDR). Among 19 FQ-resistant patients, 13 were resistant to all three tested FQ and three were resistant to two FQ, ofloxacin and levofloxacin. PZA resistance was detected in 63.4% (45/71) and 22.5% (16/71) showed resistance to both FQ and PZA .Ten different types of *gyrA* mutations and one type of *gyrB* mutation were detected in 19 phenotypic FQ-resistant isolates. Of 45 phenotypic PZA-resistant isolates, 41 different types of mutations were distributed on the *pncA* gene and/or its promoter and 10 types of which were found to be novel mutations.
Conclusions: High proportion of FQ and PZA resistance in Myanmar MDR-TB isolates highlights the need for evaluation of effective treatment regimens. Information on FQ and PZA resistance associated gene mutations may beneficial for further studies on development of rapid susceptibility assays.

SOA-14-1143-01 Evaluation of the mutations associated with resistance to bedaquiline in Mycobacterium tuberculosis isolates in Peru

D Santos Lazaro,[1] Z Puyen,[1] [1]Instituto Nacional de Salud, Public Health, Lima, Peru. e-mail: zpuyeng@gmail.com

Background: Bedaquiline (BDQ) is one of the last drugs that has been recommended for the treatment against tuberculosis (TB). Peru incorporated this drug, in 'program conditions', since 2018. Therefore, the objective of the study was to perform an a priori evaluation of the presence of mutations associated with BDQ resistance in strains of TB circulating in Peru.
Methods: A total of 100 *M. tuberculosis* strains stored at Peruvian 'National Reference Laboratory of Mycobacteria' were selected: 50 XDR, 15 Pre-XDR, 15 MDR, 10 isoniazid monoresistant, and 10 pan-susceptible strains. Whole Genome Sequencing was performed using the Miseq technology. Genomic assembly was done with BWA v0.7.12 (reference genome: H37Rv [NC_000962.3]). Duplicated reads were identified and removed with the program Picard-tools v1.119. ′Variant calling′ was made with GATK v4.0.12, and a ′Hard filtering′ (DEPTH ≥ 10; QUAL ≥ 30; AF ≥ 0.75) was performed by VCFtools v0.1.15. Single Nucleotide Variants (SNVs) and insertions/deletions (INDELs) at genes associated with BDQ resistance were evaluated: Rv0867c, *pepQ* (Rv2535c) and *atpE* (Rv1305).
Finally, functional variant annotation was made by SnpEff v4.3.
Results: Of the total of strains, six (6%) contains mutations associated with BDQ resistance. No INDELs was found and the 100% (n = 6) of this mutations were SNVs of "*missense*" type. The Rv0867c gene showed 3 SNVs: L117R, N98D y R135Q and the pepQ also 3 SNVs: D57Y, V45L and F46L. No mutations were found at *atpE* gene. Each strain contained just one SNV. Of these, three strains were classified as XDR, two as MDR and one as Pre-XDR (Levofloxacin resistant).
Conclusions: This study shows that the presence of mutations that confer resistance to BDQ is low (6%) in *M. tuberculosis* Peruvian strains. Likewise, half of them are associated with low level resistance. Therefore, the use of BDQ in the treatment of MDR and XDR TB is highly recommended.

SOA-14-1144-01 Use of Xpert MTB/RIF for the detection of Mycobacterium tuberculosis and resistance to rifampicin from sputum samples in Peru

J Giraldo,[1] M Alarcon,[1] C Osorio,[1] E Valencia,[1] D Santos Lazaro,[1] Z Puyen,[1] [1]Instituto Nacional de Salud, Public Health, Lima, Peru. e-mail: zpuyeng@gmail.com

Background: In 2018, the Xpert MTB / RIF (Xpert) assay was implemented in priority populations in Peruvian National Health System. The objective of the study was to evaluate the performance of the Xpert assay for its use in the diagnosis of *M. tuberculosis* (MTB) and resistance to rifampicin (R) from sputum samples.
Methods: A total of 200 sputum samples were evaluated, of which 100 were from new patients with suspected TB (group 1) and 100 from patients with suspected MDR-TB (group 2). To obtain sensitivity and specificity, the results were compared with the BACTEC MGIT 960®. For the discordant results to R, Genotype MTDRplus and sequencing of the rpoB gene were made.
Results: For group 1, 61 were positive for MTB and for group 2, 55 were resistant to R using Xpert. The sensitivity and specificity for the detection of MTB was 100% (95% I.C., 92.5-99.85%) and 97.5% (95% I.C., 85.27-99.87%), respectively; and for the detection of resistance to R was 100% (95% I.C., 91.73-99.83%) and 97.83% (95% I.C., 87.03-99.89%), respectively. We detected discordant results (4) for the resistance to R between two methodologies, of which 3 were confirmed as resistant to R by sequencing (2) and Genotype (1), the last sample could not be evaluated. In the two samples that the rpoB gene was sequenced, the D516Y and L511P mutations were detected, only one sample was evaluated by Genotype MTBDRplus and resistance inferred to R was detected, evidencing the absence of the WT3 probe (codons 514-515). Finally probes A (2) and B (2) of Xpert were the ones that detected the mutation in these (4) discordant results.
Conclusions: The Xpert MTB / RIF is a reliable and efficient test for the detection of MTB and resistance to R, therefore its use and implementation in Peru is recommended.

SOA-14-1145-01 The contribution of GeneXpert MTB/RIF in the diagnosis of extra-pulmonary tuberculosis

I Bouzouita,[1] A Ghariani,[1,2] H Draoui,[1] L Essalah,[1] N Marzouk,[1] E Mehiri,[1,2] L Slim-Saidi,[1,2] [1]National Reference Laboratory for Mycobacteria, A. Mami Pneumology Hospital, Ariana, Tunisia, [2]University of Monastir, Faculty of Pharmacy, Monastir, Tunisia. e-mail: leilaslimsaidi@gmail.com

Background: The extrapulmonary-tuberculosis (EP-TB) constitutes the most frequent tuberculosis (TB) form in Tunisia. This form represents 60.0% of the total of TB cases recorded in the country. The diagnosis of EP-TB is problematic due to the paucibacillary nature of extrapulmonary-samples. In this study, we evaluated the contribution of GeneXpert MTB/RIF (Cepheid, USA) in the diagnosis of EP-TB over 6 years.
Methods: During 2013-2018, 958 extrapulmonary specimens were tested by GeneXpert MTB/RIF at the National Reference Laboratory for Mycobacteria in Ariana, Tunisia: lymph nodes (425), pleural liquid and pleural biopsies (171), cerebrospinal fluids (113), osteoarticular and disco vertebral specimens (66), abscesses

(81), gastrointestinal specimens (38) and other extrapulmonary samples (64). The results found by GeneXpert were compared with microscopy and culture.

Results: Among the 958 extrapulmonary samples tested, 439 (45.8%) were found to be positive by microscopy, and/or culture, and/or GeneXpert. The GeneXpert was positive for 371 EP samples (84.5%) and 8 cases were found to be resistant to rifampicin.

The positivity of GeneXpert was in line with the microscopy and/or culture for 224 EP samples (51.0%).

Among the EP-TB cases, 259 (59.0%) were negative by microscopy but were positive by GeneXpert and 147 EP-TB cases (33.4%) were detected only using the Xpert MTB/RIF.

Sixty-five samples (14.8%) confirmed to be positive by microscopy and/or culture, were negative by GeneXpert. The Xpert detected 93.0% of lymphadenitis TB cases, 89.7% of abscesses TB and 86.3% of meningitis TB cases. However, this molecular tool revealed only 51.7% of pleural TB cases.

Conclusions: We showed in this study that one third of EP-TB cases found in the NRL for mycobacteria in Tunisia, was detected owing to the Xpert MTB/RIF. This tool constitutes a very useful method for the rapid diagnosis of EP-TB especially lymphadenitis and meningitis TB and TB abscesses.

E-POSTER SESSION (EP)

EP-06-C13 How are we doing?: tobacco control compliance post regulations

EP-06-150-01 Comparison of undercover investigation results on illegal smoking in public areas in Beijing, 2016-2018

J Duan,[1] S Wu,[2] S Huang,[3] Y Huang,[1] X Zeng,[4] [1]Beijing Center for Disease Prevention and Control, Tobacco Control Office, Beijing, China, [2]Beijing Health Commission, Health Promotion Office, Beijing, China, [3]Huilan Think-Tank, Data Analysis, Beijing, China, [4]Beijing Center for Disease Prevention and Control, CDC, Beijing, China.
e-mail: cdcdjl@126.com

Background: Beijing Smoking Control Regulations (the Regulations) took effect in 2015. Smoking is prohibited in indoor public places, workplaces and public transportation. In order to evaluate the implementation of the smoking control in public places in the past years, we carried this study out to analyze tobacco control effect in some key places.
Methods: During the past 3 years (2016-2018), we invited the third party using field observation method every winter (Oct-Dec) to do undercover observations of smoking phenomenon in 8 public areas (the government agencies, medical institutions, office buildings, hotels, restaurants, KTV, internet cafe, long-distance bus station) and taxi's in Beijing. By analyzing and comparing the incidence of illegal smoking from 2016 to 2018, we evaluated the effects of tobacco control in public places in Beijing.
Results: In 2018, we collected data from 1214 public sites, and the illegal smoking rate was 4.9%, which decreased 39.5% compared with in 2017 (8.1%) and 71.3% in 2016 (17.1%). The places where people were found smoking accounted for 0.4%, decreased 73.3% compared with in 2016 (1.5%). The number of places with indoor containers for soot was 1.2%, dropped 47.6% compared with in 2016 (2.3%). Cigarette butts were found in 4.8% places, reduced 69.8% from 2016 (15.9%). The top three places with violations in 2018 were internet cafes (17.6%), office buildings (8.3%) and hostels (7.8%). From 2016 to 2018, the top three places that illegal smoking rate reduced were KTV (87.5%), restaurants (83.2%) and office buildings (71.5%). Smoke could be smelled in 2.7% of taxis, and 4.5%of taxis weren´t forbidden smoking.
Conclusions: Illegal smoking in public places in Beijing has been significantly reduced, and the effect of the Regulations is remarkable. Although the tobacco control effect of office buildings, internet cafes, KTV and taxis has been greatly improved, the supervision and law enforcement should be further strengthened.

EP-06-151-01 Increasing compliance with smoke-free legislation in Bali, Indonesia: the importance of other tobacco control policies

K Suarjana,[1] MK Duana,[2] WG Artawan,[1] H Mulyawan,[1] T Singh Bam,[3] [1]Udayana University, Public Health, Denpasar, Indonesia, [2]Udayana University, Udayana Central, Denpasar, Indonesia, [3]The Union Asia Pasific, Tobacco Control, Singapore, Singapore.
e-mail: suarjana@unud.ac.id

Background: Since 2011, Bali Province has implemented smoke-free legislation (*Kawasan Tanpa Rokok*). Factors such as community education, sustainable enforcement, and presence of other tobacco control policies could determine the compliance with this legislation. The study aims to describe the trend of compliance with the smoke-free legislation and its association with the presence of other tobacco control policies.
Methods: We conducted a serial survey to assess the trend of compliance at all smoke-free venues including health facilities, schools, worship places, children playgrounds, work places and public places. We involved 1100 smoke-free venues or 1400 building in average in each period, with total of 7700 smoke-free venues were observed in 7 periods of study. Sample were selected using proportional probability to size. Data were collected six monthlies (semester) through observation using check-list.
Results: The study succeeded to observe 7700 smoke-free venues. The compliance was 11.8% on second semester of 2013 as the baseline. During 2014 - 2015, all 9 districts in Bali have implemented district level smoke-free legislation. Moreover, in the middle of 2014, the Ministry of Health also implemented Pictorial Health Warning regulation. Hence, the compliance then increased significantly from 17,2% (first semester of 2014) to 60% (second semester of 2015). Increasing trend continued slightly in 2016 (70,6%) and in 2017 (74,3%). Meanwhile, in 2016 one of district (*Klungkung*) also implemented outdoor tobacco advertisement ban legislation and then had better compliance compare to other districts in Bali.
Conclusions: The compliance with Bali smoke-free legislation remains suboptimal, despite showed increasing trends over time. The presence of other tobacco control policies, either at local or national level could make the people more potentially exposed to tobacco control program, increase their awareness and their compliance eventually.

EP-06-152-01 Analysis of the influence of law enforcement on tobacco control in Beijing, Tianjin and Shijiazhuang on public health consciousness and behavior

X Zeng,[1] J Duan,[2] Y Huang,[2] [1]Beijing Center for Disease Prevention and Control, Disease Prevention and Control, Beijing, China, [2]Beijing Center for Disease Prevention and Control, Tobacco Control Office, Beijing, China.
e-mail: hyyshero@126.com

Background: To analyze the impact of the implementation of tobacco control laws and regulations in Beijing, Tianjin and Shijiazhuang (BTS) on the public´s awareness of their health rights, expectations of tobacco control laws and regulations, and willingness to quit smoking, and to evaluate the law enforcement effects in the three cities.
Methods: From July to October 2018, an online questionnaire survey was conducted on the public in BTS. The questionnaire was released on the news client channels and a survey platform with more than 6 million users, and we invited and motivated the residents of BTS to participate in the survey by sending links randomly and setting gifts for the respondents, and collected 17,230 effective questionnaires.
Results: Most of people in BTS chose that "the operators and managers of the venues should stop the smokers when found someone smoked in the no-smoking place", with the proportion of 75.8%, 45.0%, 52.1%, respectively; followed by "I can discourage smokers from smoking". Public generally believed that "enhancing the supervision of comprehensive smoking bans in public places", "increasing the penalties for smoking personnel/institutions in public places", and "strengthening the propaganda of tobacco control" can better play the role of regulations/regulations; most of public in Beijing(67.2%) and Shijiazhuang(40.5%) chose enhancing the supervision; while more Tianjin netizens(37.8%) chose strengthening the propaganda. 58.3% of smokers in Beijing chose to "really willing/consider to quit smoking", followed by Shijiazhuang (57.4%) and Tianjin (46.4%).
Conclusions: The public in BTS have a clear understanding of their rights empowered by smoking bans, and expressed different requirements for the implementation of local tobacco control laws and regulations, and smokers have high willingness to quit smoking. Therefore, it is necessary to strengthen law enforcement, expand the coverage of popularization of law, continuously improve the smoking cessation service, and help the public to develop a healthy lifestyle.

EP-06-153-01 Strengthen implementation of graphic health warnings and increase the size of GHW on tobacco products in Bangladesh through advocacy, capacity building and monitoring

MB Rahman,[1,2] SH Patwary,[1,3] F Zaman,[1] M Mohi Uddin,[1] BR Das,[1] [1]Dhaka International University, Tobacco Control and Research Cell, Dhaka, Bangladesh, [2]Dhaka International University, Department of Business Administration, Dhaka, Bangladesh, [3]Government of the Peoples Republic of Bangladesh, Bangladesh National Parliament, Dhaka, Bangladesh.
e-mail: shameemlaw@hotmail.com

Background and challenges to implementation: Graphic Health Warnings (GHW) has been implemented from 19 March 2016. After successfully completed the project from 1st May 2016 again started it from 1st September 2017. It was much challenged but implemented the issue with the limited resources with highly committed team. Smaller round shape, different size of pack are the major challenge even paper, round shape tin/plastic casket/box with attach additional paper, poly packet are using for packaging.
Intervention or response: The major mission of the projects were, building capacity of enforcement officials, increase the size of GHWs , introducing uniform packaging and monitoring the evaluation. Several strategies were followed that are- Policy and follow-up meetings were conducted with different stake holders. Organized 5 (Five) divisional workshop with all district levels high govt. officials under each division. Conducted research and organized public support events. Conduct one assessment survey for need of uniform packaging. Organized two days workshop with IGTC, Bloomberg School of Public Health, John Hopkins University for update the Research Protocol for Compliance Monitoring.
Results and lessons learnt: 16 Parliament Members issued endorsement letter, two govt. organization and 5 (Five) Divisional Commissioner issued order for monitoring the implementation and sensitized 200 Government high officials. 15 human chain, awareness and signature campaign were organized and collect 2000 signature. Developed a model of uniform pack and 5 cycle of compliance monitoring was completed. Story was developed and circulates by popular news channel Jamuna Television and in the website and facebook page of The Union.
Conclusions and key recommendations: Implementation of GHWs has increased but sales single stick is still great barrier. Smokeless tobacco and *Bidi* has still challenged because un-regulated even government cannot trace; most of the SLT industry are illegal and does not provide accurate address. So, government should take initiative to stop sales single stick and should ban illegal company and enact uniform packaging model for effective implementation.

EP-06-154-01 Assessment of health warning label compliance on bidi packages in five states in India

S Saraf,[1] K Welding,[1] JE Cohen,[1] K Smith,[2] [1]Johns Hopkins Bloomberg School of Public Health, Institute of Global Tobacco Control, Baltimore, MD, United States of America, [2]Johns Hopkins Bloomberg School of Public Health, Health, Behavior and Society, Baltimore, MD, United States of America. e-mail: ssaraf3@jhu.edu

Background: Bidis are the most commonly smoked tobacco product in India. They contain three to five times the amount of nicotine as a regular cigarette, and are relatively inexpensive. The health warning labels (HWLs) on tobacco products in India must cover 85% on both sides of the pack, of which 60% should be pictorial health warning and 25% should be textual health warning; be located at the top (widest) edge of the pack; and must display specific features such as text in a contrasting background color, full color graphic and a complete HWL (label elements). This study examines the level of compliance of HWLs on bidi packages with the Indian law.
Methods: In 2017, a systematic protocol was used to collect unique bidi packages from 5 states: Maharashtra, Uttar Pradesh, Assam, Rajasthan, and Karnataka. Within each state, five towns were selected across three different population tiers, one semi-urban and two rural. To assess compliance, we used 3 indicators: health warning size, location, and label elements.
Results: 71 state-unique bidi packages were purchased. 39 did not have appropriate in-rotation HWLs. Of the 32 that had a correct HWL, 17 packs had either one or two HWLs obstructed by product wrapping. Three packs had the HWL positioned at the correct location; 1 pack met the 85% coverage requirement; and, 2 packs had the appropriate label elements. Overall, no pack complied with all three compliance indicators. There were issues with the printing quality of the graphics; 69% (n=22) packs had HWL images that were either blurry, faded or had heavy tint, making the HWL appear unclear.
Conclusions: Findings from the study suggest that bidi manufacturers are not complying with India's HWL law. Despite Indian law aligns well with the FCTC, this limited implementation undermines the potential health benefits of HWLs.

EP-06-156-01 Taxation of all tobacco products at the highest rate under the new Goods & Service Tax (GST) regime through high-level political & policy advocacy

B Mukhopadhyay,[1] [1]Voluntary Health Association of India (VHAI), Tobacco Control, Delhi, India.
e-mail: bhavna@vhai.org

Background and challenges to implementation: Tobacco products are globally recognized as "sin goods" on account of their serious adverse impact on public health. Higher taxes discourage Tobacco use and serve as additional revenue for countries.
Goods and Services Tax (GST) is a new system of taxation in India which will replace the all indirect taxes and simplify the taxation procedure, an opportunity for Tobacco to be taxed at the highest rate. India has the second largest number of tobacco users (275 million or 35% of all adults in India) in the world - of these at least 1 million die every year from tobacco related diseases.
Article 6 of the FCTC enlists price and tax measures as an essential strategy for reducing demand for tobacco products.
Intervention or response: VHAI team sensitized all senior policy makers, in the Finance ministry , including the GST council members- Finance Minister (FM) and key state FMs, with Evidence and research based representations. **1200 letters were sent** and 40 one to one meetings held to advocate for ALL tobacco products (including Bidi) to be taxed at the highest GST rate. Arguments were tweaked on basis of parliamentary sessions, political changes, tracking the GST council meetings and Tobacco industry interference.
Results and lessons learnt: Tobacco products got taxed at the highest demerit rate of 28% + Cess. For Cigarettes, the cess was further increased.
Conclusions and key recommendations: Keeping the tobacco products at the highest GST rate - 28 percent plus higher cess will have a major impact on the prices of the tobacco products.

EP-06-157-01 Initiative to address smoking dependence and promote smoking cessation in Georgia

N Maglakelidze,[1] M Maglakelidze,[2] L Sturua,[1] I Chkhaidze,[3] T Maglakelidze,[3] [1]National Center for Disease Control and Public Health of Georgia, Noncommunicable Diseases, Tbilisi, Georgia, [2]Institute for Advanced Sustainable Studies, n/a, Potsdam, Germany, [3]Georgian Respiratory Association, n/a, Tbilisi, Georgia.
e-mail: n.maglak@gmail.com

Background and challenges to implementation: High smoking prevalence is a significant problem in Georgia. The set of new tobacco control regulations include range of demand and supply reduction measures on tobacco products in order to address tobacco related health and economic burden. This created a need for

comprehensive cessation support for the smokers who constitute one third of the population. Practically non-existing cessation infrastructure was identified as a major challenge to address.

Intervention or response: The project aim was to strengthen existing smoking cessation infrastructure in Georgia through creating a national smoking cessation policy framework by developing comprehensive smoking cessation national strategy and guidelines, building healthcare professional capacity to provide smoking cessation support and increasing access to treatment for tobacco dependence.

Initial situational analysis was conducted based on which national cessation strategy and cessation clinical guidelines were developed. In targeted regions 300 PHC specialists were trained in delivering smoking cessation brief interventions and specialized tobacco dependency treatment centers were piloted.

Results and lessons learnt: As a result Georgia has:

- A national cessation strategy that is expected to be approved by Ministerial Resolution, with focus on primary care, mandatory recording, brief advice
- Cessation guidelines
- Begun to train trainers and healthcare workers in cessation
- Efforts to include medications in Essential Medicines List
- Efforts to increase awareness in opinion leaders and HCWs

Conclusions and key recommendations: Smoking cessation is an integral part of comprehensive tobacco control measures and it is important to integrate these services in existing healthcare systems. it is recommended to conduct initial situational analysis to facilitate the planning process of building cessation infrastructure and to develop a mid-term cessation strategy. Brief advice should be part of the essential list of interventions on primary healthcare level as one of the most cost-effective measures, especially in resource constrained settings.

EP-06-158-01 Navigating the legislative process in advancing tobacco control: a country perspective -Georgia

L Sturua,[1] N Maglakelidze,[1] A Gamkrelidze,[2] A Zoidze,[3] [1]National Center for Disease Control and Public Health of Georgia, Noncommunicable Diseases, Tbilisi, Georgia, [2]National Center for Disease Control and Public Health of Georgia, n/a, Tbilisi, Georgia, [3]Parliament of Georgia, Health and Social Affairs Committee, Tbilisi, Georgia. e-mail: lela.sturua@ncdc.ge

Background and challenges to implementation: One third of Georgian population are smokers which has a detrimental effect on health and economic development of the country. 2.4% of annual GDP is spent on direct and indirect costs related to smoking. Georgia is a Party to the WHO FCTC since 2006 but only few of the international tobacco control obligations were met. After several futile attempts to pass a comprehensive legislative initiative it was clear that innovative approaches to advance the policies were necessary.

Intervention or response: In 2016-2017 Georgia mobilized for a breakthrough in tobacco control. The measures taken to mobilize support for the policy change include:

- Putting health coalition together under the leadership of the Parliamentary Committee of Healthcare and Social Issues
- Opportunistic and strong public communication
- Presenting the scientific evidence specific for the country
- Exposing tobacco industry: transparent, open and highly public debate with tobacco industry reps and business associations
- Timely support from WHO and FCTC Secretariat, Bloomberg Philanthropies
- Trojan horse tactics: "converting" local tobacco manufacturers

Results and lessons learnt: As a result a so called "new generation" tobacco control legislation was passed by the Parliament of Georgia in 2017. This success is due to convergence of factors such strong coalition, solid scientific evidence, strong political will and emergence of policy advocates within the Parliament.

Conclusions and key recommendations: Georgia case study is a clear example of how strong coalitions and outstanding leadership can lead to the desirable policy changes. To do so it is recommended to be equipped with strong scientific evidence and use every opportunity to interact and communicate with all stakeholders, engage NGOs and CSOs, communicate with public in an open and transparent manner, instigate ownership and encourage individual parliament members to fight alongside.

EP-07-C6 TB in pregnancy: optimising diagnosis and treatment

EP-07-159-01 Treatment of latent tuberculosis infection among pregnant or post-partum women with HIV: uptake of World Health Organization policy in 38 high-burden TB-HIV countries

T DeAtley,[1] A Baddeley,[2] P Werner,[3] A Kanchar,[2] D Falzon,[2] M Zignol,[2] M Rangaka,[4] [1]Brown University, Behavioral and Social Sciences, Providence, RI, United States of America, [2]World Health Organisation, Global TB Programme, Geneva, Switzerland, [3]McGill University, Political Science, Montreal, QC, Canada, [4]University College London (UCL), Institute of Global Health, London, United Kingdom. e-mail: teresa_deatley@brown.edu

Background: Tuberculosis disproportionately affects women of reproductive age with serious consequences to both the mother and the child. The World Health Organization (WHO) recommends tuberculosis preventive treatment (TPT) to people living with HIV, including for pregnant/postpartum women. Uptake and coverage of this policy recommendation in reproductive health services is unclear. We did a policy review to assess the uptake of TPT policy in pregnant/postpartum HIV-infected women in 38 WHO high burden HIV/TB countries.
Methods: A systematic policy review of latent tuberculosis infection (LTBI) treatment and reported practice for pregnant/postpartum women with HIV. Data sources for policy recommendations included TB national guidelines and HIV/AIDS/ART national guidelines, augmented by results from a previous survey on policy uptake held at the WHO. Policy recommendations assessed were in line with those in the WHO's *2018 Updated and Consolidated Guidelines for Programmatic Management for LTBI*.
Results: Uptake of WHO policy to provide TB preventive therapy among women with HIV accessing reproductive health services was moderate. 63% (24 of 38 countries included in this review) provided at least one clinical guideline or policy recommendation on the treatment and management of LTBI among pregnant/postpartum women living with HIV. There was considerable difference as to the stages in pregnancy that TPT should be provided. Seventeen (45%) countries provided clinical monitoring recommendations for pregnant and postpartum women. Data sources did not report coverage (% eligible treated).
Conclusions: There is moderate uptake of TPT policy for pregnant/postpartum women with HIV. However, coverage remains unclear. Failure to provide TPT is a missed opportunity for TB prevention. Conflicting evidence on adverse pregnancy outcomes of TPT may affect implementation. National programmes should scale up current WHO recommendations, ensuring strengthened capacity to provide TPT and adequate measures for effective monitoring of coverage, timing of TPT and for early detection and management of adverse events.

EP-07-160-01 Assessing TB-related knowledge and stigma and associated risk factors among pregnant women in low-resource settings of Pune, India

S Mehta,[1] M Murrill,[1] N Suryavanshi,[1,2] R Bhosale,[3] S Naik,[3] N Patil,[2] A Gupta,[4] J Mathad,[5] R Shivakoti,[6] M Alexander,[7] [1]Johns Hopkins University School of Medicine, Center for Clinical Global Health Education, Baltimore, MD, United States of America, [2]Byramjee-Jeejeebhoy Government Medical College, Johns Hopkins University Clinical Research Site, Pune, India, [3]Byramjee-Jeejeebhoy Government Medical College, Department of Obstetrics and Gynaecology, Pune, India, [4]Johns Hopkins School of Medicine, Center for Clinical Global Health Education, Baltimore, MD, United States of America, [5]Weill Cornell Medical College, Department of Obstetrics and Gynaecology, New York City, NY, United States of America, [6]Columbia University Mailman School of Public Health, Epidemiology, New York City, NY, United States of America, [7]Byramjee Jeejeebhoy Government Medical College, Johns Hopkins University Clinical Research Site, Pune, India. e-mail: mehtashivani4@gmail.com

Background: Pregnant women have a high risk of tuberculosis (TB) disease, but TB knowledge and stigma have rarely been investigated in this population. We assessed the overall prevalence of TB-related self-stigma and knowledge among pregnant women at a government hospital in India. We also determined factors associated with TB related self-stigma and knowledge.
Methods: We conducted a prospective cohort study of pregnancy and TB immunology between 2016-2019. At enrollment, a semi-structured TB knowledge and attitude questionnaire, adapted from a recent TB knowledge, attitude, and practice survey guide, was administered to 202 pregnant women attending an antenatal clinic at Byramjee Jeejeebhoy Government Medical College (BJGMC) in Pune, India. Baseline information including demographics, HIV status, TB knowledge (6 questions) and TB-related self-stigma (2 questions), was summarized using descriptive statistics (Table). Based on responses, patients were categorized as having a stigmatizing attitude towards TB (score< 2) and inappropriate knowledge (score< 6). Univariable and multivariable logistic regression models were fit to investigate risk factors for stigmatizing attitude and inappropriate TB knowledge.
Results: The median age of the participants was 23 years (IQR 21-26). Twenty-five percent (n=51) were HIV positive, 76% (n=153) had a monthly income below Rs.10255 and 25% (n=50) were either illiterate or only had a primary school education. Forty-four percent (n=89) had a stigmatizing attitude towards TB while 64% (n=129) had inappropriate knowledge regarding

TB. When adjusting for age, income, education, and HIV status, multivariable regression showed positive significant association of inappropriate TB knowledge with stigmatizing attitude (OR=17.61; 7.34-42.26).
Conclusions: The majority of pregnant women in this study had inappropriate TB knowledge, which was associated with stigmatizing attitudes. TB-endemic countries, like India, should integrate TB education interventions into routine antenatal care. Greater efforts on increasing TB knowledge through education may decrease stigma, which can ultimately prevent delayed diagnosis and decrease TB morbidity/mortality in mothers and infants.

Survey Questions		Total n = 202, %
Knowledge Question 1	TB is caused by germs called bacteria	190 (94)
Knowledge Question 2	TB is spread from one person to another through the air	199 (99)
Knowledge Question 3	TB can be transmitted through the blood	130 (64)
Knowledge Question 4	HIV-infected persona have low risk of developing TB	102 (51)
Knowledge Question 5	TB disease can be cured	183 (91)
Knowledge Question 6	TB can affect other parts of the body besides the lung	157 (78)
Stigma Question 1	Do you think it is shameful to have TB?	123 (61)
Stigma Question 2	If you were to develop TB disease, would you hide the disease from others?	144 (71)

[Frequency of Correct Responses for Knowledge and Attitude Survey Questions]

EP-07-161-01 Does treatment of infertile women with probable genital tuberculosis improve fertility outcome?

S Naik,[1] A Chandanwale,[2] D Kadam,[3] P Sambarey,[1] G Dhumal,[4] A Deluca,[5] D Jain,[4] A Gupta,[5] V Mave,[4]
[1]B.J. Government Medical College, Obstetrics and Gynecology, Pune, India, [2]J.J. Government Medical College, Orthopedics, Mumbai, India, [3]B.J. Government Medical College, Medicine, Pune, India, [4]B.J. Government Medical College, CTU, Pune, India, [5]Johns Hopkins Bloomberg School of Public Health, CCGHE, Baltimore, MD, United States of America. e-mail: shilunnaik@yahoo.co.in

Background: In India, 5-13% of female infertility is due to genital tuberculosis (GTB). Early diagnosis and initiation of treatment may improve fertility outcomes. However, most patients are diagnosed late due to lack of symptoms. Therefore, we evaluated an intensified diagnostic approach for early diagnosis and treatment of GTB cases among women with infertility in India.
Methods: Between April 2016 and June 2018 consenting women seeking infertility care underwent an intensified diagnostic approach for GTB, including thorough history of present or past TB, clinical evaluation, ultrasonography, tuberculin skin test (TST), and Erythrocyte Sedimentation Rate (ESR). Women with clinical findings consistent with GTB, positive TST and ESR (TST $\geq$ 10 mm and ESR $\geq$ 20) were further evaluated using laparohysteroscopy and tissue sampling for microbiology especially TB-PCR. GTB cases were defined as likely (microbiologically confirmed and probable GTB) and unlikely GTB (possible and no GTB). Using descriptive statistics, clinical and laboratory characteristics were compared. Fertility outcome was assessed among likely GTB group initiated on anti-TB treatment (ATT).
Results: Of 185 women seeking infertility care, likely GTB was identified among 29 (15.7%) and unlikely GTB in 156 (84.3%). Of 29 likely GTB, 6 (20.7%) had confirmed TB and 23 (79.3%) were probable GTB. Compared to unlikely GTB group, likely GTB cases had past history of TB ($p < 0.001$); positive TST ($p=0.002$) and elevated ESR ($p=0.001$). Among the likely TB group, all 6 confirmed GTB patients were started on ATT and 2 (33.3%) conceived. Of 5 probable GTB, started on ATT, 3 (60%) conceived.
Conclusions: Approximately 1/6th of women seeking infertility care met the criteria for likely GTB. Among probable GTB group, there is higher conception rate after ATT initiation. This indicates the utility of intensified approach in identifying probable GTB among infertile women, in high TB burden countries such as India.

EP-07-163-01 Inappropriate postpartum weight loss may predict development of active TB: findings from a cohort study in Pune, India

M Alexander,[1] R Bhosale,[2] S Naik,[2] N Gupte,[1,3] D Jain,[1] N Patil,[1] N Pradhan,[1] V Mave,[1] A Gupta,[1,4] J Mathad,[1,5]
[1]BJ Medical College/John Hopkins University, Clinical Trial Unit, Pune, India, [2]BJ Government Medical College, Dept. of Obstetrics and Gynecology, Pune, India, [3]John Hopkins University, Johns Hopkins School of Medicine, Baltimore, MD, United States of America, [4]JH School of Medicine, Infectious Diseases, Baltimore, MD, United States of America, [5]Weill Cornell Medical College, Center for Global Health, New York, NY, United States of America.
e-mail: mallikaalexander@gmail.com

Background: Active TB develops mostly in the early postpartum period. Symptoms are atypical in this population; expected weight dynamics discourage use of weight loss as TB screen. The goal of this study was to identify predictors of active TB in postpartum women.
Methods: We conducted a longitudinal study of HIV+ and HIV- pregnant women with TB infection (TBI) in Pune, India. Women were enrolled during pregnancy and followed postpartum. At each visit, we administered WHO TB symptom screen, including inappropriate weight loss (>5% in HIV+, >10% in HIV-). Women with positive screen underwent sputum Gene Xpert/

culture, chest Xray and abdominal ultrasonography. Poisson regression was used to assess independent risk factors.

Results: Overall, 227 women, 78 HIV+, (45% IGRA+) 149 HIV- (85% IGRA+), none on TB prophylaxis, completed at least one follow-up visit. All HIV+ were on ART for a median of 9 months (median CD4: 447 (342 - 632), viral load < 40 (0 - 156)). Significantly more HIV+ women reported TB symptoms (58% vs. 39%, p=0.01) during follow up visits. 35 HIV+ and 30 HIV- women were investigated for TB; 9 (14%) were diagnosed with active TB, 3 (33%) within 90 days postpartum. TB incidence rate was 50/1000PY (16 - 115) for HIV+ and 18/1000PY (5 - 46) for HIV- women.

Of 218 women screened postpartum, 74 (34%) had inappropriate weight loss (46% HIV+ vs 31% HIV-, p=0.03), which was the most common presenting symptom among the 8 postpartum TB cases (63%). In multivariate analysis, incident TB risk was 3 times higher in women with significant weight loss (p=0.18). Higher mid-upper arm circumference was protective of TB (IRR 0.56 (0.32 - 0.97), p:0.04) while TB exposure increased risk (IRR 6.0 (1.7 - 50.5, p=0.01)).

Conclusions: Among pregnant women with LTBI, inappropriate weight loss during postpartum was a sensitive tool in detecting active TB.

EP-07-164-01 Performance of QuantiFERON-TB Gold in Tube (QFT-GIT) and QuantiFERON-TB Gold Plus (QFT-Plus) for detection of Mycobacterium tuberculosis infection in pregnant women in India

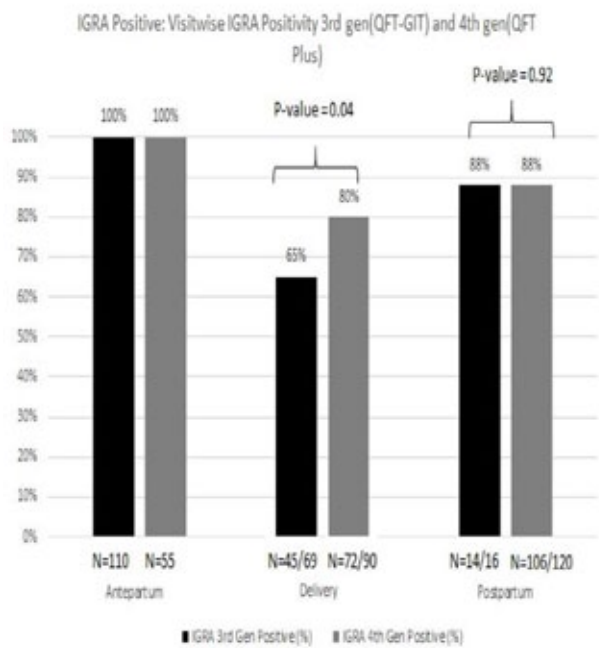
V Kulkarni,[1] R Bhosale,[2] D Jain,[1] P Deshpande,[1] S Naik,[2] M Alexander,[1] N Patil,[1] N Gupte,[1,3] A Gupta,[3] JS Mathad,[4] [1]Byramjee-Jeejeebhoy Government Medical College-Johns Hopkins University Clinical Research Site, Clinical Trial Unit, Pune, India, [2]Byramjee-Jeejeebhoy Government Medical College, Obstetrics & Gynecology, Pune, India, [3]Johns Hopkins University School of Medicine, Medicine, Baltimore, MD, United States of America, [4]Weill Cornell Medical College, Medicine, New York, NY, United States of America.
e-mail: vandanakulkarni_5@hotmail.com

Background: Pregnant women have twice the risk of tuberculosis (TB) intrapartum and immediately postpartum. Best practices for TB screening in this population are unknown as immune changes compromise both symptom screen and latent TB tests. The study's objective was to determine if 4th generation QuantiFERON® Gold Plus (QFT-Plus) which assesses both CD4 and CD8 responses, is more reliable than 3rd generation QuantiFERON® Gold In-tube (QFT-GIT), which only assesses CD4 responses.

Methods: We conducted longitudinal cohort study of HIV-infected and uninfected pregnant women with TB infection (TBI) at a government hospital in Pune, India. Women with TBI (i.e. positive QFT-GIT or QFT-Plus) at entry were enrolled with repeat testing at delivery and 6 months postpartum. The proportion of TB infection was cross-sectionally compared between both tests at each timepoint using univariable analysis. We also compared longitudinal test performance in subset tested only by QFT-Plus at all time points.

Results: We enrolled 165 women with TBI. During pregnancy, 110 (67%) were tested with QFT-GIT and 55 (33%) with QFT-Plus. Compared to QFT-GIT, QFT-Plus returned higher proportion of positive results at delivery (80% vs. 65%, p= 0.04) though no difference at 6 months postpartum (Figure). The change in proportion positive between antepartum and delivery was significant for QFT-GIT (p= 0.04) but not QFT-Plus. Proportion positive recovered postpartum with both assays. The longitudinal subset of women tested by QFT-Plus showed no significant difference in proportion of TBI at all timepoints (84% vs 66% vs 68%, p=>0.61).

Conclusions: The QFT-Plus assay showed consistent performance across the stages of pregnancy suggesting that: (1) CD8 cells do not decrease as much as CD4 cells during pregnancy; and (2) 4th generation QFT-Plus may be more reliable compared to 3rd generation QFT-GIT, especially at delivery. TB endemic countries should consider integrating QFT-Plus into antenatal care to provide targeted TB prevention therapy.



[IGRA Positive: Visitwise IGRA positivity 3rd gen (QFT-GIT) and 4th gen (QFT-Plus)]

EP-07-165-01 Prevalence and cost of systematic screening for pulmonary tuberculosis among pregnant women in Cotonou, Benin

M Adjobimey,[1] S Ade,[2] P Wachinou,[3] M Esse,[4] L Yaha,[5] W Bekou,[4] JR Campbell,[6] G Agodokpessi,[3] D Affolabi,[7] C Merle,[8] [1]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Prevention, Cotonou, Benin, [2]Centre National Hospitalier Universitaire Borgou, Pneumologie, Parakou, Benin, [3]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Pneumologie, Cotonou, Benin, [4]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Statistique, Cotonou, Benin, [5]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Recherche, Cotonou, Benin, [6]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [7]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Bacteriologie, Cotonou, Benin, [8]World Health Organisation, Special Programme for Research and Training in Tropical Diseases, Geneva, Switzerland.
e-mail: menoladjobi@yahoo.fr

Background: The prevalence of tuberculosis (TB) among women in Benin is 25 per 100,000, but it is known that pregnant women are at an elevated risk for TB. In Benin, the prevalence of TB in pregnant women is unknown and, like many other low-income countries, there is no specific screening strategy for detecting TB among these women. The objectives of this study were to estimate the prevalence of TB in pregnant women and the cost of systematic TB screening at routine prenatal appointments in this at-risk population in Cotonou, Benin.
Methods: This was a quantitative cross-sectional study combined with a cost evaluation. Pregnant women were consecutively recruited in eight prenatal consultation centers in Cotonou from April 2017 to April 2018. All pregnant women symptomatic with cough gave sputum to be tested with GeneXpert. The cost analysis was conducted from a government perspective. Cost elements were collected prospectively during the study in 2017 USD. The costs collected were related to training for the midwives, time to perform symptom screening, monitoring of the centers for new sputum samples and their transport to the central laboratory, and GeneXpert.
Results: In total, 4,070 pregnant women were screened for TB symptoms during the study. Among those screened, 94 (2.3%) were symptomatic with cough. Among those symptomatic, HIV prevalence was 5.3% and mean (SD) age was 26 (5) years. Overall, TB was detected via GeneXpert in 2 (0.05%) women screened, resulting in a TB prevalence of 49 per 100,000. The additional cost for TB symptom screening per pregnant woman was $0.71 and per TB case detected was $1435.92.
Conclusions: TB prevalence in pregnant women was elevated compared to that of other women in Benin. Systematic TB symptom screening in this population was feasible in Benin, with a low cost per pregnant woman screened.

EP-07-166-01 Experience using new and repurposed rifampicin-resistant TB drugs in five pregnant patients

R Acquah,[1] E Mohr,[1] J Furin,[2] J Hughes,[3] M Loveday,[4] V De Azevedo,[5] V Mudaly,[6] A Reuter,[1] [1]Medecins Sans Frontieres, DR-TB, Khayelitsha, South Africa, [2]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [3]Desmond Tutu TB Centre, Department of Paediatric and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, [4]South African Medical Research Council, Health Systems Research Unit, Durban, South Africa, [5]City of Cape Town Department of Health, Primary Health Care Health Department, Cape Town, South Africa, [6]Western Cape Provincial Department of Health, Health Programmes, Cape Town, South Africa.
e-mail: msfocb-khayelitsha-tbdoc@brussels.msf.org

Background: Tuberculosis (TB) is the leading cause of maternal mortality worldwide, and rifampicin resistant TB (RR-TB) in pregnancy is a neglected health problem. Pregnant women are often excluded from clinical trials, and consequentially the evidence for the use of new and repurposed RR-TB drugs in pregnancy is scarce. We aim to describe our experience of using delamanid, linezolid, and/or bedaquiline in pregnant women with RR-TB.
Methods: Persons diagnosed with RR-TB and exposed to either delamanid, linezolid, and/or bedaquiline during pregnancy from January 2014 to March 2019 in Khayelitsha, South Africa were included in this retrospective file review. We report on drug exposure, pregnancy outcomes, serious adverse events (SAEs), and interim treatment outcomes.
Results: Five patients aged 18-29 years were identified between January 2014 and March 2019 and are summarized in Table 1. All five had confirmed multi-drug resistant tuberculosis with no second line drug resistance and received a new drug either to substitute for an injectable agent, or to make an effective regimen with at least four effective drugs for the mother. The mean drug exposure during pregnancy was 79 (range 7-163) days. There were no reported serious adverse events during the pregnancy or post-partum period (until discharged from TB care or the end of the study period).
Conclusions: There is limited experience with most second-line drugs in pregnancy, with some drugs being contraindicated and others possibly unsafe based on animal studies. While more evidence would be reassuring, the experience in this small group supports improving access to new and repurposed drugs for pregnant women with RR-TB. The inclusion of pregnant women in clinical trials, as well as pregnancy drug registries is vital to ensure evidenced based safe and effective treatment options are available for mothers with RR-TB.

EP-08-C8 Matching people and numbers: role of TB data quality in ending TB

EP-08-167-01 Assessing the timeliness of and underreporting to China's national tuberculosis surveillance systems

T Li,[1] L Yang,[1] X Du,[1] H Guo,[2] SE Smith,[3] A Wang,[3] W Chen,[1] H Zhang,[1] [1]Chinese Center for Disease Control and Prevention, National Center for Tuberculosis Control and Prevention, Beijing, China, [2]US Centers for Disease Control and Prevention, Division of Global Health Protection, Beijing, China, [3]US Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis, Atlanta, GA, United States of America. e-mail: litao1@chinacdc.cn

Background: In 2017, WHO estimated 116,000 (13%) TB cases in China were unknown to the national TB program. Our objective was to have local health departments quantify under-reporting and assess timeliness of reporting TB cases to the national TB surveillance systems: Infectious Disease Reporting System (IDRS) and TB Information Management System (TBIMS) through operationalizing a tool-kit developed by the national TB program.

Methods: This retrospective review includes cases identified in 2016 from six counties each in Guangdong, Henan, Heilongjiang, Jiangsu, Sichuan, and Yunnan provinces. County staff were trained to use the tool-kit to link cases identified from facility-specific health and laboratory information systems with cases reported in IDRS and TBIMS. Underreporting was calculated as the percentage of cases not reported to IDRS or TBIMS. Untimeliness was calculated as the percentage of cases reported to IDRS or TBIMS >24 hours after medical record documentation. Multivariable logistic regression with alpha=0.05 was used to examine factors associated with underreporting.

Results: Of 4,327 pulmonary TB (PTB) cases identified, 366 (8.5%) and 1,238 (28.6%) were not reported to IDRS and TBIMS, respectively (Table). Of 371 extrapulmonary TB (EPTB) cases identified, 139 (37.5%) and 213 (57.4%) were not reported to IDRS and TBIMS, respectively. Yunnan had the highest underreporting to both IDRS (19.9%) and TBIMS (50.9%). Of 171 cases reviewed in IDRS and 170 cases in TBIMS, 12.3% and 6.5%, respectively, were found to be untimely. EPTB, clinically-confirmed PTB, and migrants were statistically more likely to be underreported to both systems.

Conclusions: We found that more than one in four PTB cases were not reported to TBIMS in participating sites. This gap is much larger than the estimated missing TB notifications (13%). We recommend expanding access to TBIMS, including this data matching exercise into county-level routine work, and developing operational guidelines for reporting EPTB.

		Underreported to IDRS		Underreported to TBIMS	
Category	Total TB Cases	n	% (95% CI)	n	% (95% CI)
PTB	4327	366	8.5 (7.6-9.3)	1238	28.6 (27.3-30.0)
EPTB	371	139	37.5 (32.5-42.4)	213	57.4 (52.4-62.7)
Guangdong	819	50	6.1 (4.5-7.7)	283	34.6 (31.3-37.9)
Jiangsu	379	52	13.7 (10.3-17.2)	112	29.6 (25.0-34.3)
Henan	441	33	7.5 (5.0-9.9)	43	9.8 (7.0-12.6)
Heilongjiang	320	6	1.9 (0.4-3.4)	7	2.2 (0.6-3.8)
Sichuan	932	4	0.4 (0.0-0.8)	87	9.3 (7.5-11.2)
Yunnan	1807	360	19.9 (18.1-21.8)	919	50.9 (48.6-53.2)

[Underreporting by type of TB and province to IDRS and TBIMS]

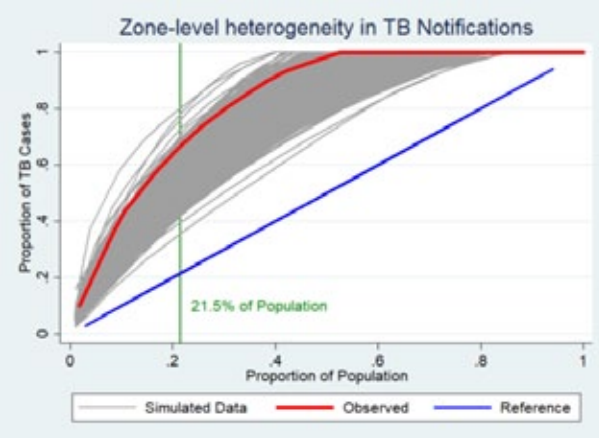
EP-08-168-01 Using spatial heterogeneity of TB notification rates to identify high-risk areas in Kampala, Uganda

K Robsky,[1] PJ Kitonsa,[2] J Mukiibi,[2] O Nakasolya,[2] D Isooba,[2] A Nalutaaya,[2] P Salvatore,[1] E Kendall,[3] A Katamba,[2] D Dowdy,[1,3] [1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America, [2]Makerere University, Clinical Epidemiology and Biostatistics Unit, Kampala, Uganda, [3]Johns Hopkins School of Medicine, Epidemiology, Baltimore, MD, United States of America. e-mail: krobsky1@jhu.edu

Background: TB risk is geographically heterogeneous; this heterogeneity may be useful for targeting case finding activities within high burden areas. We used population-adjusted TB notification rates to identify high risk areas that might be prioritized for case finding activities in a well-defined community within Kampala, Uganda.

Methods: We enrolled adult TB patients living within 32 contiguous zones diagnosed at four local TB Diagnosis and Treatment Units between May 2018 and January 2019. We estimated zone populations with a census, constructed a Poisson distribution of zone-level notification rates (per 100,000 population), and performed 1,000 stochastic simulations to estimate the number of TB cases per zone that might be expected by chance assuming no underlying spatial heterogeneity of TB risk. We compared the observed proportion of TB cases living within zones that constituted the highest-risk 20% of the population to the proportion of simulated notifications occurring in same combined population within the highest-risk simulated zones.

Results: We enrolled 30 cases within the study area (estimated population of 48,780). Zone-level TB notification ranged from 37 per 100,000 population to 331 per 100,000 population; 20 zones reported no TB cases in the study period.



[Zone-level heterogeneity in TB Notifications]

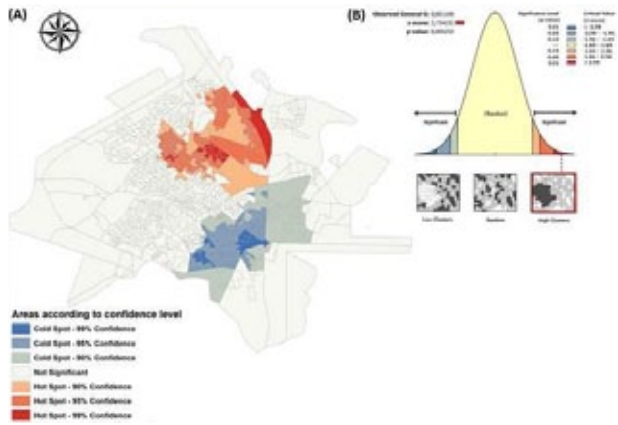
Six zones with the highest notification rate constituted 66.6% (95% confidence interval 47.2-82.7%) of TB cases and 21.5% of the population. In comparison, 53.6% (95% simulation interval 43.3-67.5%) of TB cases fell within the highest-risk 21.5% of the population among simulations that assumed no spatial heterogeneity.
Conclusions: We identified high risk zones using data routinely collected at health facilities and show that it may be possible to detect more than 60% of TB cases by screening 20% of the population, if the spatial distribution of TB risk is stable over time. Geographically prioritized case finding may be an efficient way to detect prevalent TB in urban high-burden settings.

EP-08-169-01 Spatial association of abandonment of tuberculosis treatment and temporal trend of this event in municipality of the interior of São Paulo, Brazil

T Zamboni Berra,[1] LH Arroyo,[2] HL Andrade,[2] AC Vieira Ramos,[2] F Meneguetti Pieri,[2] AA Rêgo de Queiroz,[3] A Rolim Scholze,[2] LL Limirio Souza,[2] RC Fiorati,[4] RA Arcêncio,[1]
[1]University of São Paulo, Ribeirão Preto College Nursing, Ribeirão Preto, SP, Brazil, [2]University of São Paulo, Ribeirão Preto College of Nursing, Ribeirão Preto, SP, Brazil, [3]Federal University of Rio Grande do Norte, Federal University of Rio Grande do Norte, Ribeirão Preto, RN, Brazil, [4]University of São Paulo, Ribeirão Preto Medical School, Ribeirão Preto, SP, Brazil. e-mail: ricardo@eerp.usp.br

Background: To identify areas of spatial association of tuberculosis treatment abandonment and to classify the temporal trend of this event in a municipality in the interior of the state of São Paulo, Brazil.

Methods: An ecological study carried out in Ribeirão Preto, a Brazilian endemic municipality in the state of São Paulo. The population was composed of all TB cases reported TBWeb in the period from 2006 to 2017 who abandoned treatment. The cases of TB were geocoded and the Getis-Ord Gi and Gi * analysis was performed.
The time trend of treatment abandonment in the period was classified using the Prais Winsten technique.
Results: There were 2259 cases of TB reported in the period and 157 cases with cessation of treatment as an outcome, of which 146 were geocoded (93%). Through the technique Getis-Ord Gi and Gi *, it was possible to identify hotspots in the Central, West and North regions and coldspots in the Eastern region. The analysis of the time series in the period showed that the rate of treatment abandonment in the municipality increased (1.6% per year - 95% CI: 0.02 - 3.48).
Conclusions: Areas were identified in the municipality with a spatial association for the abandonment of tuberculosis treatment, while other areas seem to be protection for this event. With the analysis of time series it was possible to identify that the rate of treatment abandonment of tuberculosis is increasing in the municipality during the period under study.
The present work contributes to the identification of vulnerable areas for the abandonment of TB treatment and also indicates that actions need to be improved to advance in terms of the elimination goal of tuberculosis.



[Spatial clustering of treatment abandonment for Tuberculosis, Ribeirão Preto - São Paulo - Brazil]

EP-08-170-01 Feasibility of geotagging of tuberculosis patients notified to national tuberculosis programmes for hotspot identification: early experience from Kolkata, India

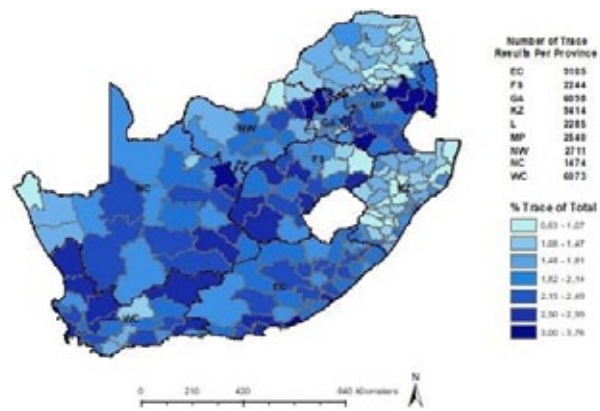
P Shukla,[1] R Swamickan,[2] A Shah,[2] [1]World Health Partners, Health, New Delhi, India, [2]USAID, Health, New Delhi, India. e-mail: prachi@worldhealthpartners.org

Background and challenges to implementation: Tuberculosis (TB) depicts heterogeneous spatial patterns with localised clustering of TB cases either due to ongoing person-to-person transmission or reactivation of latent infection in a community sharing risk factor. Identification of TB hotspots for targeted control activities requires geotagging of either house or neighbourhood of each TB patient detected in a defined area. In this regard, USAID supported Tuberculosis Health Action Learning Initiative (THALI) project by World Health Partners (WHP) in association with West Bengal TB program geotagged TB patients notified in the selected districts of Kolkata, India with aim to understand the process of carrying out geotagging and use of the information in program setting.
Intervention or response: All TB patients notified during July 2018 to March 2019 from 6 districts of Kolkata, were aimed for geotagging. 22 field staff traced the patient address and geotagged the patient´s house using Geo-mapping application built on android tablet during their home visit to the patient. Patient consent was obtained prior to geotagging. The data were used to deduce hotspots using online ArcGIS software.
Results and lessons learnt: 6,640 (95.8%) TB patients were successfully geotagged. Major reasons for failure were patients' hesitation to give consent and lack of internet connectivity in the remote areas. We deduced 46 hot spots with ≥ 9 TB patients falling per KM^2. THALI TB control activities such as active case finding, health camps and sensitization were prioritized in these identified hotspots.
Conclusions and key recommendations: Under project setting it was feasible to geotag the residence of notified TB patients. Considering National notification portal 'NIKSHAY' capturing this information, there is a need for future efforts to effectively use geotag information and prioritize TB control activities.

EP-08-171-01 Spatiotemporal analysis of Xpert MTB/RIF Ultra "trace" laboratory results from South Africa

L Scott,[1] P Ajayi,[1] G Eisenberg,[1] S Ndlovu,[2] P da Silva,[1,2] W Stevens,[1,2] [1]University of the Witwatersrand, Molecular Medicine and Haematology, Johannesburg, South Africa, [2]National Health Laboratory Service, Molecular Medicine and Haematology, Johannesburg, South Africa. e-mail: lesley.scott@wits.ac.za

Background: South Africa commenced the rollout of Xpert MTB/RIF Ultra (Ultra) in October 2017, with ~2.18 million tests performed in the public sector up to March 2019. A result category called 'trace' reports remnants of *Mycobacterium tuberculosis* DNA due to the assays increased sensitivity over Xpert MTB/RIF. Although several controversies presently surround the understanding of 'trace', this study aims to visualise and analyse the temporal trend of trace results in sub-districts across South Africa over a 12-month period.
Methods: National Health Laboratory Service test results were extracted from the central data warehouse and trace results aggregated at sub-district levels (n=213) between March 2018 and February 2019. These were merged with sub-district Geographic Information System (GIS) shapefiles and percentage of total tests calculated. Global Moran's I statistic was used to assess the spatial dependency of trace results across sub-districts and joinpoint regression was used to examine the temporal trends at provincial levels.
Results: A total 2,178,063 Ultra tests were performed and 41,944 (1.93%) reported with 'trace'. Figure 1 shows geographic variability of trace reported across the country, with KwaZulu-Natal Province reporting the highest number of trace results (n=9414), while Mpumalanga Province reporting the highest trace percentage (2.55%) (figure 1). Global Moran's I spatial autocorrelation revealed that observed trace distribution across the sub-districts are not due to random chances (I = 0.348; p-value < 0.000). Mpumalanga Province experienced the most temporal change which peaks in December 2018 (3.5%, p-value< 0.000).



[Spatial Distribution of laboratory 'trace' results in South Africa]

Conclusions: Geospatial mapping of aggregated laboratory results add value to disease surveillance and should be routinely monitored to target health care and implement local responses. The aggregated trace result may indicate hot spots of TB transmission, which requires further investigation for patient care.

EP-08-172-01 Transactional data model to ensure data quality in Nikshay 2.0 - the national information system of India's TB Control Programme

M Mathews,[1] S Achanta,[1] J Jaju,[1] R Ramachandran,[1] M Ray Chaudhury,[2] KS Sachdeva,[3] R Rao,[3] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]Everwell Health Solutions Pvt. Ltd, Nikshay ICT Cell Bangalore, Mumbai, India, [3]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: mathewm@rntcp.org

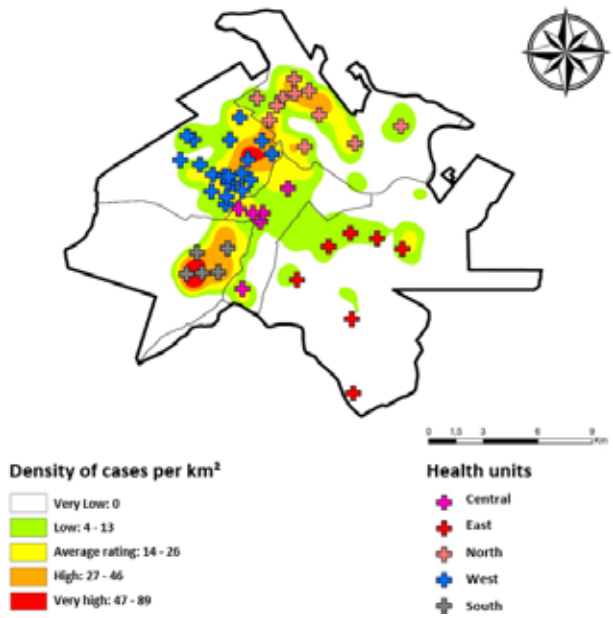
Background and challenges to implementation: Ensuring quality of the data reported to the national surveillance system is critical for programme implementation and interventions. Since 2012, the online surveillance system of the Revised National TB Control Programme of India, Nikshay, reported case-based information. With the expansion of the program in 2016, resulted an explosion in the quantity of information needed. When collecting large data sets as discrete reports, information systems are at risk of accumulating problems of redundancy, invalid data and mismatch. To address this challenge, Nikshay2.0, the second-generation information system was built on the 'Transactional Model'.
Intervention or response: The Transactional Data Model in Nikshay2.0, involves different stakeholders interacting with each other to exchange information. Compared to the reporting model, where a single user reports the complete required data; here specific data elements are fed by different users/devices who generate them to exchange it with other stakeholders; eventually iteratively building the patient record over time. New data is matched up to the related data existing in the system, and checks and balances are embedded to ensure logical fit. Whenever erroneous, duplicate or discordant data gets entered, users will find it difficult to proceed without making the correction. This results in organic data cleaning and auto-validation. Reports are generated by abstracting out necessary elements, either as aggregates or as critical events.
Results and lessons learnt: Since the launch of Nikshay 2.0, about 0.4 million invalid patient records sets have been identified and cleaned. Of these 0.4 million patient records that are de-duplicated, validated and corrected, 50% (n=0.2 million) belong to the year 2018; about 1/10th of the true notifications.
Conclusions and key recommendations: The Transactional Data Model is an organic method to ensure data quality. National TB Programmes of the world may adopt similar methods to ensure data quality.

[Figure showing work flow for auto validation / triangulation of health record elements]

EP-08-173-01 Spatial distribution and temporal trend of tuberculosis in municipality of the interior of the state of São Paulo, Brazil

TZ Berra,[1] IS Assis,[1] DT Santos,[1] LH Arroyo,[1] LLL Souza,[1] AR Scholze,[1] JD Alves,[2] JF Martoreli Júnior,[1] IC Pinto,[1] RA Arcêncio,[1] [1]University of São Paulo, Ribeirão Preto College of Nursing, Ribeirão Preto, SP, Brazil, [2]Federal Institute of Mato Grosso, Nursing Department, Barra do Garças, SP, Brazil. e-mail: ricardo@eerp.usp.br

Background: Tto analyze the spatial distribution of Tuberculosis cases, their relationship with health services and to classify the temporal trend of the incidence of the disease.
Methods: An ecological study carried out in Ribeirão Preto-SP. The population was composed of all TB cases reported TBWeb in the period from 2006 to 2017. Cases of TB and health units were geocoded and point density analysis was performed. The temporal trend of TB incidence in the period was classified using the Prais Winsten technique.
Results: There were 2259 cases of TB reported in the period and 2094 were geocoded, as well as 49 health units. The West and North districts had the largest number of cases and health units. The Kernel intensity estimator identified that the South and West districts present a higher density of TB cases. The analysis of time series in the period showed that the incidence rate of TB in the municipality was decreasing (-2.2% per year - 95% CI: -3.17 - -0.91).
Conclusions: The North and West districts had a higher number of TB cases and a larger number of health units. The Kernel intensity estimator confirmed these areas with a higher density of TB cases, together with the Southern District. With the time series analysis, it was possible to identify that the incidence of TB in the municipality showed a decreasing trend in the period, which may indicate that policies and strategies for TB control are being successful or that new cases are not being diagnosed. The present work contributes to the identification of vulnerable areas for TB and to subsidize actions aimed at the control and elimination of the disease.



[Density of TB cases per Km² Ribeirão Preto-SP (2006-2017)]

EP-08-174-01 National Tuberculosis Program data improvement efforts: transitioning from Excel to an electronic register, 2017-2018

I Nasseco,[1,2] JL Conjera,[1] A Soto,[3] R Makombe,[4] S Lisa,[5] J Jone Zacarias,[6] [1]Family Health International 360, Challenge TB Mozambique, Monitoring and Evaluation, Maputo, Mozambique, [2]Family Health International 360, Challenge TB Mozambique, Monitoring and Evaluation, Nampula, Mozambique, [3]Family Health International 360, Challenge TB Mozambique, CTB, Maputo, Mozambique, [4]Family Health International 360, Challenge TB Mozambique, Technical, Pretoria, South Africa, [5]Family Health International, HQ, Thailand, Thailand, [6]Minsitry of Health, Monitoring and Evaluation, Maputo, Mozambique. e-mail: jconjera@fhi360.org

Background and challenges to implementation: Ensuring data quality has always been a challenge for Mozambique's National TB Program (NTP). Prior to 2018, NTP relied on Excel-based aggregated data for reporting on TB indicators. The data management system involved collecting Excel-based district-level aggregated data; NTP then further aggregated these data at the provincial and national levels to produce NTP reports. This system proved unreliable due to delays in obtaining data, data-entry errors, and inconsistency among data reported.

Intervention or response: In 2018, with support from Challenge TB (CTB) Mozambique, the NTP began using the open-source DHIS 2 electronic data management software to ensure that data collection and reporting meet minimum data quality standards. The transition from Excel to DHIS 2 has ensured that data entered at health facilities (HFs) can be accessed and reviewed at district, provincial, and national levels. CTB provided technical assistance to HFs in supported areas to transition from manual, Excel-based data collection and reporting to using DHIS 2.

Results and lessons learnt: CTB-supported provinces where the first to report data through DHIS2 (SISMA) at 88.4 percent in 2017 and increased to 94.4 in 2018 on all reported indicators. In 2018, reporting rate above 94% for patient notification, 90% treatment outcomes, 92% notification of MDR TB. Data validation in 2018 found the discrepancy rate was < 2%.

Conclusions and key recommendations: DHIS 2 is essential to NTP's efforts to improve data quality and obtain timely information for decision making. The high reporting rate shows that the HF staff have the capacity to use DHIS 2. NTP should ensure that resources such as tablets and recharge vouchers are available. Financial resources for quarterly data validation meetings should be made available before the closure of the system each quarter.

EP-08-175-01 Integrating Xpert MTB/RIF machine test results with case-based information portal Nikshay: an indigenous solution from revised National TB Programme, India

J Jaju,[1] M Mathews,[1] S Achanta,[1] S Anand,[1] Y Patel,[1] N Kumar,[1] R Kumar,[2] KS Sachdeva,[3] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]World Health Organization, Country Office, Nikshay ICT Cell, New Delhi, India, [3]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: jajuj@rntcp.org

Background: India's National Strategic Plan for TB Elimination 2017-25 envisions increased case detection using rapid molecular diagnostics. About 1200 Xpert MTB/RIF machines have been deployed countrywide. Universal Drug Susceptibility testing is being scaled up and it is projected that approximately 2.5 million Xpert MTB/RIF tests will be conducted in 2019. Since these tests are largely automated and the output machine generated, there exists an opportunity to directly read the machine output, thereby reducing manual intervention and ensuring data quality. Nikshay, the case based web based management tool holds test level information and the machine output could be matched against it. Therefore, an indigenous solution was developed to integrate machine output with Nikshay.

Methods: The Xpert MTB/RIF machine generates text files with complex test related information (test data). The files range in formats based on the machine and system version. An algorithm was indigenously developed to read this complex information containing over 100 variables in a hierarchical data structure. The algorithm was built into the Nikshay application and the first version was tested in December 2018. After further refinement of the algorithm, training to end -users was imparted and an improved version was released in March 2019.

Results: As on 19th April 2019, the solution has read almost 272 thousand test details, from 20,124 files originating from 453 machines in 434 health institutions. Of these tests, 80243(~30%) were Mycobacterium Tuberculosis positive and of these 7% were Rifampicin resistant.

MTB Detection	No. of tests	%
MTB Detected	80243	30%
MTB Not Detected	182788	67%
Error / Invalid	8932	3%
Total		**271963**

Rif Resistance	No. of tests	%
Not Detected	74311	93%
Detected	5261	7%
Indeterminate	671	1%
Total		**80243**

[Xpert MTB/RIF -Nikshay Integration results]

Conclusions: The solution developed could successfully import test data into Nikshay. Further analysis of program data would be necessary to understand how this can improve quality of data, save hours of manual data entry and improve timeliness of test reports.

EP-08-176-01 Transitioning from a parallel standalone TB programme-based reporting system to a web-based national reporting system increased TB case notification

T Kiyemba,[1] T Nyombi,[2] A Nkolo,[3] E Quinto,[4] S Turyahabwe,[5] [1]University Research Company, Monitoring, Evaluation and Learning, Kampala, Uganda, [2]University Research Co., LLC (URC)/United States Agency for International Development (USAID) Defeat TB Project, Health Systems Strengthening, Kampala, Uganda, [3]University Research Co., LLC (URC)/United States Agency for International Development (USAID) Defeat TB Project, Overall, Kampala, Uganda, [4]National TB and Leprosy Control Programme, Monitoring & Evaluation, Kampala, Uganda, [5]National TB and Leprosy Program(NTLP), TB, Kampala, Uganda.
e-mail: tkiyemba@gmail.com

Background and challenges to implementation: For the period 2003 to 2017, the National TB and Leprosy program in Uganda relied on a standalone MS-Access & Excel -based reporting system managed by District TB and Leprosy Supervisors (DTLS) who moved throughout to each health facility capturing data on TB patients notified to compile the district quarterly report for submission to NTLP. This system was fraught with challenges including limited funding for the DTLS to reach all facilities and was laborious.
There was also divided attention in supporting this system and the Ministry of Health's national HMIS and MoH DHIS2.

Intervention or response: The NTLP decided to completely phase away the parallel TB reporting system and rely on the national MoH DHIS2. A circular was sent to all districts including the 3 Urban TB districts of Kampala, Wakiso and Mukono supported by the USAID Defeat TB project. All Health workers were trained on the definitions for the TB data elements in the HMIS reports and on submission of reports in DHIS2.
Results and lessons learnt: The number of persons with TB notified by NTLP increased from 44,805 to 55,835 between 2017 and 2018 (11,030 additional notifications compared to 3,166 additional notifications between 2016 and 2017). Historical Data Quality review sessions have also indicated under-reporting rates of 11% and 8% associated with the DTLS reporting system for 2017 and 2018 respectively.
Conclusions and key recommendations: Working with a web-enabled and nationally institutionalized information system for management of TB data ensured more sites are reached for reporting and more dedicated focus was directed to compilation of more complete HMIS reports by all stakeholders including the DTLS for decision making, planning and projection for key logistics and resources necessary to support persons with TB.

EP-09-C2 TB and mental health

EP-09-177-01 Female tuberculosis (TB) patients with stigma are at increased risk of persistent depression: time to integrate mental health screening into TB care

N Suryavanshi,[1] M Sane,[1] S Gaikwad,[2] M Paradkar,[1] V Mave,[1,3] P Chandrasekaran,[4] SBY Shiv kumar,[5] A Gupta,[3] N Gupte,[1,3] B Thomas,[6] for CTRIUMPH RePORT India study [1]Byramjee Jeejeebhoy Government Medical College/Johns Hopkins University, Clinical Trial Unit, Pune, India, [2]Byramjee Jeejeebhoy Government Medical College, Department of Pulmonary Medicine, Pune, India, [3]Johns Hopkins University, School of Medicine, Baltimore, MD, United States of America, [4]National Institute for Research in Tuberculosis, ICMR, Department of Clinical Research, Chennai, India, [5]Johns Hopkins University, India Office (CCGHE), Pune, India, [6]National Institute for Research in Tuberculosis, ICMR, Department of Social and Behavioral Research, Chennai, India.
e-mail: nishisuryavanshi@hotmail.com

Background: Epidemiology of persistent depression (PD) among newly diagnosed adult pulmonary tuberculosis (PTB) patients is unknown. Characterizing factors associated with PD will help in early identification of risk groups and initiated on anti-depression interventions.
Methods: Newly diagnosed adults (>18 years) with drug sensitive PTB, at anti-TB treatment (ATT) initiation were enrolled in prospective cohort and followed for 18

months. Demographic, psycho- socio-behavioral (stigma) and clinical data were collected at entry and follow-up using pre-tested questionnaires. Validated shorter version of Center for Epidemiological Studies Depression Scale (CESD-10) was administered by trained counselors at ATT initiation and completion. PD was defined as CESD greater than 9 at both times. Patients with PD and no depression at any timepoint were included in the analysis. Univariable and multivariable logistic regression was used to identify independent risk factors.

Results: Of the 461 patients, 254 were included in this analysis, of which 199 (78%) were never depressed and 55 (22%) had PD, with median (IQR) depression score 15 (12-19) at baseline and 14 (11-16) at ATT completion, 82 (32%) were females, 109 (43%) were older than 40 years, 87 (34%) were alcohol dependent, and 26 (10%) reported TB associated stigma. Overall prevalence of PD was 22% (17%-27%), and among: older age 29% (21%-39%), females, 30% (21%-42%), stigma 46% (27%-67%) and sleeplessness 40% (29%-53%). In a multivariable analysis (aOR; 95% CI), females (6.85; 2.44-19.28); age>45 years (5.78; 1.36-24.51); alcohol dependence (3.44; CI 1.25-9.47), and stigma (3.06; 1.02-9.14) were independently associated with PD. Females with stigma were more likely to be persistently depressed as compared to men (aOR=5.44; 95% CI 1.87-15.87); p-value=0.002.

Conclusions: In our cohort PD was high, and independently associated with females who reported stigma. Thus, there is an urgent need to integrate depression screening at ATT initiation and provide appropriate interventions for optimal TB care.

EP-09-178-01 Psychological support improves treatment adherence among drug-resistant tuberculosis patients: experience from Jingzhou City, China

Y Liao,[1] [1]Jingzhou Chest Hospital, MDR-TB Division, Jingzhou, China. e-mail: 84705658@qq.com

Background and challenges to implementation: MDR-TB patients usually felt isolated and were lack of family support. They may face discrimination and stigma from family, community and society. This will cause patients' negative emotion and psychological status, which will influence patients' treatment adherence and quality of life. From August 2018, under the USAID Control and Prevention of Tuberculosis (CAP-TB) Project, Jingzhou Chest Hospital has launched a comprehensive supportive care package for MDR-TB patients in Yichang City to provide high quality counselling and psychological support.

Intervention or response: Jingzhou Chest Hospital recruited two peer educators. After trained, peer educators as well as professional nurse counsellors, conducted one-on-one counselling and thematic small group activities on psychological problems and anti-stigma, using Hospital Anxiety and Depression (HAD) Scales. A community-based organization called 57 zone was developed by doctors, counsellors, MDR-TB patients, and their family members. Counsellors also provided online counselling at 57 social media group.

Results and lessons learnt: From August 2018 to February 2019, 43 accepted psychological intervention. After intervention, the patients' HAD scores were significantly lower than the control group (11 vs. 16). The intervention group's drug adherence rate is 79.07% (34/43), which is significantly higher than the control group 52.77% (38/72).

Conclusions and key recommendations: Under counsellors' help, MDR-TB patients overcame psychological problems. The drug adherence was improved. The psychological support was proved to play a positive role on MDR-TB patients' rehabilitation. More and more MDR-TB patients feel care from health providers and their own community, which helped their confidence on fighting with disease.

EP-09-179-01 Mental health among multidrug-resistant tuberculosis (MDR-TB) patients in Pune city, India: a gender-based analysis

J Jagtap,[1] M Faqih,[1] Y Dumbre,[1] A Dixit,[2,3] M Farhat,[3,4] S Atre,[1] [1]Dr. D.Y. Patil Medical College and Vidyapeeth, Pimpri, Respiratory Medicine, Pune, India, [2]Boston Children's Hospital, Division of Infectious Disease, Boston, MA, United States of America, [3]Harvard Medical School, Department of Biomedical Informatics, Boston, MA, United States of America, [4]Massachusetts General Hospital, Division of Pulmonary and Critical Care, Boston, MA, United States of America.
e-mail: jayshrigudadhe@gmail.com

Background: India carries the highest burden of multidrug-resistant TB (MDR-TB) cases. Despite the protracted treatment path experienced by MDR-TB patients and the toxicities including psychiatric side effects of some MDR-TB drugs, there is limited study of adjustment and mental health among this population. We aimed to characterize psychological symptoms among MDR-TB cases registered under the Revised National TB Control Program (RNTCP) in Pune City.

Methods: As part of a larger mixed-methods study on pathways to TB care, we consented 123 patients with MDR (55 men and 68 women) and conducted in-depth interviews using both a survey tool and an interview guide to collect qualitative and quantitative data. We coded the presence of the symptoms related to following conditions: depression, anxiety, somatization, psychotic symptoms and suicidal ideation using the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5.

Results: Of the total, 117 (95%) reported ≥1 psychological symptom (Table 1). About 71% of cases were young adults, 15 to 35 years old, and 55% were women.

The most common symptoms were depression (68%), anxiety (64%) and somatization (27%). Narratives indicated that women had depression and anxiety due most commonly to familial stress including divorce, husband's remarriage, household stigma and distance from children.

Men had anxiety due to familial stress as well as due to financial and occupational stress and societal isolation. Of the 123 cases, 45% reported treatment interruption of ≥2 weeks due to a psychological symptom. Treatment interruption was more common among men than women (60% vs. 32%; P=0.0019). Ninety percent of patients reported no referral to a mental health provider for their symptoms.

Conclusions: Our study underscores the need for improving counselling skills among RNTCP care providers and/or the establishment of referral mechanisms for mental health. Our data suggests this may help prevent treatment interruptions and improve outcomes.

Psychological symptoms	Men (n=55)	Women (n=68)	Total (n=123)
	n (%)	n (%)	n (%)
Depression	33 (60.0)	50 (73.5)	83 (67.5)
Anxiety	36 (65.5)	43 (63.2)	79 (64.2)
Somatic symptoms	17 (30.9)	17 (25.0)	34 (27.6)
Psychotic symptoms	4 (7.3)	3 (4.4)	7 (5.7)
Suicidal ideation	2 (3.6)	8 (11.8)	10 (8.1)

[Table 1 Gender wise distribution of psychological symptoms among patients with MDR-TB]

EP-09-180-01 Association between tuberculosis and depression on negative outcomes of tuberculosis treatment: a systematic review

P Ruiz,[1] R Cachay,[1] A de la Flor,[1] A Schwalb,[1] C Ugarte,[1] [1]Universidad Peruana Cayetana Heredia, Instituto de Medicina Tropical Alexander von Humbold, Lima, Peru. e-mail: cesar.ugarte@upch.pe

Background: Depression is considered a frequent comorbidity of tuberculosis (TB) and is associated with poor adherence to treatment of multiple disorders. We aim to review the evidence that supports the association between depressive disorders and negative treatment outcomes of TB.

Methods: We performed a systematic review and meta-analysis which evaluated depressive disorders directly or indirectly within psychological distress and negative treatment outcomes of drug-sensitive pulmonary TB defined as loss to follow up or death. Also, we evaluate poor adherence to TB treatment. Sources included PubMed, Global Health Library, EMBASE, Scopus and Web of Science from inception to October 2018. This study was registered in PROSPERO (CRD42018111058).

Results: Eight articles were selected among 2856 hits; four measured depression using ICD-10, PHQ-9 and CES-D scales, and the other measured psychological distress using K-10. By analyzing depression and psychological distress together, we found an association with negative outcomes of TBT (6 articles, n=9082, OR:2.16, IC95%:1.19-3.93). Only depression showed association with negative TB treatment outcomes (3 articles, n=2315, OR:4.09, IC95%:2.67-6.28) in contrast to psychological distress (3 articles, n=6767, OR:0.94, IC95%:0.83-1.07). Also, an association between depression and death during TB treatment (2 articles, n =973, OR:2.85, IC95%:1.52-5.36), and between depression and loss to follow up was found (2 articles, n=973, OR:8.70, IC95%:6.50-11.64). Finally, we found no evidence of association between depression and psychological distress with TB treatment adherence (4 articles, n=10886, OR:1.38, IC95%:0.70-2.73).

Conclusions: We found evidence that supports the association between depressive symptoms and psychological distress with negative TB treatment outcomes. However, information is scarce for specific outcomes such as death, loss to follow up and poor adherence. Further studies should be conducted to evaluate the dynamics of depressive symptoms during TB treatment, to provide evidence for interventions with person-centered approach to TB and depression care.

EP-09-181-01 Trajectories of depressive symptoms during treatment and negative outcomes among persons with tuberculosis in Peru

P Ruiz,[1] C Loret de Mola,[2] L Otero,[1] C Ugarte,[1] [1]Universidad Peruana Cayetana Heredia, Instituto de Medicina Tropical Alexander von Humbold, Lima, Peru, [2]Universidade Federal do Rio Grande, Faculdade de Medicina, Pelotas, RS, Brazil. e-mail: cesar.ugarte@upch.pe

Background: Depression is associated with non-adherence to tuberculosis (TB) treatment and loss to follow up, which increase the risk of multidrug resistant-TB development. We describe the trajectories for depressive symptoms during drug-sensitive TB treatment (TBT) and their association with negative outcomes.

Methods: We analyzed data from a prospective cohort of persons with the first episode of drug-sensitive pulmonary TB. Latent class growth analysis was used to identify trajectories of depressive symptoms during the first half (month 1 to 3) of TB treatment. Logistic regression was used to test the hypothesis that these trajectories are associated with negative outcomes of TB treatment, defined as death or treatment loss to follow up. Interaction with frequent use of alcohol (FUA) defined as drinking at least one alcoholic beverage once per week was explored.

Results: Data from 280 individuals were analyzed. Three trajectories for depressive symptoms were found; (69%) showed improvement of symptoms, (20%) showed in-

creasing symptoms and one with constant high levels (11%) of depressive symptoms. FUA was reported in 18,8% (57) individuals, and 14% (8) of them had negative treatment outcomes.
In adjusted models, individuals with an increasing trajectory of depressive symptoms during the intensive phase treatment had 3.9 times the chance of negative outcomes than those with an improvement of symptoms (OR= 3.9, IC95%: 1.1-13.9). FUA seemed to modify this effect (p=0.144). This association remained significant only in the presence of FUA (OR= 13.3, IC95%: 1.32-134.9).
Conclusions: Increasing depressive symptoms during the first half of TBT were associated with higher chances of negative outcomes. Strategies should be evaluated and implemented to include a comprehensive approach for providing a person-centered approach to TB and depression care, thereby reducing the risk of negative TB treatment outcomes.

EP-09-182-01 Assessing depression outcomes in multidrug-resistant tuberculosis (MDR-TB) patients as part of a comprehensive treatment programme in Lima, Peru

C Conteras,[1] M Aguilar,[1] H Campos,[1] S Perea,[1] L Lecca,[1] J Wilson,[2] C Flanagan,[2] M Rich,[2] KJ Seung,[2] C Mitnick,[3] [1]Socios En Salud (SES), Program, Lima, Peru, [2]Partners In Health, Clinical Programs, Boston, MA, United States of America, [3]Harvard Medical School, Department of Global Health & Social Medicine, Boston, MA, United States of America. e-mail: ccontreras_ses@pih.org

Background: Since February 2016, Socios En Salud has been treating patients in Lima, Peru with multidrug-resistant tuberculosis (MDR-TB) with bedaquiline as part of the endTB Observational Study. Throughout treatment, endTB patients receive clinical support in coordination with the Ministry of Health, as well as social and mental health support. The Patient Health Questionnaire (PHQ-9) depression module was administered. Patients exhibiting signs of depression were referred for mental health interventions, including psychoeducation, emotional support groups or occupational therapy. This study describes the change in PHQ-9 scores of endTB patients receiving a mental health intervention during their MDR-TB treatment, and relationships of mental health conditions and treatment outcomes.
Methods: Eighty-two endTB patients met the inclusion criteria for this analysis (completed 3 or more visits, had final treatment outcomes, and received a mental health intervention).
This analysis used a Wilcoxon Signed Rank Test to quantify changes in PHQ-9 scores, comparing baseline to treatment midpoint (9-12 months) and treatment end (18-24 months). Additionally, we considered whether any mental health factors were associated with loss to follow-up.
Results: At midpoint and treatment end, there was a significant improvement in PHQ-9 scores ($p < .005$) as compared to baseline. However, there was no significant improvement between midpoint and treatment end. The median within-person change at midpoint and treatment end compared to baseline was 2.0 [IQR: 0.0-6.5] and 4.0 [IQR: 0.0-8.0], respectively. Participants with baseline anxiety as measured by the Self-Reported Questionnaire (SRQ-18) were significantly positively associated ($p < .05$) with loss to follow-up.
Conclusions: These results demonstrate that a comprehensive MDR-TB treatment program, including clinical, social, and mental health support, may improve depression levels. Further study is needed to evaluate how changes in mental health conditions may impact MDR-TB treatment outcomes.

EP-09-184-01 Responding to the substance use challenge in rifampicin-resistant tuberculosis: preliminary outcomes of a primary healthcare substance use management model in Khayelitsha, South Africa

A Reuter,[1] E Mohr,[1] E Rodriguez,[1] V De Azevedo,[2] AK Domingo,[3] P Isaakidis,[4] L Snyman,[5] M Vermeulen,[6] L Weich,[7] L Trivino-Duran,[8] [1]Medecins Sans Frontieres, DR-TB, Khayelitsha, South Africa, [2]City of Cape Town Department of Health, Primary Health Care Health Department, Cape Town, South Africa, [3]Stellenbosch University, South Africa, Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch, South Africa, [4]Medecins Sans Frontieres Southern Africa Medical Unit, HIV/TB/HepC, Cape Town, South Africa, [5]Medecins Sans Frontieres, HIV/DR-TB, Khayelitsha, South Africa, [6]Medecins Sans Frontieres, EndTB Clinical Trial, Khayelitsha, South Africa, [7]Stellenbosch University, Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch, South Africa, [8]Medecins Sans Frontieres, Coordination Office, Cape Town, South Africa. e-mail: msfocb-khayelitsha-tbdoc@brussels.msf.org

Background: Substance use (SU) is associated with poor rifampicin-resistant tuberculosis (RR-TB) treatment outcomes. In 2017, Medicines Sans Frontieres and department of health integrated screening, brief intervention and referral to treatment (SBIRT) into the RR-TB treatment programme. Here we describe early experiences of the use of the SBIRT.
Methods: This was an observational cohort of patients with RR-TB who were screened for SU between October 2017-March 2019 in Khayelitsha, South Africa. Screening was conducted using the ASSIST or the AUDIT. Patients who scored moderate or high-risk were referred to a SU support group; those with moderate or high-risk alcohol use and considered eligible by a clinician, were offered naltrexone. Here we describe the number screened, risk category, and number started on naltrexone.

Results: Overall, 102 RR-TB patients were screened for SU, 48 (47%) were females and the median age at RR-TB diagnosis was 37 years (interquartile range [IQR] 31-45); 79 (77%) were HIV co-infected. Ninety two (90%) patients reported SU, with 37/92 (40%) using more than one substance; 65/92 (71%) scored moderate or high-risk for at least one substance. Overall patients reported using the following: 86/92 (93%) alcohol, 40/92 (43%) tobacco, 11/92 (12%) cannabis, 4/92 (4%) mandrax, 3/92 (3%) methamphetamines, and 1/92 (1%) cocaine. Twenty two (35%) of the 65 moderate or high-risk patients attended a support group at least once.
Of the 86 patients that reported alcohol use, 35 (41%), 16 (18%), and 35 (41%) scored low, moderate, and high-risk, respectively. Of the 51 patients that scored moderate or high-risk, 48 (94%) received a brief intervention, 34/48 (71%) were offered naltrexone and 17/34 (50%) initiated naltrexone.
Conclusions: Moderate and high-risk SU was common among the RR-TB patients screened; alcohol was the most common substance reported. Integrating SBIRT, pharmacotherapy and support groups into primary health RR-TB care could be beneficial.

EP-09-185-01 Invisibility of the mental distress experienced by TB patients in primary healthcare in Zambia

T Mainga,[1,2] M Gondwe,[1] RC Stewart,[3,4] I Mactaggart,[5] K Shanaube,[6] H Alyes,[6,7] V Bond,[1,8] [1]ZAMBART, Social Science, Lusaka, Zambia, [2]London School of Hygiene & Tropical Medicine, Public Health and Policy, London, United Kingdom, [3]University of Malawi College of Medicine, Mental Health and Community Health, Blantyre, Malawi, [4]University of Edinburgh, Division of Psychiatry, Edinburgh, United Kingdom, [5]London School of Hygiene & Tropical Medicine, International Centre for Evidence in Disability, London, United Kingdom, [6]ZAMBART, Research Directorate, Lusaka, Zambia, [7]London School of Hygiene & Tropical Medicine, Clinical Research, London, United Kingdom, [8]London School of Hygiene & Tropical Medicine, Global Health and Development, London, United Kingdom.
e-mail: gbond@zambart.org.zm

Background: TB patients often experience mental distress that could result in adverse treatment outcomes. The mental distress of TB patients in Zambia has not been viewed as a public health priority and remains under-researched. In this qualitative research study in urban Zambia, we aimed to detail how TB patients, health workers and other TB stakeholders currently view mental distress linked to TB and the availability of mental health services.
Methods: The study draws on qualitative data collected in 2018 as part of Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for active TB - trial (TREATS) being conducted in 8 urban communities across Zambia. The data came from focus group discussions with Neighborhood Health Committees (n=96) and stakeholders (n=57), and in-depth interviews with TB health workers (n=9) and patients (n=81) recruited through the clinic TB registers. Thematic analysis was conducted.
Results: TB patients most commonly suffer from mental distress due to associations between TB and death, physical frailty brought about by TB, and TB stigma. The implications of mental distress among TB patients include denial of diagnosis, poor adherence to medication and reduced quality of life. Mental health is largely invisible and misunderstood in the Zambian public health sector. For example, TB stakeholders and health workers commonly described mental distress experienced by TB patients as *"madness/craziness characterized by violence"*, which they attributed to a side effect of TB medication. Corresponding mental health services in the country are limited in scope and access.
Conclusions: TB patients in Zambia that experience mental distress have little to no avenues of support as their co-morbidity is largely ignored or misunderstood by primary care providers and TB stakeholders and there is limited access to specialized services. Sensitization of stakeholders and primary care givers and development of specialized services could improve TB treatment outcomes.

EP-09-186-01 Factors influencing poor adherence to MDR-TB treatment: patients' and providers' perspectives

N Arefin Saki,[1] M-U Alam,[2] PK Modak,[1] MAH Salim,[1] MS Bashar,[1] AH Khan,[1] MS Islam,[1] [1]National Tuberculosis Control Program, DGHS, Dhaka, Bangladesh, [2]Interactive Research and Development, Health, Dhaka, Bangladesh.
e-mail: nazis.arefin@yahoo.com

Background: Lost to follow-up of multidrug-resistant tuberculosis (MDR-TB) is a major challenge faced by national TB programs worldwide. In Bangladesh, 64(7%) MDR-TB patients were lost to follow-up among 918 enrolled in 2016 cohort. This study explores factors influencing poor adherence to MDR-TB treatment and care.
Methods: A semi-structured open-ended interviews were conducted with MDR-TB patients aged >18 years, as well as healthcare providers involved in MDR-TB care between June and December 2018, in different districts of Bangladesh. Purposive sampling was used to recruit participants from diverse backgrounds included: 50 MDR-TB patients (32 males and 18 females), 15 community DOT-providers and 5 district level supervisors. All the patients were lost to follow-up at any point of time during treatment and aged 23-57 years. Qualitative content analysis identified themes evolving from interviews.
Results: Among 50 patients, 29(58%) were lost to follow-up during intensive phase of treatment and 26 of them showed concern about injections. 41(82%) patients

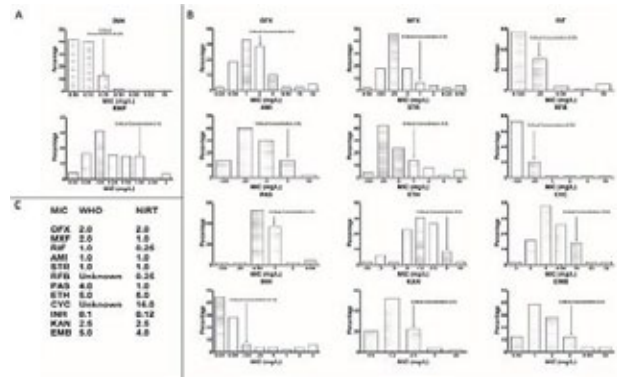
identified adverse events as a factor for non-adherence, especially minor adverse events were often ignored. Male patients were more likely to express concern over poor attitudes from DOT-providers than females.
Some DOT-providers and all supervisors reported workloads and lack of means for transportation as a barrier to follow-up the patients. 78% of the patients and all providers identified the monetary support provided by the national program insufficient and payment method were complicated. Majority of the patients (62%) and all healthcare providers found social stigma as one of the major causes for non-adherence.
Conclusions: Introduction of all oral MDR-TB regimen and prompt management of adverse events should be encouraged. Training of the DOT-providers and health education to patients should be conducted regularly.
Further evaluation is required to revise the monetary support with simple payment mechanism. More community engagement may reduce stigma and keep the patients adhere to treatment.

EP-10-A3 TB diagnostics innovation

EP-10-187-01 Re-evaluation of the critical concentration of anti-TB drugs among M. tuberculosis isolates from south Indian population using wild-type MIC distribution

AS Shainaba,[1] VND Azger,[1] MK Rajesh,[1] B Mahizhaveni,[1] B Angayarkanni,[1] R Geetha,[2] AK Hemanth Kumar,[2] T Kannan,[3] S Govindarajan,[1] T Srikanth Prasad,[4] [1]National Institute for Research in Tuberculosis, Department of Bacteriology, Chennai, India, [2]National Institute for Research in Tuberculosis, Department of Clinical Pharmacology, Chennai, India, [3]National Institute for Research in Tuberculosis, Department of Statistics, Chennai, India, [4]National Institute for Research in Tuberculosis, Research in Tuberculosis, Chennai, India. e-mail: asshainaba@gmail.com

Background: Critical concentration of anti-TB drugs is required for determining drug susceptibility. World Health Organisation (WHO) recommended cut-offs are universally followed to determine the susceptibility. It is evident that there might be changes in critical concentration which is dependent upon isolates prevalent in each community.
The present work focussed to determine critical concentration of drugs using both solid and liquid media among wild type strains from Chennai.
Methods: Wild type isolates from patients before start of treatment were used for MIC determination using Middlebrook 7H11 agar plates (solid), MGIT960 (liquid) and MycoTBI plates and sample sizes were 276, 96 and 50 respectively. Briefly bacterial cells of 0.5 Mcfarland turbidity was spotted/added to corresponding media in the presence and absence of tenfold diluted drugs along with 100 times diluted culture as control. Based on earlier reports critical concentration is defined as the lowest concentration of a drug that will inhibit ≥95% of strains. Isoniazid and Rifampicin were assayed in 7H11 plates and MGIT960 whereas Ofloxacin, Amikacin, Streptomycin, Ethambutol, Moxifloxacin, P-aminosalicilic acid and Kanamycin were assayed using MycoTBI. Pharmacodynamics were calculated using serum levels for Isoniazid and Rifampicin available for 8 patients.
Results: Critical concentration for Rifampicin was found to be identical to that recommended by WHO in both media. But critical concentration for Isoniazid in MGIT960 was found to be 0.25 mg/l as against 0.1 mg/l. Critical concentration of Moxifloxacin, Ethambutol and P-aminosalicilic acid were also dissimilar to that of recommended levels using MycoTBI. Rifampicin levels were sub therapeutic in 5 of 8 patients using MICs of corresponding infected strains.
Conclusions: Critical concentration for Isoniazid, Moxifloxicin, P-aminosalicilic acid and Ethambutol were dissimilar to the recommended concentration that could lead to over diagnosis of resistance.
Further studies in different regions of India are essential. Further, pharmacodynamics analysis, that identify rifampicin sub-therapeutic levels, were possible with MIC determinations.



[MIC distribution of various drugs for wild type strains]

EP-10-188-01 Genomic analysis of M. tuberculosis strains with discordant rifampin susceptibility in molecular/phenotypic tests

L Solari,[1,2] D Santos,[2] Z Puyen,[2] [1]Universidad Peruana de Ciencias Aplicadas, Escuela de Medicina, Lima, Peru, [2]Instituto Nacional de Salud, Centro Nacional de Salud Publica, Lima, Peru. e-mail: lelysol@hotmail.com

Background: Molecular tests are used to evaluate antituberculosis drug- susceptibility; however, discordant results with phenotypic testing are occasionally seen. This could be explained by mutations not detected by

the molecular method. We aimed to identify which are the most frequent mutations conferring rifampin resistance in discordant Peruvian specimens.
Methods: We included *Mycobacterium tuberculosis* (MTB) strains from the Laboratory of Tuberculosis of the National Institute of Health showing sensitivity to rifampin in the Genotype MTBDR-plus test, but resistant (discordant) with the proportions method in Middlebrook 7H10 agar. We performed whole genome sequencing and analyzed rpoB for the presence of mutations not identified by Genotype MTBDR-plus. The genes rpoA and rpoC were also analyzed. Only sequenced strains with a minimum depth of 50 were considered.
Results: 14 MTB strains were included and in 13, rpoB mutations were identified. In 2 strains, 1 mutation was identified, 11 strains had 3 mutations and 1 strain had 5 mutations. The most frequent mutations were rpoB V170F in 6 patients, rpoB D103D in 3, rpoB I491F in 2 and rpoB A960E in 2. Mutations rpoB H194R, rpoB E250G, rpoB F424V, rpoB L430R, rpoB L452P, rpoB V695L were present in 1 patient each. A total of 39 mutations were identified between rpoB, rpoA and rpoC genes. rpoAR182W mutation was found in 1 patient. rpoCG594E was found in 6 patients, rpoCA542A in 5 and rpoCV483A in 2. The following mutations were found in single patients: rpoCV483G, rpoCL516P, rpoCE518Q, rpoCG571R, rpoCE1033K, and rpoCE1113D.
Conclusions: We found rpoB mutations in 13/14 (93%) of Peruvian strains with discordant results. The most frequent was rpoB V170F. We were also able to find concomitant mutations in rpoC and rpoA. The identified mutations in rpoB could be candidates to be included in molecular tests for rifampicin susceptibility to be developed for Peru.

EP-10-189-01 Six-week culture conversion predicts tuberculosis treatment outcomes

N Pradhan,[1] A Kagal,[2] N Gupte,[3,4] S Gaikwad,[5,6] M Bharatwal,[7] A Gupta,[4] J Golub,[4] V Mave,[3,4]
[1]BJ Medical College/John Hopkins University, Clinical Trial Unit, Pune, India, [2]Byramjee-Jeejeebhoy Government Medical College, Microbiology, Pune, India, [3]Byramjee-Jeejeebhoy Government Medical College-Johns Hopkins University Clinical Research Site, Clinical Trial Unit, Pune, India, [4]Johns Hopkins University School of Medicine, Department of Medicine, Baltimore, MD, United States of America, [5]Byramjee-Jeejeebhoy Government Medical College-Johns Hopkins University Clinical Research Site, Pulmonary Medicine, Pune, India, [6]Byramjee-Jeejeebhoy Government Medical College, Pulmonary Medicine, Pune, India, [7]Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pulmonary Medicine, Pune, India.
e-mail: neetapradhanpune@gmail.com

Background: Eight-week culture conversion is used as a surrogate marker for treatment response in tuberculosis (TB) clinical trials. However, as the length of TB treatment reduces, an earlier surrogate marker is needed. Therefore, we sought to identify the earliest time point that can predict TB failure as outcome using MGIT.
Methods: As part of a prospective cohort study of patients with pulmonary TB, with or without Diabetes Mellitus in India, sputum collected for all enrolled participants every two weeks after TB treatment initiation through 8 weeks and then monthly until 6 months, underwent smear microscopy and growth on MGIT. Univariable and multivariable logistic regression was performed to assess whether 2, 4 or 6-week culture conversion predicted TB treatment failure. Failures were evaluated at months 5/6 of treatment initiation and were defined as microbiological evidence and/or clinical evidence of TB.
Results: Of the 718 participants with culture positive TB at baseline, 652 (91%) were cured/completed treatment, 66 (9%) failed treatment. Overall, median age was 32 (IQR, 24-45), 472 (66%) were males and 202 (28%) had diabetes. After adjusting for age, gender, body mass index, diabetes, tobacco and alcohol use, culture conversion at 6 weeks (adjusted odds ratio (aOR, 2.07; 95% CI: 1.10 - 3.91,C statistic- 0.67), 8 weeks (aOR, 1.81; 95% CI: 0.94 - 3.48) and 12 weeks (aOR, 4.44; 95% CI: 1.88 - 10.45) and 16 weeks (aOR, 8.0; 95% CI: 3.52 - 18.16) predicted TB treatment failure (Table). Two (aOR, 1.57;95%CI :0.82-3.01) and four-week culture conversion did not predict failure
Conclusions: The earliest culture conversion that predicted failure was at 6 weeks and potentially can be used as an earlier surrogate endpoint than the current standard of 8 weeks. Unsurprisingly, the odds of treatment failure increased with later TB culture conversion, however earlier culture results did not. Future studies should confirm our findings.

EP-10-190-01 Comparative accuracy of Fujifilm SILVAMP TB LAM™ and Alere Determine™ TB LAM for diagnosis of childhood tuberculosis in paediatric urine specimens

E Nkereuwem,[1] MP Gomez,[1] D Jobe,[1] B Saidy,[1] T Togun,[2] R Szekely,[3] A Macé,[3] C Denkinger,[3] B Kampmann,[1,2] [1]Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine, Vaccines and Immunity Theme, Fajara, Gambia, [2]London School of Hygiene and Tropical Medicine, Infectious and Tropical Diseases, London, United Kingdom, [3]Foundation for Innovative New Diagnostics (FIND), Head Quarters, Geneva, Switzerland.
e-mail: enkereuwem@mrc.gm

Background: Diagnosis of childhood tuberculosis (TB) is difficult due to the pauci-bacillary nature of the disease and difficulty in obtaining sputum samples. Therefore, development of non-sputum-based diagnostic tools is vital.

	MRS				CRS			
	HIV positive		HIV negative		HIV positive		HIV negative	
Test	FujiLAM	AlereLAM	FujiLAM	AlereLAM	FujiLAM	AlereLAM	FujiLAM	AlereLAM
Sensitivity [95% CI]	54.8% [28.7–81.5]	36.6% [13.8–70.4]	70.2% [28.7–81.5]	26.6% [13.8–70.4]	31.9% [18.9–47.0]	29.3% [16.3–44.6]	33.2% [23.7–43.5]	15.3% [1.7–37.5]
Specificity [95% CI]	75.9% [61.8–86.9]	80.4% [66.3–91.0]	86.0% [79.4–91.0]	89.2% [80.7–94.7]	71.4% [46.8–91.5]	92.8% [72.6–99.8]	85.7% [76.2–92.2]	89.3% [81.0–94.7]

[EP-10-190-01 Table 1: Sensitivity and specificity of FujiLAM and AlereLAM in HIV positive and HIV negative children using MRS and CRS]

We compared the performance of the new Fujifilm SILVAMP TB LAM™ (FujiLAM) and commercial Alere Determine™ TB LAM (AlereLAM) for diagnosis of childhood TB using urine samples.

Methods: Urine samples were collected from children (<15 years) with symptoms suggestive of TB prospectively recruited in The Gambia, Mali, Nigeria and Tanzania from January 2017 to December 2018. FujiLAM and AlereLAM tests were performed on all samples.

We estimated pooled sensitivity and specificity that account for heterogeneity across sites by performing bivariate random effects meta-analysis using microbiological reference standard (MRS), and a composite reference standard (CRS) of all children diagnosed with TB.

Results: Of the 415 children included (median age: 5.6 years [IQR 2.3-9.4]), 61 (14.7%) had confirmed TB, 115 (27.7%) had unconfirmed TB, 239 (57.6%) were unlikely TB and 61 (14.7%) were HIV positive. Using the MRS, FujiLAM demonstrated a sensitivity and specificity of 66.7% [95% CI 48.5 − 83.8] and 83.9% [95% CI 76.5 − 89.6] respectively, compared to AlereLAM's 31.7% [95% CI 9.9 − 60.8] and 87.9% [95% CI 79.1 − 93.8]. With the CRS, sensitivity and specificity of FujiLAM were 32.9% [95% CI 24.6 − 41.9] and 83.3% [95% CI 71.8 − 91.7] respectively, compared to 20.2% [95% CI 12.3 − 29.4] and 90.0% [95% CI 81.6 − 95.6] with AlereLAM.

Among HIV positive children, sensitivity and specificity of FujiLAM were 54.8% [28.7 − 81.5] and 75.9% [61.8 − 86.9] respectively using MRS, compared to AlereLAM with sensitivity and specificity of 36.6% [13.8 − 70.4] and 80.4% [66.3 − 91.0] respectively (Table 1).

Conclusions: FujiLAM showed promising results and may add important value for the diagnosis of childhood TB.

EP-10-191-01 Development of new format interferon-γ release assay, cost-effective and easy-to-use immunoassay for screening of tuberculosis infection

J-R Kim,[1] TS Shim,[2] HY Kang,[1] JH Je,[1] DH Choi,[3] HJ Kim,[1] [1]Korean Institute of Tuberculosis, Research & Development, Cheongju-si, Korea, Republic of, [2]University of Ulsan College of Medicine / Asan Medical Center, Department of Pulmonary and Critical Care Medicine, Seoul, Korea, Republic of, [3]Boditech Med Inc, Central Lab, R&D Center, Chuncheon-si, Korea, Republic of.
e-mail: cdh@boditech.co.kr

Background: The identification of latently infected individuals is an important component for the elimination of tuberculosis (TB). There are two main tests, the tuberculin skin test (TST) and the interferon-gamma (IFN-γ) release assays (IGRAs) for the diagnosis of latent TB infection. IGRA has higher specificity than TST. Commercial IGRAs require high cost and complex methods to measure IFN-γ. To solve these problems, we have developed a new type of IGRA, cost-effective and easy-to-use rapid assay. The new IGRA consists of tube set (Nil, antigen, Mitogen), fluorescent immunoassay (FIA) detection system, and lateral flow assay (LFA) to measure IFN-γ.

Methods: The new antigen tubes were prepared using synthesized peptides derived from the sequence of CFP-10 and ESAT-6. The tube set and the LFA were evaluated in study participants including latently infected individuals and active TB patients and their results were compared to QuantiFERON-TB Gold In-tube (QFT-GIT) or QuantiFERON-TB Gold plus (QFT-plus).

Results: The pattern of IFN-γ production by the new antigen tube compared to the antigen tube of QFT-GIT showed equivalent potency in 155 study participants, mainly including TB laboratory workers. Using the ELISA (cut off, 0.35 IU/ml), the concordance between the new antigen and the antigen of QFT-GIT was 94.6%. In 53 participants, including active TB patients, the ability to measure IFN-γ of FIA based on LFA was also similar to that of ELISA. The overall percent agreement between FIA based on LFA and ELISA of QFT-plus was 96.2%.

Conclusions: Measurement of IFN-γ responses by FIA based on LFA is much simpler and faster (within 15 minutes) compared to the current conventional tests. It may

be particularly beneficial in resource-limited places that require cost-effective laboratory diagnostics. This study suggests that the new type of IGRA can be more conveniently applied to diagnose TB infection.

EP-10-193-01 Comparison of diagnostic sensitivity of different immunological tests in tuberculosis (TB) diagnosis

A Starshinova,[1] A Panteleev,[2] V Zhuravlev,[3] I Dovgaluk,[4] P Yablonskiy,[5,6] [1]St. Petersburg State University, Laboratory of Mosaic of Autoimmunity, St. Petersburg, Russian Federation, [2]First Pavlov State Medical University of Saint Petersburg of the Ministry of Health of Russian Federation, Phthisiopulmonology, St. Petersburg, Russian Federation, [3]Research Institute of Phthisiopulmonology, Laboratory, St. Petersburg, Russian Federation, [4]Research Institute of Phthisiopulmonology, Phthisiopulmonology Department of Children, St. Petersburg, Russian Federation, [5]Research Institute of Phthisiopulmonology, Director, St. Petersburg, Russian Federation, [6]St. Petersburg State University, Medical Faculty, St. Petersburg, Russian Federation.
e-mail: starshinova_777@mail.ru

Background: Developing of new immunological tests (DST tests, IGRA tests) over the last years allows benchmarking study of all methods, including tuberculin skin test, to be carried and allows to find the most informative tests for LTB diagnosis.
Main objective: To compare diagnostic significance of immunological tests (tuberculin skin test (TST), TB recombinant allergen test (Diaskintest (DST)), QuantiFERON TB Gold, and ELISPOT) in TB diagnosis.
Methods: During 2014-2015, follow-up study was conducted that included 949 patients from 1 to 65 years old with suspected pulmonary and intrathoracic lymph node TB. Patients were examined by QuantiFERON TB Gold (QFT) and ELISPOT.
Furthermore all subjects passed TST and DST. Patients were divided into five groups: I group (n=55) - pulmonary TB (TB bacteria (+)); II group (n=295) - pulmonary TB without bacterial excretion; III group - (n=69) - TB and HIV. Also there were two groups of comparison - patients with HIV (IV) (n=50) and healthy subjects with positive results of TST (V) (n=329).
Results: TB patients demonstrated comparable amount of positive results with slight ELIPSOT superiority (89,2%), in QFT (74.5%) and DST (72.7%). All tests (DST, QFT, ELISPOT) demonstrated comparable diagnostic value (87.9%, 86.2%, 89.7%) with exception of TST (58.8%).
Diagnostic sensitivity of IGRA-tests in TB diagnosis on the background of HIV is significantly lower than without HIV (ELISPOT (69.1% against 97.1%); QFT (61.3% against 76.5%)).
More significant differences in diagnostic sensitivity were observed for in vitro tests (DST test (11.9% against 79.4%) ($p<0.001$).
Conclusions: Study data shows that all immunological methods are comparable by their sensitivity in TB diagnosis. Even ELISPOT` displays higher levels of sensitivity, its results can be compared with DST, QFT and TST.

EP-10-194-01 Plasma cytokines as biomarkers for diagnosis and monitoring therapeutic responses in paediatric tuberculosis

PK Nathella,[1] S Hissar,[2] V Banurekha,[2] S Kalpana,[3] J Ganesh,[4] D Baskaran,[2] S Swaminathan,[5] S Babu,[1,6] [1]National Institutes of Health-National Institute for Research in Tuberculosis - International Center for Excellence in Research, ICER-Immunology, Chennai, India, [2]National Institute for Research in Tuberculosis, Department of Clinical Research, Chennai, India, [3]Institute of Child Health and Hospital for Children, Pediatrics, Chennai, India, [4]Government Stanley Medical College and Hospital, Department of Pediatrics, Chennai, India, [5]World Health Organisation, Department of Digital Health, Geneva, Switzerland, [6]NIAID-NIH, LPD, Bethesda, MD, United States of America.
e-mail: pavankumarn@nirt.res.in

Background: Pediatric tuberculosis (TB) is estimated to constitute approximately 20-40% of the TB caseload in high-burden countries. There is also a greater challenge in confirming the diagnosis of pediatric TB due to the paucibacillary nature of TB disease in children.
However, progress toward a robust point-of-care test has been limited, and novel biomarker discovery remains challenging. Hence, this study evaluated the plasma cytokines as biomarkers in paediatric tuberculosis and the response to anti-tuberculosis therapy (ATT).
Methods: Children who were microbiology positive (confirmed TB) or those negative (unconfirmed TB) for M.TB but with symptoms that suggested tuberculosis were studied at baseline and at the end of ATT. Multiplex ELISA was performed to examine the systemic levels of Type 1 (IFNγ, IL-2 and TNFα), Type 17 (IL-17A and IL-22), other pro-inflammatory (IL-6, IL-12, GM-CSF IL-1a and IL-1β) and anti-inflammatory (IL-4, IL-5, IL-13 and IL-10) cytokines in these children along with latent TB infected (LTBI) and uninfected children as healthy controls (HC).
Results: Plasma levels of IFNγ, TNFα, IL-2, IL-17, IL-22, IL-1α, IL-6, and IL-10, were statistically significant and found higher in confirmed TB and unconfirmed TB in comparison to individuals with LTBI and HC. Receiver operating characteristics curve analysis revealed that IFNγ, IL-2, TNFα, IL-17A, IL-22 and IL-10 can act as markers distinguishing TB disease from LTBI and HC.
Moreover, IFNγ, IL-2, TNFα, IL-22, IL-1β, IL-6 and IL-10, levels were significantly higher in TB group with abnormal chest X-ray compared to normal X-ray. Finally, the plasma levels of IFNγ, TNFα, IL-2, IL-17, IL-22, IL-1α, IL-1β and IL-6 exhibited a significant two-fold reduction following ATT.

Conclusions: Our data demonstrate that paediatric TB is characterized by elevated levels of Type 1, Type 17 and other pro-inflammatory cytokines, suggesting that factors mentioned above could serve as accurate immune biomarkers for diagnosis and monitoring therapeutic responses.

EP-10-195-01 Structural switching electrochemical DNA aptasensor for the rapid diagnosis of tuberculous meningitis

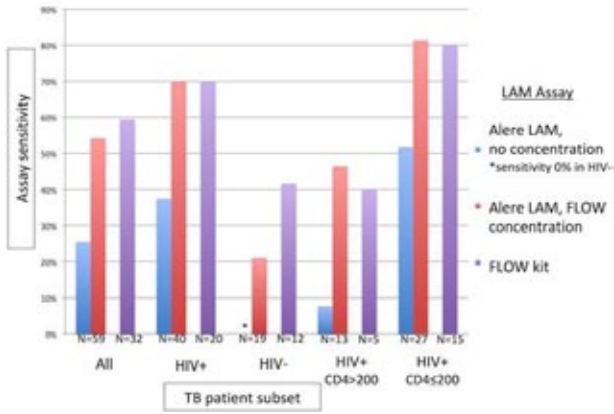
TK Sharma,[1] R Das,[2] A Dhiman,[3] SK Mishra,[4] S Haldar,[1] N Sharma,[5] A Bansal,[5] Y Ahmad,[6] A Kumar,[4] JS Tyagi,[3] [1]Translational Health Science and Technology Institute, Centre for Biodesign and Diagnostics, Faridabad, India, [2]AptaBharat Innovation Pvt. Ltd., R & D, Faridabad, India, [3]AIIMS, Biotechnology, New Delhi, India, [4]IIT Indore, Bioscience and Biomedical Engineering, Indore, India, [5]Dr Ram Manohar Lohia Hospital, Biochemistry, New Delhi, India, [6]Uttarakhand Technical University (UTU), Pharmacy, Dehradun, India. e-mail: tarun@thsti.res.in

Background: Tuberculous meningitis (TBM) is the most devastating manifestation of extrapulmonary tuberculosis. About 33% of TBM patients die due to very late diagnosis of the disease. Conventional diagnostic methods based on signs and symptoms, cerebrospinal fluid (CSF) smear microscopy or liquid culture suffer from either poor sensitivity or long turnaround time (up to 8 weeks). Therefore, in order to manage the disease efficiently, there is an urgent and unmet need for a rapid and reliable diagnostic test.
Methods: In the current study, to address the diagnostic challenge of TBM, a highly rapid and sensitive structural switching electrochemical aptasensor was developed by combining the electrochemical property of methylene blue (MB) with the molecular recognition ability of a ssDNA aptamer. To demonstrate the clinical diagnostic utility of the developed aptasensor, a blinded study was performed on 81 archived CSF specimens using differential pulse voltammetry.
Results: The electrochemical aptasensor developed in the current study can detect as low as 10 pg HspX in CSF background and yields a highly discriminatory response (P,0.0001) for TBM and not-TBM categories with ~95% sensitivity and ~97.5% specificity and has the ability to deliver sample-to-answer in ~30 minutes.
Conclusions: In summary, we demonstrate a new aptamer-based electrochemical biosensing strategy by exploiting the target-induced structural switching of H63 SL-2 M6 aptamer and electroactivity of aptamer-tagged MB for the detection of HspX in CSF samples for the diagnosis of TBM. Further, the clinical utility of this sensor could be extended for the diagnosis of other forms of tuberculosis in the near future.

EP-10-196-01 A point-of-care test to concentrate and detect urine LAM for TB diagnosis: results from the first in-human study of FLOW-TB

AE Shapiro,[1] T Wittwer,[2] NW Ngwane,[3] ZP Magcaba,[3] B Mullins,[2] R Aamotsbakken,[2] S Berry,[2] DJ Beebe,[2] DPK Wilson,[3,4] PK Drain,[1] [1]University of Washington, Global Health and Medicine, Seattle, WA, United States of America, [2]Salus Discovery, Madison, WI, United States of America, [3]Umkhuseli Research and Innovation Management, Pietermaritzburg, South Africa, [4]University of KwaZulu-Natal, Edendale Hospital, Pietermaritzburg, South Africa. e-mail: aeshapir@uw.edu

Background: There is a critical need for rapid, non-sputum-based diagnostic tools for TB. Persons with active TB shed lipoarabinomannan (LAM), a mycobacterial glycolipid, into urine. Sensitivity of existing assays to detect LAM is limited, in part due to testing small amounts of urine. An assay that concentrates and detects LAM from larger volumes of urine may improve diagnostic sensitivity.
Methods: We developed the FLOW TB assay as a two-step process to concentrate LAM from urine using antibody capture from passive flow, then elute concentrated LAM for read-out on a lateral flow assay (LFA). We collected urine from South African adults with Xpert-confirmed TB within 72 hours of TB treatment initiation. We tested urine with Alere Determine TB-LAM (Alere-LAM) before and after FLOW concentration, and separately with an integrated FLOW concentration and FLOW LFA (FLOW kit). We determined the sensitivity of each method compared to the reference standard of a positive Xpert-MTB/RIF test.
Results: 59 TB-positive adults (51% men; median age 40 (IQR 31-52) years) including 40 HIV-positive (median CD4 93, [IQR 42-330]) and 19 HIV-negative adults provided urine samples. Alere-LAM was positive in 15/59 (25%) specimens. Using FLOW to concentrate urine increased diagnostic sensitivity of Alere-LAM from 0% to 21% among HIV-negative adults, and from 38% to 70% among HIV-positive adults. The FLOW kit detected LAM in 19/32 (59%) specimens tested. Overall, the FLOW kit detected LAM in 42% (HIV-negative) and 70% (HIV-positive) persons. Sensitivity of all assays was higher in persons with lower CD4 counts; the FLOW kit was 80% sensitive in persons with CD4< 200.



[Diagnostic sensitivity of urine LAM assays in TB+ patients, South Africa]

Conclusions: FLOW concentration increases the sensitivity of LAM detection by more than 2-fold. The FLOW kit has 70% sensitivity for TB in HIV-positive persons, making it an attractive candidate for a point-of-care TB test in high-HIV-prevalence settings.

POSTER DISCUSSION SESSION (PS)

PS-15-C11 Global education and training activities

PS-15-655-01 Does tuberculosis related operational research through SORT IT training contribute to policy and/or practice change? A retrospective cohort study

P Thekkur,[1,2] AMV Kumar,[1,2] S Satyanarayana,[1,2] AD Harries,[1,3] R Zachraiah,[4] [1]International Union Against Tuberculosis and Lung Disease (The Union), Centre for Operational Research, Paris, France, [2]The Union South East Asia Office (USEA), Centre for Operational Research, New Delhi, India, [3]London School of Hygiene and Tropical Medicine, LSHTM, London, United Kingdom, [4]World Health Organization, Special Programme for Research and Training in Tropical Disease (TDR), Geneva, Switzerland.
e-mail: pruthu.tk@theunion.org

Background: The Structured Operational Research Training IniTiative (SORT IT) simultaneously integrates training of public health professionals with implementation of operational research (OR). Participants enrolled in SORT IT courses have undertaken OR on topics prioritised by their national TB programmes. We aimed to determine the number and proportions of enrolled SORT IT participants with TB-related research, course completion rates and impact of their OR studies on policy and/or practice.
Methods: We conducted a retrospective cohort study using SORT IT monitoring data routinely collected by the SORT IT global partnership and archived at the Centre for Operational Research, The Union. The participant-wise details on OR proposals developed, the course completion and publication status are recorded in the database.
After 18 months of completion of SORT IT course, e-mail based self-administered survey form was sent to participants requesting for details on the influence of their research on policy and/or practice. The data censor date was 31st March 2019.
Results: Of the 640 participants enrolled in the 60 completed SORT IT courses, 282 (44%) developed 295 TB-related research proposals. Among them, 224 (79%) completed the SORT IT course and submitted 265 manuscripts. Of the 208 manuscripts submitted before 18 months of censor date, 193 (93%) have been published.
Policy impact of 190 (91%) out of 208 manuscripts were self-reported by the participants and 141 (74%) had contributed to change in either policy and/or practice. Changes to policy and/or practice ranges from as small as including a monitoring indicator at the institution level to change in diagnostic and treatment modalities globally.
Conclusions: Nearly three out of four OR studies on TB contributed to policy and/or practice change. The SORT IT model can be integrated within national TB programmes and can contribute to evidence-informed decision making.

PS-15-656-01 Overcoming knowledge and practice gaps in the global tuberculosis workforce: the ECHO experience in 12 countries

B Struminger,[1] NV Nhung,[2] MK Kimenye,[3] AS Adakun,[4] A Armistad,[5] D Fortune,[6] J Carter,[7] A Colorado,[8] N Kiria,[9] R Sarin,[10] [1]University of New Mexico Health Sciences Center, ECHO Institute and Department of Internal Medicine, Albuquerque, NM, United States of America, [2]Vietnam National Tuberculosis Program, National Lung Diseases Hospital, Hanoi, Viet Nam, [3]Ministry of Health, National Tuberculosis, Leprosy, and Lung Disease Program, Nairobi, Kenya, [4]Mulago National Referral Hospital, Department of Medicine, Kampala, Uganda, [5]University of New Mexico Health Sciences Center, ECHO Institute, Albuquerque, NM, United States of America, [6]New Mexico Department of Health, TB Prevention Program, Santa Fe, NM, United States of America, [7]Brown University, Warren Alpert Medical School, Pulmonary Medicine, Providence, RI, United States of America, [8]Americas TB Coalition, Patient Advocacy, San Diego, CA, United States of America, [9]National Center for Tuberculosis and Lung Disease, Office of the Director, Tblisi, Georgia, [10]National Institute of Tuberculosis and Respiratory Diseases, Office of the Director, New Delhi, India.
e-mail: bstruminger@salud.unm.edu

Background and challenges to implementation: With approximately one third of the world population infected with tuberculosis (WHO, October 2017), countries burdened by TB need to adapt effective strategies to combat TB in their local context. One similarity throughout all contexts is the need for continuous professional development and training of TB health workers in evidence-based best practices to meet the demands of TB elimination globally.
Intervention or response: An increasing number of TB programs around the world are implementing Project ECHO [Extension for Community Healthcare Outcomes] virtual communities of practice to build the capacity of their workforce to identify, care and treat persons with TB. The ECHO tele-mentoring model is a cost effective, time efficient, low-dose, high-frequency, evidence-based education and training intervention designed to strengthen the knowledge and practice of clinical and programmatic teams in underserved communities. The learner-centered model supports development of case-based virtual communities of practice and learning that connect national and international experts

with site level TB practitioners for workforce development and collaborative problem solving to improve quality of and access to care.

Results and lessons learnt: Within four years, 12 countries have successfully implemented more than 25 TB ECHO programs: Viet Nam (2), the United States (8), Georgia (2), Guatemala (1), Panama (1), Honduras (1), Kenya (3), India (6), Mozambique (1), Namibia (1), Uganda (1) and Tanzania (1). The programs focus on drug resistant TB, TB Data 4 Action, Pediatric TB, TB Infection, TB/HIV, TB Advocacy, and TB nurse case management. Thirteen of the 25 programs have conducted 361 ECHO sessions and attracted almost 8,000 attendees.

Conclusions and key recommendations: The ECHO model's growing uptake and continuous implementation of more than 25 programs supporting TB workforce capacity building in 12 countries across four continents illustrates its adaptability and sustainability in a wide variety of contexts; the sustainability is due in large measure to its cost-effectiveness, time efficiency, and responsiveness to learner needs.

PS-15-657-01 On-site trainings and evaluation of tuberculosis (TB) control activities in Turkey: TB field teams programme

F Kara,[1] E Kabasakal,[2] S Ozkan,[3] S Gogen,[2] A Yildirim,[2] S Ozkara,[4] [1]Ministry of Health, General Directorate of Public Health, Ankara, Turkey, [2]Ministry of Health, General Directorate of Public Health, Department of TB, Ankara, Turkey, [3]Ministry of Health, Ankara Provincial Health Directorate, Yenimahalle Camlica Family Health Center, Ankara, Turkey, [4]Ataturk Chest Diseases Hospital, Tuberculosis Clinic, Ankara, Turkey.
e-mail: suozkan@gmail.com

Background and challenges to implementation: The program planned to evaluate and identify deficiencies of tuberculosis(TB) control activities for providing essential on site trainings of health workers. Since central trained work force was inadequate, expert volunteers recruited all across the country, trained on communication, conflict management, problem solving, life coaching and leadership.

Intervention or response: TB field teams formed following five-days of interactive trainings of 82 participants. TB Department representatives, chest diseases specialists, microbiologists, dispensary physicians and health workers took part in teams. Considering the size, population and number of registered TB patients of the provinces, 3 to 5 days of on-site evaluations and training carried out by various numbers of teams. The program funded by Ministry of Health. Field teams visited provincial health directors, TB control units, medical faculties, hospitals, TB laboratories, family physicians and identified current situation, provided required trainings and recommendations on-site within a specific program. Additionally, the teams visited randomly selected TB patients at their homes, interviewed with opinion leaders, visited refugee camps if available. Obtained information discussed and reported by team members each day. Finally, a feedback meeting held with all the stakeholders and reported to the Ministry of Health.

Results and lessons learnt: Total 1264 units visited, 3824 health workers trained on-site within 25 provinces between 2016 and 2018. Considering 81 provinces; the population of the visited 25 provinces corresponds to 58% of country population and number of registered TB patients corresponds to 65% of total registered TB patients in Turkey.

Conclusions and key recommendations: By knowledge and experience transfers of expert teams, some false practices corrected, motivations of the field health workers increased, deserved importance to TB by provincial directors ensured. As there could be various province-specific needs, diverse and specified interventions provided to each province such as combining TB units in idle status, improving bacteriological examination at provincial level. Good practices shown as examples to other provinces.

PS-15-658-01 Tuberculosis infection control knowledge and attitudes of healthcare workers, China

C Zhang,[1] SE Smith,[2] H Guo,[3] ML Pearson,[2] PA Jensen,[2] J Cheng,[1] [1]Chinese Center for Disease Control and Prevention, National Center for Tuberculosis Control and Prevention, Beijing, China, [2]US Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis, Atlanta, GA, United States of America, [3]US Centers for Disease Control and Prevention, Division of Global Health Protection, Beijing, China. e-mail: zhangcy@chinacdc.cn

Background: Effective implementation of proven TB infection control (TBIC) measures is the primary strategy to prevent TB transmission in healthcare settings. Inadequate knowledge and misconceptions about TBIC among healthcare workers (HCWs) may result in poor adherence to recommended measures. Before implementing a comprehensive quality improvement program, using the TB Building and Strengthening Infection Control Strategies (TB BASICS) model, we wanted to understand HCWs' knowledge and attitudes regarding TBIC.

Methods: In December 2017, we administered a survey to HCWs at nine TB-designated facilities in six provinces of China as part of the baseline assessment. Knowledge was assessed using 11 multiple-choice questions; nine attitudes regarding TBIC were assessed using a 4-point Likert scale. Demographic and job information were collected. Descriptive statistics were used to summarize responses.

Results: Of 3584 HCWs offered the survey, 3293 (91.9%) responded. Respondents had a median age of 31 years (IQR: 26-39); 2514 (76.6%) were female and 2457 (74.7%) were physicians or nurses (25.9% and

48.8%, respectively). The average knowledge score was 60.5%; 81.8% of HCWs responded that TB was transmitted by droplets, rather than airborne (18.5%). The vast majority of HCWs felt that they had a good understanding of the facility's IC policies and that they had been adequately trained in IC measures. However, 58% felt they had a limited role in improving TB IC at their facility. There was a general sense of workplace health and safety, but 96.2% would not report their TB symptoms to anyone at the facility (Table).

Conclusions: HCWs felt they were adequately trained in, and understood, TB IC policies and procedures, but actual TBIC knowledge and perceived self-efficacy were low. Ongoing training and supportive mentorship are needed to address critical knowledge gaps and misconceptions that may negatively affect HCW's adherence to precautions needed to prevent TB transmission in healthcare facilities.

Statement	Agree/Strongly agree
I believe my health facility is concerned about my health and safety	91.1%
I believe I have a good understanding of my health facility's infection control policy	94.1%
If I develop symptoms of TB, I would not tell anyone at work	96.2%
I have been adequately trained in infection control measures by my facility	91.1%
I think our patients will resist wearing a surgical mask, so I don't offer it or ask them to wear one	6.5%
This facility is adequately equipped to safely take care of TB patients	85.3%
My facility has put measures in place to protect me from TB	82.3%
I feel comfortable educating patients about TB and how to prevent TB spread	97.8%
I feel I have a limited role in improving TB IC at this facility	58.3%

[Attitudes of HCWs toward TBIC, China]

PS-15-659-01 Engaging private sector providers through group and one-to-one sensitisation in India

D Livingstone,[1] A Victor,[1] [1]World Vision India, Health, Chennai, India. e-mail: david_livingstone@wvi.org

Background and challenges to implementation: TB diagnosis and treatment in the Indian healthcare system is quite diverse and complex made up of many types of care providers in public and private sectors. Studies suggest that nearly 80% of the first-contact health care and about 50% of TB care occurs in the private sector. The private sector has been the center of attention for TB interventions in the country and multiple ways to engage and support the private sector have been taken up by the RNTCP.

Intervention or response: In order to increase the uptake of notification among private providers, sensitization clinics were conducted for private practitioners. Practitioners who did not make it to sensitization clinics were sensitized in person. Sensitization and notification details of 1353 practitioners engaged by the project from 67 cities were obtained and the data analysed. Later 337 practitioners (245 Notifying and 92 not notifying) were interviewed to understanding barriers and enablers for notification.

Results and lessons learnt: It was noticed that 472 of the 1214 previously non notifying practitioners started notifying. Therefore sensitization helped increase notification among practitioners by 339%.

The type of sensitization among currently notifying practitioners showed 24% were sensitized in a group, 69% were sensitized 'one to one' and 7% had both types of sensitization. Among the 742 practitioners who are currently not notifying the type of sensitization showed 99.5% (n=739) were sensitized in a group.

The most reported barrier to notification was lack of man power. The highest enablers for notification were social responsibility and dedicated follow up by project staff.

Conclusions and key recommendations: Sensitization clinics or CME's can help increase knowledge on TB and its treatment guidelines but may not necessarily translate in increase in notification. Repeated follow up with the provider in addition to sensitization clinics/CME is required to create a behavior change.

PS-15-660-01 Impact of educational intervention on knowledge and awareness of TB among secondary school students in The Gambia

OA Owolabi,[1] S Njie,[1] A Touray,[1] MI Gibba,[1] S Barry,[1] A Tunkara,[1] M Davies,[1] S Donkor,[1] TO Togun,[2] J Sutherland,[1] [1]Medical Research Council Unit Gambia at the London School of Hygiene and Tropical Medicine, Vaccine and Immunity, Banjul, Gambia, [2]London School of Hygiene & Tropical Medicine, Clinical Research, Faculty of Infectious Diseases, London, United Kingdom. e-mail: oowolabi@mrc.gm

Background: Health education and awareness campaign about tuberculosis (TB) can empower youths on different aspects of the disease and its management, resulting in early and appropriate care seeking behaviour through their advocacy in the community. We assessed the impact of educational intervention on knowledge and awareness about TB among youths in the greater Banjul area (GBA) of The Gambia where approximately 70% of TB cases in the entire country are notified.

Methods: A school-based interactive educational workshop was conducted among grade twelve students of the Methodist Academy Secondary School in Bakau, Banjul The Gambia. The workshop activities included illustrative demonstrations using posters, flipcharts, infographics, and fun games to convey TB messages in six domains namely:

1. basic knowledge;
2. symptoms;

3. risk factors
4. modes of transmission; and
5. treatment;
6. Care and support.

Structured questionnaires were used to assess changes in the student's knowledge and awareness about TB in the five domains before and after the workshop. Data were analysed using descriptive statistics and student paired t-test.

Results: Ninety-six students participated in the workshop out of which 92 (96%) students completed both pre- and post- test questionnaires. Sixty-eight percent of the students were females and 58% belong to the science class. The mean difference and standard error (SE) between the pre- and post-workshop test scores in the six domains are as follows: basic knowledge: +1.4 (0.2; p<0.0001); symptoms: +1.5 (0.2; p< 0.0001); risk factors: +3.1 (0.3; p< 0.0001); modes of transmission: +1.2 (0.2; p< 0.0001); treatment: +0.8 (0.1; p< 0.0001); and care and support of TB: +0.5 (0.1; p= 0.0001).

Conclusions: This school-based educational interactive workshop significantly improved the knowledge and awareness of the students especially in understanding the risk factors of TB disease. We recommend exposure of students to TB educational activities as part of the school curriculum.

PS-15-661-01 Designing a TB operational research training programme: experience from the USAID Eradicate TB Project in Zambia

R Kumar,[1,2] J Bwembya,[1] M Makasa,[3] J Simbaya,[4] P Ndubani,[5] A Schaap,[2,6] V Makwambeni,[7] J Nikisi,[8] A Mwinga,[1] [1]Zambart, Eradicate TB Zambia, Lusaka, Zambia, [2]London School of Hygiene and Tropical Medicine, Department of Clinical Research, Faculty of Infectious Disease Epidemiology, London, United Kingdom, [3]University of Zambia School of Public Health, Department of Community and Family Medicine, Lusaka, Zambia, [4]University of Zambia, Institute of Economic and Social Research, Lusaka, Zambia, [5]Frontiers Development and Research Group, Department of Research, Lusaka, Zambia, [6]Zambart, Data/Statistics Unit, Lusaka, Zambia, [7]PATH Eradicate TB Zambia, Strategic Information, Lusaka, Zambia, [8]PATH Eradicate TB Zambia, Chief of Party, Lusaka, Zambia. e-mail: ramya.kumar.mlk@gmail.com

Background and challenges to implementation: In Zambia, there is inadequate public health workforce capacity in tuberculosis (TB)-related operational research (OR). The Eradicate TB Project (ETB) established an OR training program for National Tuberculosis and Leprosy Program (NTLP) district-level employees to generate evidence to improve TB care and control.

Intervention or response: In December 2017, ETB and the NTLP selected four district teams (18 trainees) from districts with high TB notification rates, high-risk catchment populations, and motivated TB staff. Each team included clinical and laboratory staff, and some included district- and provincial-level directors. Over one year, teams received intensive hands-on mentorship to develop a research proposal, analyze data, and write study reports. Teams underwent two 10-day training sessions during the year, employing learning-by-doing pedagogy. Proposals underwent multiple levels of key stakeholder, and ethical reviews over 8 months.

Results and lessons learnt: All trainees completed the course. Two OR projects successfully identified gaps in their local TB diagnostic and care cascades, one project identified reasons for low sputum sample referrals, and the fourth identified factors associated with unfavorable TB treatment outcomes. Challenges included limited computer, scientific writing, and data analysis skills, and little to no prior research exposure among trainees. This contributed to weak initial proposal drafts, a lengthy review process, and difficulty effectively integrating revisions in response to multiple reviewers. In teams which included directors, complicated intra-group dynamics existed because members felt uncomfortable challenging their supervisors.

Conclusions and key recommendations: This training program has been effective in building the skills of district-level staff to conduct locally-relevant service delivery research. To improve the quality of studies conducted, future training programs should consider using a competitive process to select candidates with prior exposure to research and strong writing skills. An additional workshop on framing a research question can strengthen initial proposals. Simultaneous stakeholder review of proposals could also help reduce the time spent to conduct the studies.

PS-15-662-01 Using family opinion leaders to promote tuberculosis knowledge among ethnic groups in Southern Xinjiang, China

M Wang,[1] [1]Xinjiang Medical University, Nursing, Urumqi, China. e-mail: 1005483572@qq.com

Background: Xinjiang Uyghur Autonomous Region in Northwest China is China's biggest province, encompassing one-sixth of the land of China. Xinjiang has higher rates of tuberculosis in China, especially southern Xinjiang. Southern Xinjiang is larger and poorer, including four main prefectures: Kashi, Hotan, Aksu and Kizilsu four prefectures. Southern Xinjiang has higher tuberculosis incidence rate than Northern Xinjiang. Lots of ethnic groups live in southern Xinjiang, such as Uyghur and Kyrgyz. Targeted and localized TB prevention and control strategy are needed to explore in southern Xinjiang.

Methods: In tradition Southern Xinjiang society, family opinion leaders usually play a key role in a family and have great influence on other family members. Xinjiang Chest Hospital is designated tuberculosis hospital. They provided 11 times of training or supervision on 3000

health providers in southern Xinjiang. Then trained health providers provided health education to the key family opinion leaders. Then They disseminated and communicated tuberculosis information with their family members. 2278 were selected from 47 counties of 4 prefectures in Southern Xinjiang to evaluate the training effectiveness.

Results: Among 2278 participants, 83.41% were peasants. After the intervention, the tuberculosis knowledge level was improved significantly (P<0.01) from 61.96% to 90.72% in Aksu Prefecture, from 66.22% to 95.62% in Kashi Prefecture, from 51.34% to 91.26% in Hotan Prefecture, and from 31.96% to 98.54% in Kizilsu Prefecture. The acceptance of tuberculosis health education by key family opinion leaders increased significantly (*P*<0.01) from 27.1% (pre-intervention) to 77.5% (post-intervention).

Conclusions: Family opinion leaders play a significant role in TB health education in Southern Xinjiang Uyghur Autonomous Region. After accepting training from local health providers, they can influence and promote their family members' TB knowledge effectively. Further behavior changes on seeking diagnosis, treatment adherence, or infection control should be monitored and evaluated.

PS-15-663-01 An online course on "management of tuberculosis" for doctors: our experience on a new venture

V Banurekha,[1] J Saraswathy,[1] MS Jawahar,[1] NS Gomathi,[2] M Natrajan,[1] R Rao,[3] S Tripathy,[4]
[1]ICMR-National Institute for Research in Tuberculosis, Department of Clinical Research, Chennai, India, [2]ICMR-National Institute for Research in Tuberculosis, Department of Bacteriology, Chennai, India, [3]Ministry of Health & Family Welfare, Central TB Division, New Delhi, India, [4]ICMR-National Institute for Research in Tuberculosis, Director-In-Charge of ICMR-NIRT, Chennai, India.
e-mail: saraswathi.nagala@gmail.com

Background: Massive open online courses (MOOC) has opened up a novel approach for training and education. Recognising the need to disseminate information on updates and guidelines on the management of TB in a timely manner to doctors providing care for tuberculosis (TB) patients, we explored the use of this technology and present our experience.

Methods: We designed and executed an online 8-week free course on the management of TB with technical support from National Programme for Technology Enhanced learning. The course comprised of modules on TB epidemiology, diagnosis, treatment, prevention and elimination, and included lectures, case discussions, video-demonstrations and weekly assignments.

The target audience was registered medical practitioners in public and private sector. Online examination was required for receipt of a course certificate. Data collected included age, gender, affiliation, number of years in practice and TB patients seen monthly. Course evaluation questionnaire was administered at the end of each week.

Results: Of 2280 participants who registered for the course 17% were from Tamilnadu and 10% from Uttar Pradesh. Of 1086(48%) participants for whom profiles were available 48% were from the private sector and 28% cared for >10 TB patients per month (Table). The course was completed with certificates awarded to 327(14%) participants. The average final score of the participants was 81%. Course evaluation feedback from 135 respondents revealed achievement of course objectives of improvement in knowledge and approach in management of TB with an average score of 4.6 out of 5, on a scale of 1(strongly disagree) to 5(strongly agree).

Conclusions: Our 8-week online course was favourably received by the target audience. Online courses on TB have the potential to reach out to large number of participants at a time and place convenient to them and can be a potent tool in disseminating information on guidelines and updates on the management of TB.

Characteristics		n (%)
Gender (n=1086)	Male	607 (56%)
Age group (n=1071)	<40 years	889 (83%)
Qualification (n= 1046)	Post graduate	670 (64%)
Place of practice (n=979)	Government	507 (52%)
	Private	472 (48%)
Number of years in practice (n=894)	< 5	390 (44%)
	5 to 10	300 (33%)
	> 10	204 (23%)
Number of TB patients seen per month (n=824)	1 to 10	594 (72%)

[Profile of Doctors who registered for the Online course on Tuberculosis]

PS-15-664-01 Adopting the Union/MSF model of OR training for capacity building in conducting systematic reviews and meta-analysis

K Sagili,[1] S Satyanarayana,[1] S Chadha,[2] P Tharyan,[3] J Tonsing,[1] [1]International Union Against Tuberculosis and Lung Disease, TB, New Delhi, India, [2]FIND India, AMR, New Delhi, India, [3]BV Moses Centre for Research and Training in Evidence-Informed Healthcare and Health Policy, Cochrane South Asia, Vellore, India. e-mail: ksagili@theunion.org

Background: Systematic literature review is essential for any scientific research and policy making. A large body of research is published every day with varying magnitude and the generalisability; hence evidence synthesis is essential for decision makers to guide in policy decisions. There are very few researchers in India who could conduct SRs, especially in the context of TB. Hence the objective was to build the capacity of researchers in India to conduct SRs for better TB care and prevention.

Methods: The Union is a flag bearer of Operational Research (OR) training across the globe, impacting public health policy and program delivery. Adopting 'The Union/MSF' model for OR training, The Union South East Asia office in collaboration with Cochrane South Asia and national TB program organised training on SR Protocol Development (2016) and SR Analysis Writing (2017). Similar to the OR course, milestones were set for the teams to submit their protocols, complete data extraction and analysis, writing the review. To ensure the teams meet the milestones, one Union staff was part of each group as a mentor or an investigator who would do the necessary follow up.
Results: A total of 20 participants were trained who formed six teams. A brainstorming exercise was undertaken with national TB program to prioritise research questions. Six questions were finalised and the teams went ahead to develop six SR protocols in 2016. Five protocols were registered in Prospero (open database) and one with Cochrane. Participants extracted data and analysed over the next 6-9 months. The reviews were completed in about 18 months. Four out of six reviews were published, one is under review (Figure 1).
Conclusions: Adopting and customizing the proven model of The Union/MSF OR training, built capacity of researchers in conducing SR with over 80% review completion.

S.No	Review title	Current status
1	Effect of insulin, with or without oral hypoglycemic agents, (compared to oral hypoglycemic agents only) and glycemic control, stringent or not stringent, (compared to no glycemic control) on unsuccessful TB treatment outcomes among patients with TB-diabetes: a systematic review.	Shewade HD, et al. (2017) Effect of glycemic control and type of diabetes treatment on unsuccessful TB treatment outcomes among people with TB-Diabetes: A systematic review. PLoS ONE 12(10): e0186697. https://doi.org/10.1371/journal.pone.0186697
2	Shortened treatment regimens with fluoroquinolones or rifamycins versus standard regimen for drug-sensitive pulmonary tuberculosis. Grace et al	Protocol published; review under way with Cochrane Grace AG et al (2018) Shortened treatment regimens versus the standard regimen for drug-sensitive pulmonary tuberculosis. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012918.DOI: 10.1002/14651858.CD012918
3	Cost-effectiveness study of GeneXpert and LED FM for diagnosis of pulmonary tuberculosis: A Systematic Review	Sagili KD, Muniyandi M, Nilgiriwala KS, Shringarpure KS, Satyanarayana S, Kirubakaran R, et al. (2018) Cost-effectiveness of GeneXpert and LED-FM for diagnosis of pulmonary tuberculosis: A systematic review. PLoS ONE 13(10): e0205233. https://doi.org/10.1371/journal.pone.0205233
4	Chemoprophylaxis for childhood contacts of drug resistant tuberculosis patients: a systematic review	Is Chemoprophylaxis for Child Contacts of Drug-Resistant TB Patients Beneficial? A Systematic Review C. Padmapriyadarsini et al Tuberculosis Research and Treatment Volume 2018, Article ID 3905890 https://doi.org/10.1155/2018/3905890
5	Short-course treatment regimens for multidrug-resistant tuberculosis: a systematic review and meta-analysis.	Review completed and submitted for publication. Under review
6	Evaluation of Public-Private Mix programs in Tuberculosis Care and Control in South Asia: A systematic review.	Partial Data collection and extraction done; waiting for local unpublished data . Currently this review is dormant.

[Figure 1. Review titles and current status of Systematic Review protocols]

PS-15-665-01 Predictor of correct knowledge of tuberculosis in South Africa

O Oladimeji,[1] L Makola,[1] K Zuma,[2] M Mabaso,[1] S Jooste,[3] R Tadokera,[4] S Takatshana,[2] J Chicovore,[1] I Naidoo,[1] S Moyo,[3] The Fifth South African National HIV Prevalence Incidence Behaviour and. Communication Survey (SABSSM V) [1]Human Sciences Research Council, Social Aspect of Public Health Program, Durban, South Africa, [2]Human Sciences Research Council, Social Aspect of Public Health Program, Pretoria, South Africa, [3]Human Sciences Research Council, Social Aspect of Public Health Program, Cape Town, South Africa, [4]Stellenbosch University, Division of Molecular Biology and Human Genetics, Cape Town, South Africa.
e-mail: ooladimeji@alumni.harvard.edu

Background: Correct TB knowledge is crucial in making informed choices to seek TB health help. Hence, our study explored predictor of correct knowledge of TB in South Africa.
Methods: We analyzed the 2017 South African national household HIV prevalence, incidence and behavior survey data based on a multistage cross-sectional design. We computed composite scores from the multiple TB knowledge responses and dichotomized into 0=inaccurate knowledge and 1=accurate knowledge of TB. Univariate and multivariate logistic regression models were used to analyze the relationship between the primary outcome and a set of socio-demographic and TB-related variables. Odds Ratio (OR) with 95% confidence intervals (CI) and p-value ≤ 0.05 are reported for factors significantly associated with correct knowledge of TB.
Results: Out of 44,675 sub-sample of the 15 years and older participants included in our analysis. Only 30.4% reported correct knowledge of TB. There was a significant positive relationship between correct knowledge of TB and those aged 20 -24 (OR:1.23, 95%CI: 1.07-1.41), p< 0.03), 25 - 49 years (OR:1.18, 95%CI: 1.06-1.31), p< 0.03), those who attained secondary education (OR:1.39, 95%CI: 1.24-1.56), p< 0.001), tertiary education (OR:1.39, 95%CI: 1.15-1.68), p< 0.001), those who were employed (OR:1.16, 95%CI: 1.06-1.27), p< 0.001), those who were reported that that have previously been told about that they had TB (OR:1.17, 95%CI: 1.00-1.37), p< 0.048), tested HIV positive (OR:1.15, 95%CI: 1.02-1.30), p< 0.021), good self-reported health status (OR:1.13, 95%CI: 1.00-1.28), p< 0.046). Having controlled for possible confounders, there was statistically significant between educational attainment and correct knowledge of TB. The main predictor of accurate knowledge of TB was secondary education (AOR: 1.42, 95%CI: 1.17-1.74, p=0.001).
Conclusions: Our findings provide insights for government and key TB stakeholders the need to strengthen the current interventions and explore other cost effective tailored initiatives on TB-related health awareness activities.

PS-15-666-01 Blended learning in the private sector in Uganda: a case study of tuberculosis (TB) capacity-building efforts for private health providers

R Makabayi-Mugabe,[1,2] S Zawedde-Muyanja,[2] R Kikonyogo,[3] WJ Arinaitwe,[3] M Nakazzi-Kweyamba,[1] E Katwesigye,[3] H Brightman,[4] A Ocero,[1] A Nkolo,[5]
[1]USAID/Defeat TB Project, Health Systems Strengthening, Kampala, Uganda, [2]Infectious Diseases Institute, Research Department, Kampala, Uganda, [3]Infectious Diseases Institute, Training Department, Kampala, Uganda, [4]University Research Co., LLC (URC), Programs, Maryland, WA, United States of America, [5]USAID/Defeat TB Project, Technical Department, Kampala, Uganda.
e-mail: makrita2@gmail.com

Background and challenges to implementation: The 2015 national TB prevalence survey showed that 37.3% of individuals with TB symptoms sought care in private facilities. 90% of those with TB symptoms were not screened. Engaging private health providers (PHP) is a key component in the End TB strategy and they need access to the best standards of prevention, diagnosis and treatment.

Intervention or response: A blended on-line interactive six-week TB management course was developed and implemented between June and July 2018 using the WHO International Standards for Tuberculosis Care. Pre-post assessments, course evaluations as well as follow-up facility-based mentorships to assess for knowledge translation and baseline site improvement monitoring system (SIMs) as a bench mark were carried out in September and October 2018. This intervention involved 22 PHP from 20 private health facilities in Kampala.

Results and lessons learnt: There was a marked improvement in the post-test scores of 71.5% compared to 42.7% pre-test, with an average knowledge gain of 28.8%. 90% found the course relevant and the sessions effective. 70% felt the facilitators were outstanding in terms of experience and facilitating sessions. Personal experiences were positive noting it as a convenient learning modality.

There was no documented evidence of knowledge translation at the health facilities. Other challenges were; limited human resource (2-4 staff on average), inadequate lab capacity, limited use of the hub system, inadequate documentation, no quality improvement initiatives, inadequate TB related supplies. Regarding SIMs, 3 facilities out of the 20 trained had at least TB screening, TB evaluation cascade and provider-initiated counselling and testing (PITC) for adults implemented while the rest of the domains were suboptimal.

Conclusions and key recommendations: Blended learning resulted into knowledge gain among PHP. The National TB and Leprosy Program (NTLP) should continue engaging the private sector and apply a deliberate and sustained comprehensive health systems strengthening approach to improve TB services in the private sector.

PS-15-667-01 Strengthening childhood TB diagnosis in Zimbabwe: roll-out of an intervention package in 21 priority districts

P Nzombe,[1] R Ncube,[1] C Zishiri,[1] T Mapuranga,[2] C Sandy,[2] [1]International Union Against Tuberculosis and Lung Disease (The Union), TB/HIV, Harare, Zimbabwe, [2]Ministry of Health and Child Care - Zimbabwe, AIDS & TB - National TB Programme, Harare, Zimbabwe.
e-mail: czishiri@theunion.org

Background and challenges to implementation: Although childhood tuberculosis (TB) is a major cause of disease and death in TB endemic countries it is underdiagnosed due to non-specific symptoms, the paucibacillary nature of the disease, a lack of accurate diagnostic tools and limited health worker confidence and skills to collect specimens. Childhood TB (< 15 years) is estimated to account for 10% of all notified TB patients in Zimbabwe; however the country has been recording less than this proportion.

Intervention or response: In 2015, the Zimbabwean National Tuberculosis Control Programme, with support from the International Union Against Tuberculosis and Lung Disease (through the Challenge TB project), conducted a situational analysis to assess the quality of childhood TB diagnosis and treatment services in the country. Results from the analysis informed the development of the childhood TB intervention package. This included training for community and facility-based healthcare workers and procurement of childhood TB diagnostic consumables. In addition, it supported the development of guidelines and training materials, as well as information, education and communication (IEC) materials. In 2018, the intervention package was implemented in 21 districts in Zimbabwe with low TB notification rates and low treatment success rates.

Results and lessons learnt: There was an increase in the number of children diagnosed with TB in the 21 districts, from 285 in 2017 (before implementation of the package), to 333 in 2018 (after the intervention). This represents an increase of 16.8%.

Conclusions and key recommendations: Capacity building of facility-based and community healthcare workers, using guidelines, training and IEC materials, is important in strengthening TB diagnosis among children. Diagnostic tools and consumables should also be made available at all health facilities.

PS-16-B1 Optimising diagnostic tools in predictive TB

PS-16-668-01 Spoligotyping improves detection of M. tuberculosis complex in induced sputum from children in The Gambia

A Ayorinde,[1] A Mendy,[2] E Coker,[3] M Wathuo,[1] AK Sillah,[1] F Mendy,[3] U Egere,[4] B Kampmann,[5] L Tientcheu,[5] [1]Medical Research Council Unit Gambia @ London School of Hygiene and Tropical Medicine, Vaccines and Immunity, Banjul, Gambia, [2]Medical Research Council Unit Gambia @ London School of Hygiene and Tropical Medicine, Disease Control and Elimination, Banjul, Gambia, [3]Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Vaccines and Immunity, Banjul, Gambia, [4]Liverpool School of Tropical Medicine, Paediatrics, Liverpool, United Kingdom, [5]Medical Research Council at London School of Hygiene and Tropical Medicine, Vaccines and Immunity Theme, Banjul, Gambia.
e-mail: aayorinde@mrc.gm

Background: Diagnosing Tuberculosis (TB) in children remains a great challenge because they are often paucibacillary and unable to produce good sputum. Previous studies have demonstrated that direct spoligotyping of decontaminated sputum from adult is capable to identify the infecting *Mycobacterium tuberculosis complex* (MTBC) strain. We tested whether spoligotyping on decontaminated induced sputum from children in The Gambia will improve of MTBC and correlated the results to the different categories defined by conventional diagnosis as confirmed, probable and not-TB children cases.

Methods: A total of 115 induced sputa from children were processed using smear microscopy, GeneXpert and liquid mycobacteria growth indicator tube (MGIT) culture. Boiled lysate DNA extraction and Spoligotyping analysis was done on decontaminated sputum to assess the sensitive of this method in detecting MTBC presence in children samples.

Results: Of the 115 samples that were analysed by spoligotype, 29 (25%) were ''confirmed TB'', 42 (37%) were ''probable TB'' and 33 (28%) were ''Not TB'' cases, 11 (10%) had no clinical definition. For each routine diagnostic lab methods used, only 4/115 (3%) were smear positives; 18/115 (15%) Xpert positives; 13/115 (11%) culture positives and 111/115 (96%) spoligotype positives. All routine positives TB were from ''confirmed TB'' children.

However, spoligotype detected more positive TB children in ''confirmed TB'' 28(24%); ''probable TB'' 40(34%) and ''not-TB'' 33(28%). The majority of infecting lineages was Euro-American 42 (36%), and *M. africanum* West African type2 12 (10%), Indo-Oceanic 14 (12%), and East African Indian 6 (5%), East Asian Beijing 3 (3%) and Negatives 4 (3%).

Conclusions: Our results provide evidence that spoligotyping can be used to detect MTBC directly in children induced sputum with higher sensitivity but poor specificity. Further studies are required to assess whether the high rate of MTBC positive sputum in Not-TB children reflect an active disease or latent infection and their impact on transmission.

PS-16-669-01 Early CD4+ T-cell responses to PPD and CFP-10 predict recent M. tuberculosis infection

E Wahren Borgström,[1,2] G Fröberg,[1,2] M Correia-Neves,[1,3,4] F Atterfelt,[5] J Bellbrant,[2] R Szulkin,[6,7] E Chryssanthou,[8] P Andersen,[9] G Källenius,[1] J Bruchfeld,[1,2] [1]Karolinska Institutet, Infectious Diseases, Medicine Solna, Stockholm, Sweden, [2]Karolinska University Hospital, Infectious Diseases, Stockholm, Sweden, [3]University of Minho, School of Medicine, Life and Health Sciences Research Institute (ICVS), Braga, Portugal, [4]PT Government Associate Laboratory, ICVS/3B's, Braga/Guimarães, Portugal, [5]Public Health Agency of Sweden, Department of Microbiology, Stockholm, Sweden, [6]Karolinska Institutet, Family Medicine, Department of Neurobiology, Stockholm, Sweden, [7]Scandinavian Development Services, Statistics, Danderyd, Sweden, [8]Karolinska University Hospital, Department of Clinical Microbiology, Stockholm, Sweden, [9]Statens Serum Institute, Department of Infectious Disease Immunology, Stockholm, Sweden.
e-mail: gabrielle.froberg@sll.se

Background: Interferon-γ release assays QuantiFERON-TB Gold and T-SPOT.TB cannot differentiate active, latent or past tuberculosis, nor identify individuals with latent infection and increased risk of progression to active disease, such as recent infection.

The objective of this work was to identify biomarkers of recent infection following exposure to pulmonary tuberculosis to increase the positive predictive value for incipient TB.

Methods: Contacts of pulmonary tuberculosis were tested repeatedly with interferon-γ release assays and flow-cytometry. Proliferative $CD4^+$ T cell responses to antigens CFP-10, ESAT-6, Rv251c, Rv0287, Rv0288, Rv1120c, Rv1284, Rv2659c, Rv2710, Rec85a and Rec85b and purified protein derivative (PPD) were analysed. Patients with pulmonary tuberculosis and individuals with no exposure were used as controls.

The individual probability of recent and remote infection was estimated using a novel mathematical model and compared with $CD4^+$ T cell responses in a prediction model.

Results: The most specific prediction of recent infection was an early high $CD4^+$ T cell response to CFP-10 and PPD and a low $CD4^+$ T cell response to ESAT-6. High $CD4^+$ T cell responses to Rec85a, Rec85b and Rv1284 were also observed in recent infection, but did not distinguish recent from remote infection with the predic-

tion model. Proliferative responses to Rec85b were reduced in patients with active tuberculosis as compared to IGRA positive contacts.
Conclusions: Early high CD4+ T cell responses to CFP-10 and PPD and low responses to ESAT-6 may be used as biomarkers to improve positive predictive values for recent infection and thus, increased risk of incipient TB. Rec85a, Rec85b and Rv1284 are also of interest to study further in this context.

PS-16-670-01 Evaluation of novel antigens for immunodiagnostic tests of childhood tuberculosis infection: the CITRUS (ChIldhood TubeRcUlosis in Switzerland) study

NR Meier,[1,2] T Sutter,[3] M Jacobsen,[4] T Ottenhoff,[5] JE Vogt,[6] N Ritz,[2,7,8] Sara Bernard-Stirnemann Lisa Kottanattu Andrea Duppenthaler Marie Rohr Isabelle Rochat Michael Büttcher Jürg Barben Christoph Berger [1]University of Basel, Faculty of Medicine, Department of Clinical Medicine, Basel, Switzerland, [2]University Children's Hospital Basel, Mycobacterial Research, Basel, Switzerland, [3]ETH Zurich, Department of Computer Science, Zurich, Switzerland, [4]Children's University Hospital Düsseldorf, Department of Pediatrics, Düsseldorf, Germany, [5]University of Leiden, Department of Infectious Diseases, Leiden, Netherlands, [6]ETH, Department of Computer Science, Zurich, Switzerland, [7]University of Basel, Faculty of Medicine, Basel, Switzerland, [8]The Royal Children's Hospital Melbourne, Department of Pediatrics, Melbourne, VIC, Australia. e-mail: noemi.meier@ukbb.ch

Background: Microbiological methods are unable to confirm tuberculosis (TB) disease in all children. Immunodiagnostic tests have the potential to improve diagnosis of children with TB but the currently used interferon gamma release assays (IGRA) have limited sensitivity in children and are unable to distinguish between TB infection and TB disease. The aim of this study was to find novel antigens and cytokines that improve immunodiagnosis of TB.
Methods: Whole blood from children undergoing evaluation for TB exposure, infection or disease was stimulated overnight with the positive controls staphylococcal enterotoxin B and phytohemagglutinin, with classical IGRA early secretory antigenic target (ESAT)-6/culture filtrate protein (CFP)-10 fusion protein, and with 10 novel *Mycobacterium tuberculosis (*M.tb*)* antigens, or left unstimulated. Production of 11 cytokines was measured in supernatant using Luminex technology. We used different machine learning algorithms to discover patterns in cytokine production.
Results: A total of 105 children have been recruited with a median age of 8.4 years and 54% male participants. Samples from 80 children were included in this analysis grouped as follows: confirmed TB disease (n=15), unconfirmed TB disease (n=5), TB infection (n=28) and TB-exposed healthy controls (n=32). Generally, median cytokine production among study groups varied more for IL-6, IP-10 and TNF-α compared to GM-CSF, IFN-γ, IL-1RA, IL-2, IL-10, IL-13, IL-17 and sCD40L (Figure: heat map of median cytokine production from normalized data between all study groups for antigens vs. cytokines; blue to yellow = increasing difference). IV1/2 (Rv2346/47, Rv2431) induced IP-10 concentrations showed better distinction of groups compared to ESAT-6/CFP-10 induced IFN-γ concentrations.
Conclusions: This is the first study investigating a large number of novel M.tb antigens for use in TB diagnostics in children. A set of recently discovered in-vivo expressed M.tb antigens show improved potential of discriminating between healthy, TB-infected and TB-diseased children compared to the standard reference. Further analysis is in progress.

PS-16-671-01 Haematological profile and the ratio of monocytes to lymphocytes in children with tuberculosis

S Hissar,[1] M Kannan,[2] A Venkatraman,[2] T Kannan,[3] NS Gomathi,[4] S Anbalagan,[2] A Studhi,[1] L Hanna,[2] V Banurekha,[1] S Swaminathan,[1,5] [1]National Institute for Research in Tuberculosis, Clinical Research, Chennai, India, [2]National Institute for Research in Tuberculosis, HIV Lab, Chennai, India, [3]National Institute for Research in Tuberculosis, Statistics, Chennai, India, [4]National Institute for Research in Tuberculosis, Bacteriology, Chennai, India, [5]World Health Organisation, Research, Geneva, Switzerland. e-mail: drsyed@rediffmail.com

Background: Evidence from the literature shows that there is a high prevalence of haematological abnormalities among children with tuberculosis (TB). Furthermore, adult studies have shown that the ratio of peripheral blood monocytes to lymphocytes (ML ratio) is associated with risk of TB disease. The objective of this study was to evaluate the haematological profile of children with active TB and to further study the relationship between anaemia, ML ratio, ratio of peripheral blood Neutrophils to lymphocytes (NL ratio) and clinical status of children with active TB.
Methods: Children ≤ 15 years presenting to the outpatient clinics at in Chennai with symptoms suggestive of pulmonary TB between 2014 and 2018 were included. The haematological parameters, ML ratio and NL ratio were compared between children with active TB and matched controls.
Results: A total of 2078 children were screened and 593 children with median age of 5.8 years (range 3 months-15 years) were included. 55% were < 6 years of age; 59% were males. 33.7% (200/593) were diagnosed with TB; 38% (76/200) bacteriologically confirmed. Of the 593 children 32.4% (192) were anaemic. Anaemia was more prevalent among children with TB [49% (98/200)] as compared to children without TB [24% (94/393)]; p value < 0.001. Children with TB also had significantly higher neutrophil count, monocyte count

and lower lymphocyte count. (Table 1) Median ML ratio was 0.2 (0.14 - 0.31) in children with active TB, and 0.15 (0.11 - 0.2) in controls (p <0.001).
Conclusions: Our study shows significant haematological abnormalities in children with TB. The ML ratio and NL ratio, which are easily derived from routine differential full blood counts, might be helpful in the diagnosis and follow-up of children with active TB.

PS-16-673-01 Performances of LAMP, Xpert®MTB/RIF (Cepheid, USA) and MGIT-BACTEC™ MGIT 960™ culture in the diagnosis of paediatric pulmonary tuberculosis in a country with high TB prevalence

A Govindan S,[1] R Yadav,[2] PC Vaidya,[1] S Sethi,[2] RR Das,[3] A Saini,[2] N Mehra,[1] I Verma,[4] M Singh,[1] [1]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Pediatrics, Advanced Pediatrics Centre (APC), Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Medical Microbiology, Chandigarh, India, [3]All India Institutes of Medical Sciences (AIIMS), Department of Pediatrics, Bhubaneswar, India, [4]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Biochemistry, Chandigarh, India. e-mail: dr_pcv@yahoo.com

Background: The key to successful management of pediatric tuberculosis (TB) lies in early detection and proper treatment. The most difficult task in childhood TB is making the diagnosis; especially in early and latent stages. The present study was conceived with an intention to evaluate the performances of modern diagnostic tests (Loop-Mediated Isothermal Amplification (LAMP), Xpert® MTB/RIF (Cepheid, USA) and Mycobacteria Growth Indicator Tube (MGIT- BACTEC™ MGIT 960™ TB System)) against a modified version of this international consensus diagnostic definition (i.e., composite reference standard [CRS]) for better implication.
Methods: Cross-sectional analytical study was conducted in a tertiary care hospital in North India from July 2016-December 2017 involving 100 children below 14 years with suspected Pulmonary TB. Respiratory specimens (sputum, gastric lavage, bronchoalveolar lavage) were collected and subjected to LAMP, Xpert® MTB/RIF (Cepheid, USA) and BACTEC MGIT 960 culture assay.
Results: Among one hundred enrolled pediatric patients, six were excluded because of insufficient sample. Fifty-five children had confirmed and probable TB according to the composite reference standard (CRS). The sensitivity of MGIT culture, Xpert® MTB/RIF (Cepheid, USA) and LAMP assay was 9.09%, 10.91%, and 10.91% respectively when compared against the predefined CRS. The specificity for all these tests was 100%. When compared with MGIT culture, as a gold standard, the LAMP and Xpert® MTB/RIF (Cepheid, USA) assay had the sensitivity of 85.71% (95% CI: 42.13% to 99.64%) and 71.43% (95% CI: 29.04% to 96.33%), respectively. The specificity of both assays was 100%. The LAMP assay had a positive predictive value of 100% and negative predictive value of 98.78 %. The Xpert® MTB/RIF (Cepheid, USA) assay had a positive predictive value of 100% and a negative predictive value of 97.59 %.
Conclusions: We noted that both LAMP and Xpert® MTB/RIF (Cepheid, USA) assay had the comparable sensitivities and specificities.

PS-16-674-01 Diagnostic accuracy of Xpert MTB/RIF Ultra for detection of M. tuberculosis in intra-thoracic tuberculosis in children

R Yadav,[1] S Sethi,[2] P Vaidya,[3] J Mathew,[3] M Singh,[3] R Khaneja,[4] P Agarwal,[5] [1]Postgraduate Institute of Medical Education and Research, Department of Medical Microbiology, Chandigarh, India, [2]PGIMER, Department of Medical Microbiology, Chandigarh, India, [3]PGIMER, Pediatric Medicine, Chandigarh, India, [4]State TB Cell, RNTCP, Chandigarh, India, [5]WHO Country Office, TB, Chandigarh, India. e-mail: pgi.rky@gmail.com

Background: The next generation Xpert MTB/RIF ultra has shown increased sensitivity for detection of *M tuberculosis* in pauci-bacillary conditions. In this study, we assessed the diagnostic accuracy of Xpert MTB/RIF ultra for pediatric tuberculosis in high burden setting.
Methods: A total of 156 respiratory samples (Gastric aspirate/lavage n= 50; Broncho alveolar lavage n=17; sputum n= 89) from the suspected tuberculosis children (< 15 years) were collected and were processed for MGIT culture and Xpert MTB/RIF as per manufacturer's instructions. The Xpert MTB/RIF ultra were performed directly on the respiratory samples and results were interpreted as per manufacturer's instructions.
Results: Among 152 samples, 4 were rejected due to culture contamination, the valid results of Xpert Ultra were received in 151/152 (99.3%). The median age was 9.5 yrs. Tuberculosis were confirmed in 33 (21.8%) children by MGIT culture as a reference standard. The smear, Xpert MTB/RIF and Xpert MTB/RIF ultra were positive in 12/151(7.9%), 31/151(20.5) and 35/151(23.2%) samples, respectively. The sensitivity of Xpert MTB/RIF and Xpert MTB/RIF ultra were found 81.8%(95% CI, 64.5-93%) and 84.8%(95% CI, 68.1-94.9%) and the specificity were 96.6% and 94.9%, respectively. The positive and negative predictive value for Xpert MTB/RIF and Xpert MTB/RIF ultra were 87.1%(95% CI, 71.8-94.7%) and 82.3%(95% CI, 67.9-91.2%) or 95%(95% CI, 90.2-97.5%) and 95.7%(95% CI, 90.9-98.1%), respectively. The diagnostic accuracy of Xpert MTB/RIF and Xpert MTB/RIF ultra were 93.4% and 92.7%, respectively. The concordance between Xpert MTB/RIF and Xpert MTB/RIF ultra were found to be 0.95.
Conclusions: The Xpert MTB/RIF ultra has shown better sensitivity for detection of *M tuberculosis* in children but specificity needs more studies taking clinical diagnosis and mycobacterial culture both as a reference standard.

PS-16-675-01 TB detection in children in Moscow (Russia) as in low TB incidence region

V Aksenova,[1] T Sevostianova,[2] E Belilovskiy,[3] D Kudlay,[4] N Nikolenko,[5] [1]National Medical Research Center of Tuberculosis and Infectious Diseases, Children and Adolescents, Moscow, Russian Federation, [2]Moscow City Scientific and Practical Center for Tuberculosis Control, Clinical and Diagnostic Cente, Moscow, Russian Federation, [3]Moscow City Scientific and Practical Center for Tuberculosis Control, Epidemiological Department Tuberculosis Monitoring, Moscow, Russian Federation, [4]Institute of Immunology of the Federal Medical and Biological Agency, Laboratory of Personalized Medicine and Molecular Immunology №71, Moscow, Russian Federation, [5]Moscow City Scientific and Practical Center of Fight against Tuberculosis of Department of Health Care of the City of Moscow, Moscow, Russian Federation. e-mail: nynikolenko@pharmstd.ru

Background: Moscow (city of 12 million of population) has one of the lowest TB notification rate in the country for children aged 0-14 - 5.5 per 100K or 93 cases in 2018. Before 2012 in whole Russia, procedure of TB detection among children included mass screening by Mantoux test (MT) and clinical and X-ray assessment for MT positive cases. During last 5 years, for MT positive cases as for as children from TB contact, and social and medical risk groups, Moscow TB control service provides a immunological recombinant TB allergen skin test (RTAT) with subsequent clinical and X-ray assessment, which covered a significantly smaller number of children.
Aims: Evaluate results of modern TB detection tools among children in Moscow.
Methods: Data of screening of Moscow children (0-14) population by RTAT Diaskintest® (*Global investments in tuberculosis. Research and development, WHO, 2017, P.30*) were analyzed.
Results: Mantoux test covered 76.3% of children (1 282 235), 74% from which had positive results. RTAT was used in 131 000 children, with MT positive and/or belonged to TB risk groups. RTAT was positive in 3304 (2.5%) children. TB detection rate was 5.0% among them (91 children 0-14) in comparison with 0.13% for Mantoux test.
2 new TB cases among children were detected with negative reactions of RTAT. Sensitivity of RTAT was 98.4% (95% CI: 94.2-99.8).
Additionally 102 children were detected by RTAT with post TB changes, which can indicate undetected TB cases among family and close contacts of the child.
Conclusions: The introduction of a new diagnostic algorithm allowed to significantly reduce the number of children subjected to TB screening, while maintaining the accuracy of detection of the disease.

PS-16-676-01 Evaluation of Xpert® MTB/RIF (Cepheid, USA) for the diagnosis of paediatric tuberculous meningitis

S Shah,[1] SR Dhawan,[1] R Yadav,[2] PC Vaidya,[1] K Sharma,[2] N Sankhyan,[1] CK Ahuja,[3] N Mehra,[1] S Sethi,[2] [1]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Pediatrics, Advanced Pediatrics Centre (APC), Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Medical Microbiology, Chandigarh, India, [3]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Radiodiagnosis, Chandigarh, India. e-mail: nancymehra777@gmail.com

Background: Tuberculous meningitis (TBM) is one of the most devastating consequences of tubercular infection and accounts for approximately 1% of all tuberculosis (TB) cases with peak incidence age less than 4 years. Accurate diagnosis and early treatment initiation is critical to reduce Pediatric TBM-associated morbidity and mortality. The conventional techniques have low sensitivity for the diagnosis of tuberculosis. There exists scarce literature on sensitivity of Xpert® MTB/RIF (Cepheid, USA) in TBM in children.
Methods: Prospective study conducted at a tertiary care hospital in North India from January 2017 to June 2018 involving 130 consecutive children below 12 years with suspected TBM. We evaluated the sensitivity and specificity of Xpert® MTB/RIF (Cepheid, USA) in Cerebrospinal fluid (CSF) compared to Mycobacteria Growth Indicator Tube (MGIT- BACTEC™ MGIT 960™ TB System) culture. CSF samples were collected and subjected to Ziehl-Neelsen staining, Xpert® MTB/RIF (Cepheid, USA) and BACTEC MGIT culture assay.
Results: Among 130 enrolled pediatric patients, 121 were included in the study. 81 children were classified into TBM group. Xpert® MTB/RIF (Cepheid, USA) was positive only in 17 patients out of 81 patients; culture was positive in only two children and none of the children had smear positivity on Ziehl-Neelsen staining. The sensitivity, specificity, negative-predictive value (NPV) and positive-predictive value (PPV) of Xpert® MTB/RIF (Cepheid, USA) was 50%, 100%, 66.6% and 100% respectively compared to MGIT culture. The sensitivity, specificity, NPV and PPV of MGIT culture was 2.9%, 100%, 28.5% and 100% respectively. The sensitivity, specificity, NPV and PPV of Xpert® MTB/RIF(Cepheid, USA) calculated against presumptive clinical diagnosis of TBM were 20.9%, 100%, 28.5% and 100% respectively (95% CI).
Conclusions: We noted that Xpert® MTB/RIF (Cepheid, USA) was more sensitive than MGIT culture and smear, however, still has a poor sensitivity of 20.9% in the CSF samples seen in a clinical setting in a tertiary care institute.

PS-16-677-01 Gastric aspiration for GeneXpert assay: an opportunity for diagnosis of rifampicin-resistant TB in children younger than five years

F Enock,[1] EN Bassey,[2] IB Uguge,[2] S Useni,[3] M Onuoha,[4] P Nwadike,[5] [1]KNCV Nigeria/ Challenge TB, Programs, Abuja, Nigeria, [2]KNCV Tuberculosis Foundation, Programs, Abuja, Nigeria, [3]KNCV Nigeria/ Challenge TB, Technical, Abuja, Nigeria, [4]KNCV Nigeria/ Challenge TB, Monitoring and Evaluation, Abuja, Nigeria, [5]KNCV Nigeria/ Challenge TB, Laboratory, Abuja, Nigeria.
e-mail: enock.fanisi@kncvtbc.org

Background: Diagnosis of Tuberculosis (TB) in children is challenging, especially in under-fives who ordinarily cannot produce sputum. Most children with TB are diagnosed clinically with about 5% of childhood TB in under-fives diagnosed bacteriologically. Thus, making the diagnosis of Rifampicin and Multi-drug resistance TB (RR/MDR-TB) exceptionally difficult. This study shows the importance of gastric aspiration in diagnosis of RR/MDR-TB at Federal Medical Center, Niger State, Nigeria.
Methods: The study was conducted between 29th August, 2018 to March 30, 2019. A one-day orientation of childhood TB with demonstration on gastric aspiration for 11 nurses and 6 medical officers from the pediatrics department and 2 Laboratory Staff. Naso-gastric (NG)-tubes were provided and a childhood TB focal person was appointed from the pediatrics department. Children identified with presumptive TB were referred to the trained personnel for gastric aspiration. Aspirates were sent within 2 hours for laboratory analysis. Results were recorded in relevant TB registers in the pediatric department and laboratory unit.
Results: Out of 99 children identified with presumptive TB between 29th August, 2018 to 17th April 2019, 85 (85.9%) were below 5 years of age (males - 38 and female - 47) and 14 (14.1%) were above 5 years of age (male-13 and female-1). Of the 85 children below the age of five, 64 (75%) had gastric aspiration and specimens were analyzed with GeneXpert (males-27 and female-37). Two children (1 male age 3 years and 1 female age 1 year) were diagnosed with MTB detected and all were Rifampicin resistant detected. This represents a percentage of 2.9%.
Conclusions: Though, NG-Tube feeding is common in many health facilities, gastric aspirate for the diagnosis of TB has not been fully maximized. Routine gastric aspiration for GeneXpert assays could be a veritable tool for the diagnosis of RR/MDR-TB in children under five with presumptive TB in resource limited settings.

PS-16-678-01 Diagnostic accuracy of Xpert MTB/RIF Ultra Assay for the diagnosis of pulmonary TB in children: preliminary results

I Sabi,[1,2] E Sichone,[1] H Mahiga,[1] F Njeleka,[1] B Mtafya,[1] W Olomi,[1] NE Ntinginya,[1] M Hoelscher,[2,3,4] N Heinrich,[2,3,4] B Kampmann,[5] [1]National Institute for Medical Research, Mbeya Medical Research Center, Mbeya, Tanzania, United Rep., [2]CIHLMU Center for International Health, University Hospital, LMU Munich, Munich, Germany, [3]German Centre for Infection Research (DZIF), Partner Site Munich, Munich, Germany, [4]Division of Infectious Diseases and Tropical Medicine, University Hospital, LMU Munich, Munich, Germany, [5]Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Vaccines & Immunity, Fajara, Gambia. e-mail: isabi@nimr-mmrc.org

Background: Xpert MTB/RIF Ultra Assay (Ultra) was most recently recommended by WHO for the diagnosis of pulmonary TB (PTB) in children. We evaluated the diagnostic accuracy of Ultra for the detection of PTB using fresh sputum samples in children.
Methods: In this ongoing study of the Reach4Kids Africa team, children aged less than 15 years old were considered for enrollment at the Mbeya regional Referral hospital or referred from the nearby health facilities in Mbeya, Tanzania. Children with signs and symptoms suggestive of active TB disease were assessed using history, physical examination and chest X-rays. Two sputum samples were obtained using sputum induction or by spontaneous expectoration in older children. Sputum samples were analyzed using smear microscopy, Ultra and liquid culture using BD BACTEC MGIT 960. The diagnostic sensitivity, specificity and predictive values of Ultra were calculated using culture as the reference standard.
Results: Between September 2017 to October 2018, 111 children with presumed TB were enrolled. The median age was 3.6 years, 57 (50.9%) were males and 19 (17.1%) were HIV infected. Bacteriological confirmation (positive culture or Ultra) were achieved in 18 (16.2%) children. Among all children smear detected 6 (5.5%), Ultra detected 15 (13.5%) and culture detected 16 (14.6%) TB cases. The sensitivity of Ultra was 80.0% (CI, 51.9% - 95.7%) when only the 1st available sample was tested and 81.3 (CI, 54.4% - 96.0%) when the 1st and 2nd samples combined were tested. Ultra detected extra 2 cases (1 "low"; 1 "trace") in the group of children with culture negative results.
Conclusions: Compared with culture as the gold standard, Ultra demonstrated high sensitivity for the detection of PTB in children. The addition of a second sample did not increase its sensitivity.

PS-16-679-01 Diagnostic accuracy of molecular detection of Mtb in paediatric stool samples: a systematic review

AW Mesman,[1] CA Rodriguez,[1] E Ager,[2] J Coit,[1] MF Franke,[1] [1]Harvard Medical School, Global Health and Social Medicine, Boston, MA, United States of America, [2]Harvard T.H. Chan School of Public Health, Department of Social and Behavioral Sciences, Boston, MA, United States of America. e-mail: annelies_mesman@hms.harvard.edu

Background: Diagnosing pediatric TB is challenging given the difficulty for young children to expectorate sputum necessary for microbiological confirmation of *Mycobacterium tuberculosis* (*Mtb*) using conventional methods. Stool is a non-invasive sample type; however, molecular test sensitivity has been wildly variable. We aimed to estimate assay accuracy and investigate heterogeneity in available data to identify potential variables impacting accuracy and test performance.
Methods: We conducted a systematic review on *Mtb* detection in stool from pediatric pulmonary TB studies that used Xpert or other in-house molecular assays. We evaluated accuracy by comparing stool outcomes to microbiological confirmation via culture or Xpert on sputum or gastric aspirates, as well as to clinical diagnosis. We assessed study quality via the QUADAS-2 tool.
Results: We identified 419 studies, of which we included 14 in our analyses (11 Xpert, 3 in-house), with stool results from 2162 children.
We observed major heterogeneity in methodology, both in index (e.g. sample processing methods) and reference test (e.g. culture vs Xpert on sputum or gastric aspirate), as well as in study design (e.g. cohort vs case-control, collection time relative to anti-TB treatment initiation). Therefore, we did not find it appropriate to pool the data and conduct meta-analyses. Stool test sensitivity varied with wide intervals from 9%-85% (stool Xpert) and 19%-50% (stool in-house test) compared to microbiological confirmation. Stool sensitivity was highest among smear-positive children (81.5%) and very low among children with unconfirmed, clinically diagnosed TB (0%-17% across all studies). Specificity was very high with estimates of 99%-100% (Xpert) and 96%-98% (in-house tests) when based on children not diagnosed with TB.
Conclusions: Molecular assays on stool are promising and could serve as a rule-in test for TB. However, standardization of testing procedures, study design and reporting impactful characteristics as smear-status is necessary to compare protocols and identify optimal detection strategies.

PS-17-F Zoonotic tuberculosis: from basic science to One Health

PS-17-680-01 Recognition of mycobacterial mycoketides by bovine T cells from infected or vaccinated cattle

T Holder,[1] S Steinbach,[1] PJ Hogarth,[1] M Baird,[2] DA Thomas,[2] L Benedictus,[3] T Connelley,[3] A Minnaard,[4] I Van Rhijn,[5] M Vordermeier,[1,6] [1]Animal and Plant Health Agency, Bacteriology, Addlestone, United Kingdom, [2]Diagnostig, Diagnostig, Bangor, United Kingdom, [3]The Roslin Institute, University of Edinburgh, Edinburgh, United Kingdom, [4]University of Groningen, Bio-Organic Chemistry, Groningen, Netherlands, [5]Brigham and Women's Hospital/Harvard Medical School, Division of Rheumatology, Immunology and Allergy, Boston, MA, United States of America, [6]University of Aberystwyth, Centre for Bovine Tuberculosis, Institute for Biological, Environmental and Rural Sciences, Aberystwyth, United Kingdom. e-mail: martin.vordermeier@apha.gov.uk

Background: Mycobacterial lipids and glycolipids constitute an additional potential pool of antigens recognised by T cells that could complement protein-based subunit vaccines against tuberculosis. Glycolipid antigens are often recognised by human T cells in the context of non-polymorphic MHC class I-like molecules of the CD1 system. Ruminants, and, in particular, cattle, have well-developed CD1 systems, yet only few lipid containing ligands have been described as being recognised by bovine T cells.
Methods: To identify novel mycobacterial lipids and glycolipids recognised by bovine T cells from *Mycobacterium bovis* infected cattle, we screened a library of mycobacterial lipid and glycolipid ligands that included Glucose monomycolate, Trehalose dimycolates, mycolic acids and mycoketides. T cells from infected cattle were co-cultured with dendritic cells pulsed with these lipid-containing ligands and proliferation and IFN-gamma production determined.
Results: The most frequently recognised ligands identified in our screen were mannose-1, β-phosphomycoketide (MPM) and phospho-mycoketide (PM), hitherto only described to be recognised by human T cells. MPM and PM, gave rise to T cell proliferative responses in about 50 % of *M. bovis* infected animals tested, but produced little or no IFN-gamma after primary culture. However, following *in vitro* differentiation, antigen specific IFN-gamma production could be detected. Next, a group of calves was vaccinated with MPM and PM. PM and MPM induced memory T cell proliferative responses in 3/4 and 4/4 vaccinated calves, respectively, with MPM responses stronger and more durable than PM-induced responses.
In addition to proliferation, PM and MPM vaccination also resulted in IFN-gamma responses in in 1/4 and 2/4 vaccinated calves, respectively. Experiments are under

way to functionally characterise MPM and PM-specific T cells and the results of these experiments will be presented.
Conclusions: Mycobacterial mycoketides constitute potential sub-unit vaccine candidates against bovine tuberculosis whose protective efficacies should be evaluated in future cattle experiments.

PS-17-681-01 Identifying high-risk profile patients for zoonotic tuberculosis in Mubende district, Uganda

F Olea Popelka,[1] M Terry,[2] E Godfrey,[3,4] A Muwonge,[5] IR Grant,[6] L Stewart,[7] PI Fujiwara,[8] C Kankya,[3] [1]Western University, Pathology and Laboratory Medicine, London, ON, Canada, [2]Colorado State University, College of Veterinary Medicine and Biomedical Sciences, Fort Collins, CO, United States of America, [3]Makerere University, Department of Biosecurity Ecosystems and Veterinary Public Health, Kampala, Uganda, [4]Makerere University, College of Health Sciences, Department of Biosecurity Ecosystems and Veterinary Public Health, Kampala, Uganda, [5]University of Edinburgh, Division of Genetics and Genomics, The Roslin Institute and the Royal (Dick) School of Veterinary Studies, Edinburgh, United Kingdom, [6]Queen's University Belfast, Institute for Global Food Security, School of Biological Sciences, Belfast, United Kingdom, [7]Queen's University Belfast, Institute for Global Food Security, School of Biological Sciences, Belfast, United Kingdom, [8]International Union Against Tuberculosis and Lung Disease, International Union Against Tuberculosis and Lung Disease, Paris, France. e-mail: foleapop@uwo.ca

Background: Zoonotic Tuberculosis (ZTB) in humans caused by *Mycobacterium bovis (M. bovis)*, the causal agent of bovine TB, remains an important challenge in terms of diagnosis. Recently (2017), a novel lateral flow immunochromatographic device (LFD) antibody test was developed and evaluated for the specific detection of *M. bovis* in veterinary samples. The objectives of this study were to:
1) use the LFD to screen a group of human samples from TB suspect patients in Mubende district, and
2) assess sociocultural practices from patients testing positive to *M. bovis* by the LFD assay.
Methods: 125 patients having a cough for at least two weeks and a smear positive sputum test were interviewed between August 30th, 2016 and June 29, 2017 at the Mubende Regional Referral Hospital, Kasambya, Kiganda, Kassanda, Bukuya health centers. Sputum samples were collected by qualified and experienced medical personnel, cultured and then tested using the LFD test.
Results: The LFD assay detected 22 (17.6%, 95% CI: 11-25%) *M. bovis* positive sputum cultures among all TB suspect patients. More than half (56%) of these patients reported eating/drinking unpasteurized dairy products, and 78% reported eating uncooked meat. Finally, 19 of these LFD positive patients (82.6%) worked in proximity to animals (all of them as farmers). All but one of the 22 LFD positive patients (21 (95.4%), 95% CI: 77 - 99%) were confirmed as *Mycobacterium tuberculosis complex* positive by the HAIN test.
Conclusions: The results using the novel LFD assay agree with previous results published for rural areas in Africa with similar socio-cultural eating practices, and therefore, this study highlights the importance to further investigate the use of appropriate tools and methods to correctly identify *M. bovis* as the potential cause of human TB among patients in such high-risk communities.

PS-17-682-01 Developing molecular assays for estimating the prevalence of zoonotic tuberculosis in India

S Duffy,[1,2,3] S Srinivasan,[4] JS Michael,[5] V Kapur,[4,6] M Behr,[1,2,3] [1]McGill University, Department of Microbiology and Immunology, Montreal, QC, Canada, [2]McGill International TB Centre, Department of Microbiology and Immunology, Montreal, QC, Canada, [3]McGill University Health Centre Research Institute, Infectious Diseases and Global Health Program, Montreal, QC, Canada, [4]The Pennsylvania State University, Department of Animal Science, University Park, PA, United States of America, [5]Christian Medical College Vellore, Department of Clinical Microbiology, Vellore, India, [6]The Pennsylvania State University, Huck Institutes of Life Sciences, University Park, PA, United States of America. e-mail: shannon.duffy@mail.mcgill.ca

Background: The *Mycobacterium tuberculosis* complex (MTC) consists of *M. tuberculosis* (*M. tb*) and closely-related variants associated with non-human hosts, including *M. bovis* and *M. orygis*. The latter can be transmitted to humans to cause zoonotic tuberculosis (zTB). Although several MTC species can cause zTB, published human series generally look for *M. bovis*. Therefore, they may have underestimated zTB by not looking for other zoonotic subspecies. Recent reports suggest *M. orygis* may be endemic to South Asia, yet robust estimates of zTB prevalence or *M. orygis* in humans in India are lacking. We aimed to develop a screening method for rapid species-level differentiation of MTC members and to conduct a pilot study.
Methods: Two conventional polymerase chain reaction (PCR) assays were developed to differentiate between *M. tb, M. bovis,* and *M. orygis:* a three-primer PCR to detect the region of difference 9 (RD9) and a six-primer PCR to detect differences in the deletion size of RD12. A pilot study was conducted on 600 clinical samples (300 pulmonary, 300 extrapulmonary) in patients presenting with suspected TB at a large referral hospital in Vellore, India to estimate the prevalence of zTB and *M. orygis*.
Results: Of the 600 samples, 557 (92.8%) were confirmed to be *M. tb sensu stricto*. We determined that 19 (3.2%) were identified as an MTC species other than *M. tb*. Of the 300 extrapulmonary samples, 4 (1.3%) were identified as *M. orygis*.

Conclusions: This study validated a PCR-based assay to differentiate between MTC species in clinical samples and identified the presence of *M. orygis* in patients presenting at a large clinical centre in southern India. Further studies need to be conducted on representative samples from other areas of India, and other high burden countries, to accurately determine the proportion of human disease due to zTB.

PS-17-683-01 Isolation and whole genome sequencing of Mycobaterium orygis from cattle in south India

K Palaniyandi,[1] AK Refaya,[1] N Kumar,[2] M Veerasamy,[3] S Balaji,[4] S Shanmugam,[4] A Rajendran,[1] D Raj,[3] S Swaminathan,[5] S Peacock,[2] [1]National Institute for Research in Tuberculosis, Department of Immunology, Chennai, India, [2]University of Cambridge, Department of Medicine, London, United Kingdom, [3]Tamilnadu Veterinary and Animal Sciences University, TRPVB, Chennai, India, [4]National Institute for Research in Tuberculosis, Department of Bacteriology, Chennai, India, [5]World Health Organisation, Planning, Geneva, Switzerland.
e-mail: kannanvet@rediffmail.com

Background: *Mycobacterium orygis*, previously known as oryx bacilli, has been categorized as a member of *M. tuberculosis* complex which has been reported to cause tuberculosis (TB) in a wide range of animals and in human. Most of the reported cases were traced out to be South Asian origin. In this study, we describe the isolation and characterization two *M.orygis* isolates from cattle in Chennai, south India.
Methods: Post mortem examination was conducted in 6 cattle in a farm located in Chennai. Lung samples were taken in a sterile container from cattle during post-mortem examination subjected to Zhiel- Neilson (ZN) stain and inoculated onto Lowenstein-Jensen (LJ) slopes (with or without glycerol and sodium pyruvate) and mycobacteria growth indicator (MGIT) tubes supplemented with 800ul of PANTA antibiotic mixtures. Positive growth in MGIT tubes was investigated by ZN staining to confirm the presence of mycobacteria and tested using the ICT to confirm *M. tuberculosis* complex. Drug sensitivity test (DST) was performed in these cultures. Genomic DNA was extracted from these cultures and subjected to spoligotyping and whole genome sequencing.
Results: Spoligotyping identified 2 /6 isolates as *M.africanum* and further analysis by whole genome sequencing identified these isolates as *M.orygis*. Among the two isolates one isolate was phenotypically resistant to rifampicin and ethambutol.
Conclusions: Our study confirms the presence of *M. orygis* in cattle in India but was inadequate to trace their source of infection.

PS-17-684-01 Zoonosis in reverse: Mycobacterium tuberculosis in a population of captive sun bears

K Officer,[1] S Heng,[2] S Cheng,[3] [1]Free the Bears Fund, Veterinary Programme, Phnom Penh, Cambodia, [2]Institute Pasteur du Cambodge, Molecular Biology Platform, Medical Laboratory Unit, Phnom Penh, Cambodia, [3]Institute Pasteur du Cambodge, Mycobacteriology Laboratory, Phnom Penh, Cambodia.
e-mail: kirsty.officer@gmail.com

Background: The illegal wildlife trade in Cambodia sees bears kept in prolonged close contact with humans. Between 2009 and 2018 at one wildlife rescue centre nineteen sun bears (*Helartctos malayanus)* either died or were euthanased with TB caused by *Mycobacterium tuberculosis*. One staff member developed TB within the same time period. Drug susceptibility testing to four first line drugs suggested the involvement of at least two strains of *M. tuberculosis.*
Methods: 43-spacer spoligotyping and 24-locus MIRU-VNTR methods were used to genotype already cultured and confirmed *M. tuberculosis* isolates from each case. Historical temporal and spatial records were used to model possible transmission paths.
Results: Spoligotyping revealed two patterns. Sixty percent of isolates belonged to the East African-Indian (EAI) family whereas 40% belonged to the Beijing family. All the isolates belonging to the Beijing lineage were resistant to isoniazid and streptomycin, while the EAI isolates were pan-sensible. MIRU-VNTR typing distinguished three patterns. The first cluster contained all Beijing spoligotype isolates, including the human case. The second cluster contained 11 out of 12 isolates belonging to the EAI spoligotype, with the final isolate having one locus different. Contact tracing indicated transmission pathways for each infection, with the human case providing a link between two temporally separated bear cases in the Beijing spoligotype pathway.
Conclusions: Genotyping revealed two lineages of *M. tuberculosis* and confirmed involvement of a human case, with timing and exposure indicating likely transmission from bear to human and back to bear. This illustrates TB susceptibility in a wildlife species placed in contact with humans in a high TB prevalence country, with captivity creating necessary conditions for pathogen exposure and disease development. There are serious human health implications when drug-resistant zoonotic disease emerges in a previously unreported species, as well as important conservation impacts when the species is endangered.

PS-17-685-01 Outbreak of M. tuberculosis in a zoo in Israel involving Tapir and possibly humans

O Catabi,[1] Z Mor,[1,2] R Grossman,[3] N Edry,[4] S Maneshku,[1] R Sheffer,[1] Y Horowitz,[5] [1]Ministry of Health, Department of Health, Tel Aviv, Israel, [2]Ashkelon Academic College, School Health Sciences, Ashkelon, Israel, [3]National Public Health Laboratory, National Tuberculosis Laboratory, Tel Aviv, Israel, [4]The Veterinary Institute, Ministry of Agriculture, Pathology Department, Beit Dagan, Israel, [5]Safari, Veterinary, Ramat Gan, Israel. e-mail: zmor100@gmail.com

Background: *M. tuberculosis* in wild animals is rare and has not been described in Israel. This study aims to illustrate *M. tuberculosis* outbreak among Tapirs in an Israeli zoo.
Methods: This study describes an outbreak of tuberculosis in Tapirs in a zoo in central Israel, including the results of autopsies, findings from the contact investigations and molecular strain typing.
Results: *Tapirus terrestris* yard was occupied initially in the 80s′ with two animals, which were imported from Poland and Brazil. Between the years 2007 and 2018, six out of the eight Tapirs died. In autopsy, two demonstrated pathological signs compatible with pulmonary tuberculosis. Samples from pulmonary fluid from two other Tapirs were positive for *M. tuberculosis*, Beijing strain, sensitive to isoniazid and rifampin. Molecular analysis showed similar pattern. No clinical signs were detected in other two Tapirs- which are still alive, or in two Capybaras, which share the same yard.
Contact investigation found that 14 (28.6%) of the 84 zoo workers had positive tuberculin skin test, although all the workers were recommended to use N-95 mask. As the majority of the workers were Israeli-born and might not be at risk for latent tuberculosis infection, it is suspect that they acquired *M. tuberculosis* infection while working at the zoo.
Conclusions: Five of the eight Tapirs died during the study period and the *M. tuberculous* strain was identical. The source case was probably imported from Poland or Brazil. The positive skin test among a quarter of the workers suggests potential spread in the zoo.
It is recommend that zoo veterinarians should consider the possibility of tuberculosis in sick animals. In line with ′one health′ approach, workers should use personal protection aids in case of tuberculosis suspicion in animals. Close contacts should be periodically screened for tuberculosis while working close to possibly infected animals.

PS-17-686-01 Prevalence and knowledge level of zoonotic tuberculosis amongst livestock workers and tuberculosis patients in selected parts of Lagos State, Nigeria

G Ebere,[1] V Akinseye,[1] H Adesokan,[1] S Cadmus,[1] [1]University of Ibadan, Department of Veterinary Public Health and Preventive Medicine, Ibadan, Nigeria. e-mail: greaterglory2008@gmail.com

Background: Zoonotic tuberculosis (ZTB) is a significant public health disease, but has long been neglected despite the high risks for its transmission. Its burden amongst occupationally exposed individuals and tuberculosis (TB) patients in Nigeria is largely unknown.
Methods: A cross-sectional study was conducted to determine the prevalence and knowledge level of ZTB amongst livestock workers and the TB patients attending major Directly Observed Therapy Short-Course (DOTS) centres in Lagos State, Nigeria. Sputum samples collected were cultured and isolates further analysed using genus and deletion typing techniques. A semi-structure questionnaire was self-administered to assess the participants' knowledge level on ZTB. Data were analysed using descriptive statistics, univariate and multivariate logistic regression at $P \leq 0.05$.
Results: Of the total of 249 participants (livestock workers =172; DOTS centre TB patients =77), a prevalence of 2.4% ZTB was obtained, with higher proportion amongst DOTS centre TB patients (3.9%) than the livestock workers (1.7%). Participants within the age group 30-39 years (4.4%), the females (5.1%) and those with post-primary education constituted the highest affected groups. Again, only 45% of the participants had good knowledge level of ZTB. Logistic regression analysis showed that the females were about three times more likely to have good knowledge of ZTB than the males (OR= 3.309; 95%CI:1.589-6.892; p = 0.001).
Conclusions: The 2.4% prevalence obtained further reiterates ZTB as an endemic disease of public health importance. The higher prevalence observed amongst DOTS centre TB patients than the livestock workers provides an important epidemiological insight into ZTB challenge. The low knowledge level about ZTB amongst the respondents remains a factor to be considered in the drive to end TB globally by 2030. The need for increased awareness programmes and routine surveillance for ZTB amongst not just the occupationally exposed people but also the general population is advocated.

PS-17-687-01 Detection of Mycobacterium bovis and M. tuberculosis in slaughtered cattle in Baja California, México

R Muñiz-Salazar,[1] SE Sandoval-Azuara,[1] G Lopez-Valencia,[2] R Zenteno-Cuevas,[1] [1]Universidad Autonoma de Baja California, Escuela de Ciencias de la Salud, Ensenada, Mexico, [2]Universidad Autonoma de Baja California, Instituto de Ciencias Veterinaria, Mexicali, Mexico. e-mail: ramusal@uabc.edu.mx

Background: Baja California reports the highest incidence of tuberculosis (TB) rate in humans in México. However, identification of the infecting species is not performed, and consequently, there is no official information on human TB cases in México caused by *Mycobacterium bovis*. This is of critical since patients with *M.bovis* are 2.6 times more likely to die during treatment. We describe the identification of *M. bovis* and *M. tuberculosis* from granulomatous lesions suggestive of TB identified in lymph nodes and lungs of cattle slaughtered in Baja California, México.
Methods: Tissue samples were collected from cattle with granulomatous lesions suggestive of bovine TB from June-July 2013 and from January-June 2014. Samples collected were from a municipal (MP) and federal (FD) type slaughterhouse. Samples from beef and dairy cattle were subjected to hematoxylin-eosin staining and acid- and alcohol-fast bacilli to Ziehl-Neelsen staining. Positive samples were cultured and subsequently subjected to PCR amplification targeting the *mce-3* region to identify species.
Results: Three hundred nineteen samples with granulomatous lesions suggestive of bovine TB were collected from June-July 2013 (n=43) and January-June 2014 (n=276). The majority of samples (70.8%; 226) were collected from FD, while 29.2% (93) were from MP. Overall, 61.1% (195) were beef cattle breeds, including Cebu, Angus, Hereford and mix breeds. The rest were dairy cattle belonging to the Holstein breed (85; 68.5%). In total, *M. bovis* and *M. tuberculosis* were identified in 62% and 38% of microbiological isolates, respectively.
Conclusions: Molecular characterization of TB isolates is required to pedigree circulating lineages and to better identify transmission events. Circulation of both *M. bovis* and *M. tuberculosis* in cattle in México represents a major challenge for TB control in the country. Control measures aimed to prevent bacterial spread should be reinforced, including monitoring of circulating strains through proper implementation of adequate surveillance systems in cattle.

PS-18-C3 Challenges for DR-TB treatment

PS-18-689-01 Evaluating the results of a decentralised shorter treatment regimen for MDR-TB treatment in Cameroon, 2015-2018

V Mbassa,[1] J Noeske,[2] A Nana Yakam,[3] C Kuaban,[4] [1]NTP, Central Level, Yaounde, Cameroon, [2]Consultant, Independent Consultant, Douala, Cameroon, [3]University of Douala, Applied Statistics, Douala, Cameroon, [4]University of Bamenda, Faculty of Biomedical Sciences, Bamenda, Cameroon. e-mail: vincentmbassa@yahoo.fr

Background and challenges to implementation: In 2005, the Cameroon NTP implemented its PMDT component. Successive treatment regimens were from the very beginning inspired by v. Deun's experiences with alternative standardized shorter regimens (STR). In 2013, the NTP implemented the 9-months (´Bangladesh´) regimen in the framework of The Union observational study run in three specialized units. Until March of 2015, a total of 181 patients were included. Given the excellent results (85% of treatment success), the NTP decided in 2015 to decentralize the 9-months regimen as routine standard of care. The results of the decentralization process 2015-18 - including 413 patients - and challenges in notification and care are evaluated, comparing key indicators of the observational study period with those of the decentralization period.
Intervention or response: MDR-TB diagnostic facilities increased from 2 to 28 (two reference laboratories equipped for performing GeneXpert, LPA and culture and 26 GeneXpert sites). The number of treatment units increased from three to ten. Three models of care were

					Treatment outcome			Serious AE (degree >2)	
	Proportion of diagnosed RR patients treated	Median delay between diagnosis and treatment initiation	Patients with SL-DST (Fql, SLI)	Treatment success	Death	Failure	LTF	ALL	Ototoxicity
Study period	1050/1582 (66%)	36 days	86%	85%	9%	3%	3%	0.5%	7%
Decentralisation period	1069/1272 (84%)	12 days	18%	82%	13%	1%	4%	1.4%	5%

AE= Adverse drug effects; DST = Drug resistance test; Flq = Fluoroquinolone; LFT= Lost to Follow-up; M21= Control of patients 12 months after end of treatment; RR= Resistance to rifampicin; SLI = Second line injectable.

[PS-18-689-01 Table. Values of key indicators of the observational study as compared with those of the decentralization period]

introduced (hospitalization, ambulatory care and a mix of both). Accompanying measures included training of personnel and formulation of standard operational procedures (SOP).

Results and lessons learnt: The table compares the results of the observational study with those of the decentralization period.

During decentralization, the proportion of treated among diagnosed RR-TB cases increased by 20% while the median delay to treatment initiation was halved. However, the proportion of patients with a treatment success decreased at the expense of the death rate. Moreover, crucial follow-up exams (second line DST, follow-up exam at M21) were not carried out according to SOP. The rate of serious AE remained comparable.

Conclusions and key recommendations: Decentralization of standardized STR for MDR-TB in Cameroon enhanced access to diagnosis and care but, apparently, did so at the expense of quality of care and execution of essential follow-up exams. Stricter point-of-care monitoring has to ensure adherence to SOPs.

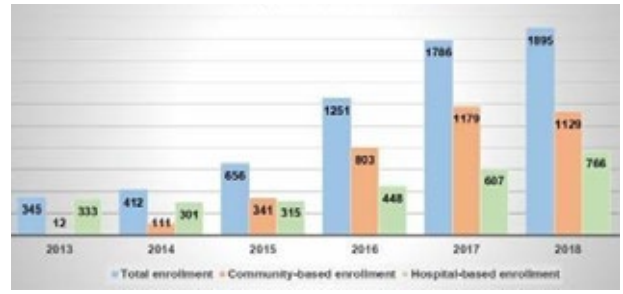
PS-18-690-01 The impact of decentralisation of the management of drug-resistant tuberculosis on patient enrolment in Nigeria

CA Ohikhuai,[1] O Chijioke-Akaniro,[2] A Agbaje,[3] F Murtala-Ibrahim,[1] [1]Institute of Human Virology Nigeria, Strategic Information, Abuja, Nigeria, [2]National Tuberculosis and Leprosy Control Programme, Monitoring and Evaluation, Abuja, Nigeria, [3]Institute of Human Virology Nigeria, Office of the CEO, Abuja, Nigeria.
e-mail: cohikhuai@ihvnigeria.org

Background and challenges to implementation: Nigeria is among the 30 high Drug-Resistance Tuberculosis (DR-TB) burden countries globally. The National Tuberculosis and Leprosy Control Programme (NTBLCP) commenced the Programmatic Management of Drug-Resistant Tuberculosis (PMDT) in Nigeria in 2010 with only hospital-based management using the 20 months standard regimen. There were delays in treatment initiation due to a limited number of treatment centers while many patients refused to be enrolled because of the long hospitalization periods and significant travel distance from their homes.

Intervention or response: The community-based model of PMDT was introduced in Nigeria in 2013 in four States and progressively scaled up nationwide by the end of 2016. This model provided an alternative for patients to be initiated on treatment in DOTS facilities nearest to them rather than being admitted in a distant hospital. The capacity of the State and the Local TB Control teams was built to implement a community-based PMDT system. Samples for baseline investigation were taken from the patient at the DOTS facility and transported to a designated laboratory. Based on the result, the teams initiate patients on the appropriate 2nd line treatment. The Local TB Control teams with technical support from the State team continue the management of the patients using the DOTS facility for monthly outpatient follow up and examination. Treatment supporters assist patients in adhering to DOTS. Patients receive financial support for transportation, feeding and monthly stipend. Quarterly surveillance data was reported, verified and analyzed by NTBLCP.

Results and lessons learnt: DR-TB patient's enrollment rose from 345 in 2013 to 1,895 in 2018 with community-based enrollment increasing from 3% in 2013 to 60% in 2018. More DR-TB patients are now willing to commence treatment.



[National DR-TB patient enrollment from 2013 - 2018 sorted by hospital or community enrollment]

Conclusions and key recommendations: Decentralization of PMDT in Nigeria has ensured that patients receive prompt patient-centered treatment and care. Further study to determine the quality of care received by patients at this level will be required.

PS-18-691-01 Closing the DR-TB treatment gap: operationalising the South Africa policy framework on decentralised and de-institutionalised management of multidrug-resistant tuberculosis in eThekwini District, South Africa

G Jagwer,[1] JJ Ongole,[1] C Dlamini,[2] P Mabota-Rapholo,[1] S Memela,[3] S Fynn,[4] [1]University Research Co., LLC (URC), USAID TB South Africa Project, Pretoria, South Africa, [2]USAID/South Africa, Health, Pretoria, South Africa, [3]University Research Co., LLC (URC), USAID TB South Africa Project, Durban, South Africa, [4]Government of South Africa, eThekwini District Municipality, Durban, South Africa.
e-mail: gregoryj@urc-sa.com

Background and challenges to implementation: South Africa diagnoses approximately 20,000 patients with Rifampicin-resistant (RR) tuberculosis (TB) annually. Routine data suggests a large proportion do not receive adequate treatment and likely contribute to drug-resistant TB (DR-TB) transmission. A key contributor to this treatment gap is physical inaccessibility to limited DR-TB treatment facilities. Systems issues such as poor reporting and human resources capacity challenges also

contribute. South Africa adopted a DR-TB decentralisation and deinstitutionalisation policy to facilitate access to treatment and address the treatment gap.

Intervention or response: To support implementation of the policy, USAID TB South Africa Project facilitated decentralisation of services to 14 of 18 government-identified DR-TB facilities in eThekwini district, KwaZulu-Natal province. DR-TB management teams were established in each based on identified critical health systems gaps. Facility-specific DR-TB packages, including in-service training and clinical systems mentorship support focusing on teams and individual providers were implemented at each site. Mentorship ensured that bi-directional referral pathways were functional and continuous quality improvement methodologies implemented. Reporting systems were established, including activation of electronic TB registers; the EDRWeb. Regular review forums were initiated.

Results and lessons learnt: Between October and December 2018, from a zero-baseline, 142 (31%) of all 538 patients initiated on DR-TB treatment were seen at project-supported decentralized sites. On follow-up at six months, 139 (98%) patients were still retained on treatment. Follow-up clinical and chart audits found 100% continued adherence to DR-TB guidelines and 92% overall achievement on data quality audits among health care workers.

Conclusions and key recommendations: Despite the limited intervention period, data indicates effectiveness of the decentralisation policy in closing treatment gaps for DR-TB patients. Interventions to expand access to treatment in high-burden and resource limited settings is essential. However, focusing on treatment alone is insufficient; targeted clinical systems mentorship is a prerequisite for expansion, quality and effective linkage of patients to treatment services.

PS-18-692-01 Implementation of decentralised drug-resistant TB care in South Africa has yielded increasing treatment successes and significant health system benefits

N Ndjeka,[1] Y Kock,[1] D Goldberg,[2] P Madhav,[2] S Bryer,[2] P Chituku,[2] [1]South Africa Department of Health, Drug-Resistant TB, TB and HIV, Pretoria, South Africa, [2]Clinton Health Access Initiative, TB Access Programme, Pretoria, South Africa.
e-mail: norbertndjeka@gmail.com

Background and challenges to implementation: South Africa has one of the highest burdens of multi-drug resistant TB (MDR-TB) globally. MDR-TB treatment was historically delivered through centralised care, which has been associated with significant health system constraints, and often poses a barrier to health-seeking in patients who, in many cases, live far from their point of access to care.

Intervention or response: In 2011, the National Tuberculosis Control Programme introduced a model of decentralised care whereby patients are able to access treatment for MDR-TB, including new and repurposed medicines, in facilities closer to their places of residence or work. Before the introduction of the policy on decentralised and deinstitutionalised management of MDR-TB there were only 17 MDR-TB treatment initiation sites. Patients across the country are now able to access decentralised care, with 636 sites across all provinces and districts active to date. The current study compares patient treatment outcomes between centralised and decentralised sites between 2011 and 2016.

Results and lessons learnt: A review of patient records in EDRweb (n=39,328) shows a steady increase in the number of patients receiving decentralised care, which was supported by the expansion of the nurse-initiation and ototoxicity programmes A steady increase was recorded in the number of patients with successful treatment outcomes receiving decentralised care, from 47% (2011) to 60% (2016). Additionally, the proportion of patients lost to follow-up in decentralised care reduced by almost half, from 30% (2011) to 18% (2016).

Conclusions and key recommendations: The decentralisation and deinstitutionalisation of care yields significant programmatic and patient benefits, with no risk to patients' outcomes. Given the considerable benefits to be realised by treating patients closer to their homes - including decanting heavily-congested centralised facilities and the reduced patient waiting times, travel costs and hours of work and wages lost - the model should be brought to full-scale in South Africa, with potential learnings for other countries facing similar constraints.

PS-18-693-01 Implementation of the new WHO drug-resistant TB treatment guidelines in Africa

D Affolabi,[1,2] M Gasana,[3] P Gandaho,[1] F Mavhunga,[3] D Falzon,[4] K Samson,[4] F Mirzayev,[4] AP Wachinou,[1] C Merle,[5] [1]West and Central African Regional Network for Tuberculosis Control, WARN-TB/CARN-TB, Cotonou, Benin, [2]Supranational Reference Laboratory for Tuberculosis, SRL, Cotonou, Benin, [3]World Health Organization, Regional Office for Africa, Brazzaville, Congo, [4]World Health Organization, Global TB Programme, Geneva, Switzerland, [5]Special Programme for Research and Training in Tropical Diseases (TDR), Research for Implementation Department, Geneva, Switzerland. e-mail: affolabi_dissou@yahoo.fr

Background and challenges to implementation: Resistance to anti-TB drugs is a major obstacle to effective TB care. An estimated 90,000 new cases of rifampicin-resistant tuberculosis (including multidrug-resistant TB; MDR/RR-TB) emerge each year in the WHO African Region. In 2017, less than 25% of MDR/RR-TB cases were reported to have been started on treatment. New (2018) WHO treatment recommendations could potentially facilitate scale up of MDR-TB treatment.

Intervention or response: During a regional workshop on MDR/RR-TB treatment expansion organized in March 2019 by WHO, the SNRL of Benin and TDR, country preparedness, barriers and operational research questions for implementing new WHO guidelines were assessed among African participating countries through self-administered questionnaires.
Results and lessons learnt: Out of 44 African countries, 38 (86.3%) plan to use shorter DR-TB regimen. All of them consider using all-oral shorter or longer regimen within the next 2 years. Most countries have, or will shortly, include all priority Group A medicines in their national essential medicines lists - levofloxacin (40/[FD1] 44), moxifloxacin (42/44), bedaquiline (35/44) and linezolid (35/44), as well as clofazimine (40/44) and cycloserine/terizidone (40/44). Laboratory capacities for drug sensitivity testing to the quinolones and injectables are available for only half of the countries, tests for baseline assessment and/or safety monitoring are not freely available for around 25% of the countries and active TB Drug Safety Monitoring and Management (aDSM) is in place in only 25% of them. Twenty-seven countries plan to conduct operational research projects to improve treatment delivery.
Conclusions and key recommendations: Principal barriers reported for implementing new WHO MDR/RR-TB treatment policies relate to laboratory capacities and aDSM. Both need to be urgently strengthened and funded. The feasibility of scaling-up new treatment regimens, their acceptability, cost and impact particularly on quality-of-life are parameters that countries should investigate through appropriately funded operational research for an effective and safe implementation of these guidelines.

PS-18-694-01 Patient challenges across three stages of DR-TB/HIV care - a longitudinal perspective from the PRAXIS study, South Africa

A Daftary,[1,2] S Mondal,[1] B Seepamore,[2,3] J Zelnick,[4] R Boodhram,[2] KR Amico,[5] G Friedland,[6] N Padayatchi,[2] MR O'Donnell,[2,7] PRAXIS Study [1]McGill University, McGill International TB Centre, Montreal, QC, Canada, [2]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa, [3]University of KwaZulu-Natal, Social Work, Durban, South Africa, [4]Touro College, Graduate School of Social Work, New York, NY, United States of America, [5]University of Michigan, Health Behavior and Health Education, Ann Arbor, MI, United States of America, [6]Yale School of Medicine, Epidemiology and Public Health, New Haven, CT, United States of America, [7]Columbia University Mailman School of Public Health, Epidemiology, New York, NY, United States of America.
e-mail: seepamoreb@ukzn.ac.za

Background: Even with bedaquiline, DR-TB entails an arduous medical journey. In the PRAXIS Study of DR-TB/HIV treatment and care, we documented patient experiences at key time-points to inform targeted interventions across the biography of their illness.
Methods: In 2017-18, 11 focus groups (FG) were held with 30 women and 20 men with DR-TB and HIV in KwaZulu-Natal; all were on bedaquiline and ART. Patients were grouped by gender and stage-in-care: *early*, < 3 months since diagnosis/hospital admission; *mid*, 4-6 months in treatment/post-discharge; *late*, >6 months in treatment/ambulatory care. Analysis borrowed from the Framework Method and Bury's theory of biographical disruption.
Results: Each stage was disrupted by a unique set of patient needs and challenges. During the *early* stage, adverse drug-effects, perceived/real abdication of responsibilities, prolonged isolation and boredom - particularly among hospitalized patients, institutional stigma, and difficulties accepting one's diagnosis were the greatest sources of disruption. Kind and informative health providers, peer-based support, and visits from family members were the greatest sources of relief. *Mid* stage was characterized by abatement in side-effects and an end to hospitalization.
But new challenges related to household obligations, burden of self-care, community stigma, and quality medical advice disrupted patients' experiences. These were alleviated by stable household support and access to basic services at local clinics. *Late* stage was distinguished by renewed concern of financial obligations and return to work, as support from grants and social networks wore thin. Stronger social protections and early preparation around treatment duration, including limitations, were felt to offer some relief.
Conclusions: This is a first attempt to delineate patient challenges with DR-TB and HIV at three critical stages. Bury's conceptual framework, used in chronic illness, illuminated distinct disruptive, reinforcing and alleviating forces. Findings informed an ongoing psychosocial intervention that addresses transitions and vulnerabilities in patients' treatment journeys.

PS-18-695-01 Programmatic effectiveness of multidrug-resistant tuberculosis care in Burundi

M Sawadogo,[1] F Ciza,[1] A Roggi,[2] O-G Nimer,[2] [1]Damien Foundation Burundi, Project, Bujumbura, Burundi, [2]Damien Foundation Belgium, Project, Bruxelles, Belgium.
e-mail: sawadgom@yahoo.fr

Background and challenges to implementation: Burundi notifes annually around of 50 multidrug-resistant tuberculosis (MDR) cases, representing 25% of estimated MDR-cases in 2018. Classed as low-income, there is a chronic lack of health-staff with a physician density of 0.03/10.000 population. Therefore, access to MDR-care is centralised. Here, we report the programmatic effectiveness of this approach.
Intervention or response: The MDR-care strategy includes: 1)Diagnosis by GeneXpert and culture at regional-laboratoires; 2)Referral of diagnosed-MDR for

hospitalisation at referral-MDR hospital; 3)Shorter Treatement Regimen (STR) including **4Km-Mfx-Pto-H-Cfz-E-Z/5Mfx-Cfz-Z-E**, with Mfx at 400 mg/day; 4) Social support: all medical and suplementary nutrition support is free of charge. We report the treatment outcomes of MDR-care strategy from May 2013 to January 2017.

Results and lessons learnt: We enrolled 191 MDR-cases: 180 (94.24%) eligible for STR. From 180 on STR, 75.8% were 15-44-years, only 1.65% under 15-years, and 16.48% were 45-64-years. 66.11% were male, 21.11% had HIV. 75.55% were previously treated with first-line treatment: 57.22% category-1 and 18.33% category-2.
A total of 157 patients were cured (87.2%) and 12 completed treatment (6.66%) resulting in 93.88% of treatment success, 9 died (5.00%) and 2 were lost to follow-up (1.11%).
The total cost of 9 months hospitalization was around 3,764,000 FBU (2002 USD) by patient including restoration, medicines, examination costs, sheets and hygiene equipment.

Conclusions and key recommendations: With a rate of 93.88% of treatment success without relapses, our MDR-care strategy has yield excellent programmatic effectiveness, reaching the End-TB goal of treatment success of 90%. Nevertheless, financial-sustainability is challenging. Therefore, decentralization of MDR-care at least for the continuation phase could be considered.

PS-18-696-01 Profile and outcomes of rifampicin-resistant TB in Nigeria: poor treatment success and high mortality

C Osakwe,[1] K Ukwaja,[2] A Lawanson,[3] O Okorie,[4] U Chukwulobelu,[5] I Alobu,[6] C Chinweuba,[7] C Okafor,[8] D Okafor,[9] V Babawale,[3] [1]Initiative for Prevention and Control of Tuberculosis and Lung Diseases, Public Health, Mararaba, Nigeria, [2]Federal Teaching Hospital Abakaliki, Internal Medicine, Abakaliki, Nigeria, [3]Federal Ministry of Health, Tuberculosis and Leprosy Control Programme, Abuja, Nigeria, [4]Ministry of Health - Abia State, Tuberculosis and Leprosy Control Programme, Umuahia, Nigeria, [5]Ministry of Health - Anambra State, Tuberculosis and Leprosy Control Programme, Awka, Nigeria, [6]Ministry of Health - Ebonyi State, Tuberculosis and Leprosy Control Programme, Abakaliki, Nigeria, [7]Ministry of Health - Enugu State, Tuberculosis and Leprosy Control Programme, Enugu, Nigeria, [8]Ministry of Health - Imo State, Tuberculosis and Leprosy Control Programme, Owerri, Nigeria, [9]Odumegwu Ojukwu University Teaching Hospital, Laboratory Services, Awka, Nigeria.
e-mail: chijiosakwe@yahoo.com

Background: Drug-resistant tuberculosis (DR-TB) undermines control efforts and the outcomes of its treatment is poorly studied in high-burden, resource-limited settings. Nigeria belongs to the 30 countries with the highest burden of DR-TB in the world. Since the scale-up of community-based DR-TB treatment, little is known about its treatment outcomes in the country. The objective of this study was to assess the profile and outcomes of patients treated for multidrug-resistant TB (MDR-TB) in Nigeria.

Methods: Retrospective cohort study of 335 patients with rifampicin-resistant TB enrolled for MDR-TB treatment using the longer regimen from 2014 to 2017 in five States in Nigeria. Demographic, clinical and laboratory data were retrieved from the treatment registers and patient charts. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated using multivariate logistic regression after controlling for confounders.

Results: Of the 335 patients, 228 (68.1%) were male and 199 (59.4%) were 40 years old or younger. Also, 114 (34%) were new and 221 (66%) were previously treated for TB; and 65 (19.4%) were co-infected with HIV. Overall, 141 (42.1%) were cured, 37 (11.0%) were classified as treatment completed, 73 (21.8%) died, 19 (5.7%) were lost to follow-up, 3 (0.9%) declined treatment, and 45 (13.4%) were still on treatment. Overall treatment success rate was 178 (53.1%). Being HIV-negative (aOR 2.1; CI 1.1 - 3.6) and being a newly-diagnosed TB case (aOR 3.1; CI 1.9 - 5.1) were independent predictors for treatment success.

Conclusions: Community-based MDR-TB was associated with poor treatment success and high mortality in Nigeria. Being HIV-negative and a newly-diagnosed TB case were independent predictors for treatment success. Further investigation is needed to characterise all the risk factors for DR-TB treatment success in Nigeria.

PS-18-697-01 Predictive factors of QT prolongation in the STREAM 1 trial

G Hughes,[1] C Cook,[1] S Ahmed,[1] A Nunn,[1] S Meredith,[1] STREAM Collaboration [1]UCL, MRC Clinical Trials Unit, London, United Kingdom. e-mail: gareth.hughes@ucl.ac.uk

Background: STREAM 1 was a randomised phase 3 trial in rifampicin-resistant participants comparing a 9-11 month "short regimen" to a "long regimen" following WHO 2011 guidelines. Severe QT prolongation was more frequent on the short regimen, defined as QT or QTcF ≥500 ms (11% v 6.4% p=014) OR an increase ≥60ms above baseline (64% v 41%). These differences may be due to high dose moxifloxacin and clofazamine in the short regimen. We explored additional predictive factors for development of severe QT prolongation.

Methods: Trial participants had 4-weekly ECG monitoring for the year after randomisation. The 282 participants randomised to the short regimen were analysed to identify factors associated with severe QT prolongation using Pearson's chi-squared test and a two-sample t test.

Results: Of the 282 participants in the short regimen, 182 had severe QT prolongation on at least one ECG; 31 had QT/QTcF of ≥500ms and 181 an increase of ≥60ms from baseline. Risk factors included a baseline QT/QTcF >450ms and recruitment from the Mongo-

lia site. There was no significant association with age, gender, BMI, hypokalaemia, diabetes or HIV infection. The median time to severe QT prolongation was 20 weeks (IQR 8.0 to 28 weeks). The median change was 104ms (IQR 83 to 137) in those with QT/QTcF ≥500ms and 67ms (IQR 63-77) in those with ≥60ms increase from baseline.

Conclusions: Whilst the baseline QT/QTcF level may be expected to influence whether it later increased, the reason for increased risk of patients from Mongolia was unclear, possibly due to genetic or environmental differences affecting pharmacodynamics of the trial medications. Although 2 patients developed a QTcF >500ms within 4 hours of their 1st dose of medication the median time of 20 weeks suggests the change takes several weeks, indeed 80% occurred at 8 weeks or later.

PS-18-698-01 Side effects and clinical outcomes among pre-extensively and extensively drug-resistant tuberculosis patients receiving imipenem/cilastatin

T Bichashvili,[1] N Tukvadze,[2] M Buziashvili,[3] Z Avaliani,[4] D King,[5] M Magee,[6] R Kempker,[7]
[1]National Center for Tuberculosis and Lung Diseases, Pharmacy, Tbilisi, Georgia, [2]National Center for Tuberculosis and Lung Diseases, Research Unit, Tbilisi, Georgia, [3]National Center for Tuberculosis and Lung Disease, Scientific Research, Tbilisi, Georgia, [4]National Center for Tuberculosis and Lung Disease, Administration, Tbilisi, Georgia, [5]Georgia State University School of Public Health, Epidemiology, Atlanta, GA, United States of America, [6]Georgia State University School of Public Health, Division of Epidemiology and Biostatistics, Atlanta, GA, United States of America, [7]Emory University School of Medicine, Infectious Disease, Atlanta, GA, United States of America. e-mail: teonabichashvili@mail.ru

Background: We sought to describe clinical characteristics and outcomes of patients receiving imipenem/cilastatin (Ipm/Cln) in an effort to provide needed data on its safety and tolerability.

Methods: A retrospective study was conducted at the National Center for Tuberculosis and Lung Diseases (NCTLD). Patients with pre-extensively (PRE-XDR) and extensively drug-resistant (XDR) tuberculosis (TB) receiving Ipm/Cln during 2014-2016 were included. Demographic and medical information, including information on adverse drug reactions (ADRs) and line-related complications were collected from medical charts and NCTLD databases.

Results: Fifty-nine patients were included. Most were male (90%) and had a history of prior TB treatment (87%). Nearly half (49%) had XDR-TB and 39% had a history of treatment failure. Among participants, 41% received Ipm/Cln as part of their initial treatment regimen while the rest initiated Ipm/Cln a median of 101 days (range: 67-157) after initiating treatment. Median duration of Imp/Cln use was 323 days (range: 158-454). The most common companion drugs were linezolid (98%), clofazimine (97%), bedaquiline (88%) and cycloserine (85%).

The main route of Ipm/Cln administration was via Port-a-cath (58%); 15% used central and 9% used peripheral venous catheters. Eleven (19%) stopped Imp/Cln as a result of ADR including two (4%) patients with seizures.

Eight (24%) patients had Port-a-cath removed/changed due to line site reactions. Hepatotoxicity developed in 8(14%) cases. Among 40(76%) culture positive patients at start of Ipm/Cln, 34(92%) had culture conversion.

Thirty six (61%) patients had a successful treatment outcome. Ten (17%) patients were lost to follow-up, two (3%) failed the treatment and 9 (16%) died.

Conclusions: Our findings show Ipm/Cln was used as an additional agent to other WHO Class A and B drugs and associated with a high rate of culture conversion. Rate of drug discontinuation due to ADR and line site reactions were high, highlighting concerns about safety and tolerability.

PS-18-699-01 Care beyond cure: improving quality of life of cured drug-resistant pulmonary TB cases through pulmonary rehabilitation

Y Dholakia,[1] CR Desai,[1] A Dalal,[1] D Adak,[1] [1]Maharashtra State Anti TB Association, Tuberculosis, Mumbai, India. e-mail: yatindholakia@gmail.com

Background: Studies have shown significant pulmonary functional abnormality and reduced quality of life in around 60 to 80% of patients who have successfully completed treatment for drug resistant TB(DRTB). Limited studies have shown Pulmonary Rehabilitation will improve physical conditioning and quality of life in such patients.

Methods: Cured DRTB cases were assessed. Detailed clinical history, X ray chest, distances covered by 6-minute walk test and PEFR was conducted. Dyspnoea grade was evaluated as per New York association scale. Eligible cases were enrolled in a structured pulmonary rehabilitation program including breath training, warm-up, endurance and strength training exercises. Cases that completed twelve sessions were assessed.

Results: 41cases of the 111 enrolled(40%) - (M=22, F=19) completed the twelve sessions of the program. Median age was 37 years (13-75yrs); 32%(13/41), 54%(22/41) and 14%(6/41) cases had mild, moderate and extensive radiological lesions. Improvement observed in the 6MWD at the end of the program was 30% (4-90%) with an improvement in absolute median distance of 60 m. (4 - 150 m.) over baseline. PEFR also showed similar improvement.

No significant difference was observed in the two parameters for severity in radiological extent of lung involvement.

Quality of life as assessed by Karnofsky score showed an improvement by a score of ten. Patients claimed an improvement in the performance of day to day activities.
Conclusions: Pulmonary Rehabilitation improves pulmonary functions in patients with post DRTB squeal. Disability in such patients due to residual symptoms like dyspnoea is reduced. There is improvement in physical conditioning and quality life. Pulmonary Rehabilitation should be included in the continuum of care after cure for DRTB cases.

PS-18-700-01 Analysis of the reasons and risk factors leading to unfavourable treatment outcomes in patients with multidrug-resistant tuberculosis in China

Y Li,[1] F Sun,[1] W Zhang,[1] [1]Huashan Hospital, Fudan University, Department of Infectious Diseases, Shanghai, China. e-mail: lalaliy@sina.com

Background: China is a high-burden country of multidrug-resistant tuberculosis (MDR-TB), with the second highest annual incidence worldwide. Nevertheless, the favorable treatment rate of MDR-TB in China is 41%, ranking last among 30 high burden countries.
Methods: Pulmonary MDR-TB patients who were confirmed by sputum culture and received the Global Fund project in six cities in Zhejiang Province, China, from January 1, 2009 to May 30, 2015 were enrolled. We determined the treatment outcomes according to the WHO definition for each participant. Multivariate logistic regression analysis was used to assess risk factors that may lead to unfavorable treatment outcomes.
Results: This study included 354 patients with MDR-TB. The overall treatment success rate was 60.7% (215/354). Of the 108 patients (30.5%) who were determined to failure, 48 (44.4%) failed to culture conversion at the end of the intensive phase; 21 (19.4%) had sputum culture reversion; and another 39 cases (36.1%) failed for adverse drug reactions. The overall rate of loss of follow-up was 7.1%. 85% of patients experienced at least one adverse event during treatment. Risk factors leading to unfavorable outcomes occurring in the early stage included aminoglycoside resistance (OR: 7.53; $P < 0.001$), involvement of bilateral lungs (OR: 2.39; $P = 0.030$), and previous treatment times ≥ 3 (OR: 9.20; $P = 0.044$); Among them, involvement of both lungs (OR: 2.38; $P = 0.047$) and aminoglycoside resistance (OR: 6.10; $P = 0.001$) were also independent risk factors for bacteriological failure. The risk factor leading to a final unfavorable treatment outcome was fluoroquinolone resistance (OR: 2.09; $P=0.030$).
Conclusions: Resistance to key drugs and low safety profile of antituberculosis drugs are important reasons for the failure of MDR-TB treatment. In addition, strengthening the treatment follow-up management of MDR-TB patients is of great significance in improving the overall treatment success rate.

PS-18-701-01 Treatment outcomes in multidrug-resistant tuberculosis patients treated for hepatitis C co-infection with direct-acting antivirals

O Kirakosyan,[1] N Khachatryan,[1] N Sargsyants,[2] H Atshemyan,[1] L Yeghiazaryan,[3] S Balkan,[4] N Melikyan,[5] M Bastard,[6] C Hewison,[4] H Huerga,[5] [1]Medecins Sans Frontieres, Medical Department, Yerevan, Armenia, [2]Armenicum Clinical Centre, Infectious Diseases Department, Yerevan, Armenia, [3]Ministry of Health, National Tuberculosis Control Centre, Yerevan, Armenia, [4]Medecins Sans Frontieres, Medical Department, Paris, France, [5]Epicentre, Epidemiology Department, Paris, France, [6]Epicentre, Epidemiology Department, Geneva, Switzerland. e-mail: helena.huerga@epicentre.msf.org

Background: Co-infection with hepatitis C (HCV) among multi-drug resistant tuberculosis (MDR-TB) patients is a risk factor for poor outcomes. We assessed the effectiveness of treating with direct-acting antivirals (DAAs) among patients co-infected with HCV and MDR-TB.
Methods: Prospective and retrospective observational cohort study including MDR-TB patients diagnosed with HCV between January 2016 and December 2018 in Armenia. A DAA regimen of either 12 weeks of sofosbuvir, daclatasvir or ledipasvir or 24 weeks of sofosbuvir, daclatasvir and ribavirin was provided. Sustained viral response to DAA treatment was measured with a HCV PCR done at 12 weeks post of completion of DAA treatment (SVR12).
Results: Of the 40 patients started on DAAs, 38 (95%) were men, 7 (17.5%) HIV-positive, 18 (46.1%) intravenous drug users, 19 (47.5%) alcohol users, and 23 (57.5%) had been or were in prison. Median age was 51 years [IQR 43-58]. HCV genotype distribution was: 19 (55.9%) genotype 3a, 10 (29.4%) genotype 1b, 4 (11.8%) genotype 2, and 1 (2.9%) genotype 4. Most of the patients, 27 (73.0%) had fibroscan FO-F1, 4 (10.8%) F2, 3 (8.1%) F3 and 3 (8.1%) F4. Of the total 40, 39 completed DAAs, and 1 patient was lost to follow-up during DAAs. Of the 39 who completed DAAs, 31 had a measure of SVR12, 2 died and 2 were lost-to-follow-up after completion of DAA, 4 were still under post DAA follow-up. Amongst the 31 patient who completed DAA and had SVR12 results, 29 (93.5%) were negative and 2 (6.5%) positive.
Conclusions: Patients with MDR-TB and HCV co-infection treated with DAAs had high rates of DAA completion and sustained viral suppression among those tested. However lost to follow-up and deaths after completion of DAA, restricted the measurement of DAA effectiveness. Treatment with DAAs should be accessible for MDR-TB patients co-infected with HCV and follow-up should be ensured.

PS-19-D10 A potpourri of tobacco issues

PS-19-703-01 The prevalence of smoking and public support for tobacco control policy in Bali, Indonesia: "it's time for acceleration"

IWG Artawan Eka Putra,[1,2] PAS Astuti,[1] IMK Duana,[1] IK Suarjana,[1,2] IKH Mulyawan,[1] TS Bam,[3] [1]School of Public Health, Faculty of Medicine, Universitas Udayana, Public Health and Preventive Medicine, Denpasar, Indonesia, [2]Faculty of Public Health, Universitas Airlangga, Epidemiology, Surabaya, Indonesia, [3]The International Union Against Tuberculosis and Lung Disease, Tobacco Control, Singapore, Singapore.
e-mail: gedeartawan@unud.ac.id

Background: Smoking Prevalence in Bali 2014 was 27.5%. Tobacco control policy to reduce the prevalence need to be strengthen. Public support to the policy is important on strengthening strategy. The study aimed to assess smoking prevalence and public support for tobacco control policy in Bali, Indonesia.
Methods: This was a cross-sectional study that conducted from January to February 2019. Samples were selected from visitor of smoke-free area (SFA) or people live in surrounding community during a compliance study. They were distributed proportionately based on SFA and regencies/city. Data was collected through face to face interview using structured questionnaire that have been tested previously. Public support is their opinion on smoke-free legislation (SFL), tobacco advertisements, promotion, and sponsorship (TAPS) ban, pictorial health warning (PHW) enlargement and price increasing. Data was analyzed descriptively using frequency relative and cross tabulation.
Results: The study succeeded to interview 1,105 people. The average of age was 37±10.8 years old and 642(58.1%) were male. The current smokers were 220(19.9%) and ex-smokers were 168(15.2%). Smoking prevalence were higher among male (33.3%) compare to female (1.3%). 970(87.8%) support the SFL implementation, 92.8% among smokers and 69.5% among non-smokers. 888(80.4%) support the TAPS ban, 86.3% among smokers and 58.6% among non-smokers. 891(80.6%) Agree PHW need to be enlarged, 87.6% among smokers and 54.5% among non-smokers. 931(84.3%) agree on price increasing, 94.8% among smokers while 43.2% among non-smokers. They suggest that ideal price per pack is 4 USD.
Conclusions: The smoking prevalence is decreasing in the last 5 years. This show the effect of recent tobacco control program. High public support show the tobacco control policy is a popular. Acceleration is needed to achieve low prevalence. SFL strengthening and TAPS ban should be initiated in all regencies/city. In national level, PHW should be enlarge and cigarette sin taxes should be increased to make more expensive.

PS-19-704-01 Prevalence, pattern, and factors associated with dual tobacco use in a rural community in South-Eastern Nigeria

U Ofonakara,[1,2] EO Ekesi,[3] T Kotey,[4] [1]Federal Teaching Hospital Abakaliki, Community Medicine, Abakaliki, Nigeria, [2]National Primary Health Care Development Agency, Primary Health Care System Development, Asaba, Nigeria, [3]Madona University, Health Economics, Okija, Nigeria, [4]University of Lagos Teaching Hospital, Community Medicine, Lagos, Nigeria. e-mail: druzooffor@yahoo.co.uk

Background: National prevalence studies have consistently shown higher rates of dual tobacco use in South Eastern Nigeria but little is known about the pattern and factors associated with the dual tobacco use . Dual tobacco use is a greater health problem than mono use and needs to be researched.
The aim of this study was to determine the pattern and factors associated with dual tobacco use, among residents of a rural community in South Eastern Nigeria.
Methods: .A cross-sectional descriptive study was carried out among 490 residents of Ukpo community selected using a two-stage sampling method. Data was collected using a pre-tested interviewer-administered questionnaires adapted from Global Adult Tobacco Survey. Odd ratios and 95% confidence intervals were computed and P values of < 0.05 were considered statistically significant.
Results: The results showed that respondents were mostly male 300(61.2%) and aged between 20 and 70 years with a mean of 42.2 ± 15.4 years. Almost a quarter of the respondents, 101 (20.6%) were ever- dual tobacco users. Also, 210(42.9%) and 110 (22.4%) used only smokeless and smoked tobacco respectively. Dry snuff (73.8%) and cigarettes (82.2%) were the most common forms of tobacco used. The primary reasons for tobacco use were: to relieve stress (61.2%); to increase levels of alertness (56.4%); for personal pleasure (55.9%) and social acceptance (52.1%). Age (p<0.0001), male gender (p<0.0001) and lower educational attainment (p<0.0001) were associated with dual tobacco use. Also (51%) were aware that dual tobacco is more dangerous to human health than mono use and only about (27.1%) were aware that tobacco use is associated with lung cancer and COPD.
Conclusions: .Efforts targeted at raising community awareness of the health effects of dual tobacco use are needed in rural communities where dual tobacco use is disproportionately high. Programmes should be directed to males with lower educational attainment.

PS-19-705-01 Intention to quit and quitting support among tobacco users in a rural community of Southeastern Nigeria

U Ofonakara,[1,2] EO Ekesi,[3] T Kotey,[4] [1]Federal Teaching Hospital Abakaliki, Community Medicine, Abakaliki, Nigeria, [2]National Center for Disease Control and Public Health of Georgia, Primary Health Care System Development, Asaba, Nigeria, [3]Madona University, Health Economics, Okija, Nigeria, [4]Lagos University Teaching Hospital, Community Medicine, Lagos, Nigeria. e-mail: onyinyeekesi@yahoo.com

Background: Prevalence studies have consistently reported higher rates of tobacco use in the South-Eastern parts of Nigeria. The prevalence rates are (1.9% Nigeria; 4.7% SE Nigeria) while the prevalence rates for smoked tobacco are 13.7% Nigeria; 9% South East Nigeria). However, little is known about the intention to quit and supports to quit tobacco use in these parts of the country. The aim of this study was to determine the pattern and factors associated with intention to quit tobacco use among residents (population; 96,517) of Ukpo community of Dunukofia LGA of Anambra State, South Eastern Nigeria.

Methods: A cross-sectional survey was carried out among 490 residents of Ukpo community selected using a two-stage sampling method. Data were collected using pre-tested interviewer- administered questionnaires adapted from the Global Adult Tobacco Survey. Odd ratios and 95% confidence intervals were computed.

Results: Respondents were mostly male (n=300, 61%) and aged between 20 and 70 years with a mean of 42.2 ± 15.4 years. Almost half (n=210, 43%) had ever used smokeless tobacco. Only 116(24%) had ever smoked tobacco.

More people (n=68, 59%) were willing to quit smoked tobacco than smokeless tobacco (n=60, 29%). Of the people who tried to quit smokeless tobacco, most did so without assistance (n= 52, 24%) or used counselling at a cessation clinic (n=50, 23%), whereas nicotine replacement therapy (NRT) was used by only 26 (12%). Of smokers who tried to quit, most used counselling at a cessation clinic (n=22, 10%). A few used NRT (n=15, 7%), while 7% tried to quit without external assistance.

Conclusions: More people are willing to quit smoked tobacco than smokeless tobacco. We recommend programmes to help people who are willing to quit tobacco use and special programs to target smokeless tobacco users.

PS-19-707-01 Tobacco use among urban-slum dwellers attending a clinical setting in Noida (India): a cross-sectional study

S Nethan,[1] V Kumar,[1] S Sharma,[2] D Sinha,[3] R Hariprasad,[1] R Mehrotra,[4] [1]ICMR - National Institute of Cancer Prevention & Research, Clinical Oncology, Noida, India, [2]ICMR - National Institute of Cancer Prevention & Research, Epidemiology & Biostatistics, Noida, India, [3]School of Preventive Oncology, Director, Patna, India, [4]ICMR - National Institute of Cancer Prevention & Research, Director, Noida, India. e-mail: suzanne.nethan@gmail.com

Background: Oral cancer is attributable to the high tobacco burden in India, which shows variation according to the place of residence of the users (urban/rural). Minimal, exclusive information exists regarding the same for 'urban-slum' dwellers (result of the rapid, large-scale mobilisation of villagers to cities for employment). The Institutional clinic screens women referred from nearby hospitals, and those motivated by community healthcare providers, for cervical, breast, and oral cancer, and their male attendants for oral cancer; tobacco cessation is provided as appropriate. The current study aims at determining the tobacco use pattern among such urban-slum dwelling attendees of our clinic in Noida (India).

Methods: A cross-sectional study was performed among the urban-slum residents visiting the clinic between December 2016-October 2018. Their basic demographic details and tobacco use history (if present) were recorded, followed by routine oral examination. The data thus collected was statistically analyzed.

Results: Among 5780 respondents (1230 males, 4550 females), 17.7% (n=1024, $p< 0.001$) consumed tobacco, with males (46.1%) having a much higher prevalence than females (10%). Overall, the majority were smokeless tobacco (SLT) users (11.8%), followed by smokers (3.3%), and dual users (2.6%), ($p< 0.001$); females showed a similar pattern. However, among males, the highest prevalence of SLT users was followed by dual users, and smokers. Among males, gutkha (20.9%) and khaini (19.2%), and among females gulmanjan (2.9%) and gutkha (2.4%) were used most commonly. All users were advised to quit tobacco.

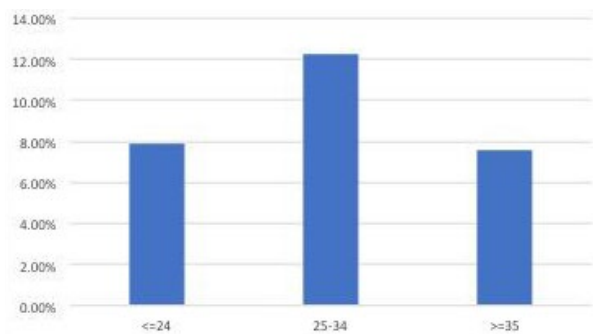
Conclusions: SLT was the most commonly consumed tobacco form in the Noida urban-slum population attending the Institute. This is one of the best examples of treating tobacco addiction from the local referrals under one roof.

However, the probable gender variation in the tobacco form and product-specific consumption patterns deems the undertaking of urban slums-specific surveys, essential. Tobacco control programmes must incorporate appropriate strategies addressing such subgroups of tobacco users.

PS-19-708-01 Colombian smokers calling it quits: the effects of a tobacco tax hike

B Llorente,[1] G Friedrich,[2] N Maldonado,[3] [1]Fundación Anaas, Research, Bogota, Colombia, [2]Universidad de los Andes, Biomedical Engineering, Bogota, Colombia, [3]Universidad Jorge Tadeo Lozano, Department of Economics, Bogota, Colombia.
e-mail: g.friedrich@uniandes.edu.co

Background: Tobacco taxes in Colombia increased two-fold between 2016 and 2017, leading to a 22% rise in the real price of cigarettes. Literature on smokers response to price indicates that this should lead to reductions in tobacco consumption by a combination of: a lower number of new smokers; current smokers quitting; and current smokers reducing consumption intensity. This study provides empirical evidence on whether the price change in Colombia is associated with the smokers' intention to quit, changes in their self-reported cigarette consumption and the amount of cigarettes they purchase.
Methods: Two surveys (DeicsCol) before and after tax hike, representative for the Colombian smoking population, provided information about cigarette consumption patterns, last purchase price and volume, intention to quit, and self reported reasons to quit. Sample design included a matching strategy, performed during fieldwork, creating a pseudo cohort. Using a paired t test we assessed changes in self-reported consumption intensity in daily and occasional smokers. A descriptive statistics approach determined main reasons to consider quitting and described other changes in smokers' behaviour.
Results: In 2017 most cited reason of intention to quit was health concerns. Prices are the second most important reason to quit, particularly for the 25-34 age group. Higher prices did not trigger widespread changes in brand: 79,7% of smokers informed they had not purchased a cheaper brand since December 2016. After tax increase cigarettes per week by smoker lowered between 3,2 and 9,8 sticks.



[Reason for quitting by age group: Price (second in importance)]

Conclusions: During the first year of the tax increase, trends in consumption are encouraging, and plausibly attributable to price changes. Results of intention to quit and reduction in smoking intensity are consistent with previous estimates of demand for cigarettes in Colombia. Results contradict tobacco industry narrative that states smokers are more willing to look for cheaper brands in the illegal market after a tax increase.

PS-19-710-01 Baseline compliance assessment of Indian Tobacco Control Act in eight districts of Madhya Pradesh, India

MK Sinha,[1] B Sharma,[1] [1]Madhya Pradesh Voluntary Health Association, Tobacco Control, Indore, India.
e-mail: sinhamukesh63@gmail.com

Background: Baseline compliance assessment gives us an idea about the actual implementation before starting an intervention it is also helpful in measuring the success of any intervention when compared with end line. The objective of the assessment was to understand the compliance of section 4,5 6a and 6b of Indian Tobacco Control Act(COTPA). Its Section 4 prohibits smoking at public places, section 5 prohibits advertisements of tobacco products, section 6a prohibits sale of tobacco to minors,6b prohibits sale of tobacco within 100 yards of educational institutions.
Methods: It was an cross sectional observational study conducted in 8 districts i.e Gwalior,Ashoknagar,Guna,Shivpuri,Datiya,Bhind,Morena and Sheopur districts of Madhya Pradesh. For assessing compliance of section 4 of seven types of public places were observed. A total of 640 public places were observed.For assessing compliance of section 5 and 6a a total of 160 shops were observed in 8 districts.
Results: Availability of No Smoking signage's was highest in Ashoknagar district 14% and least in Datiya,Bhind,Morena,and Sheopur districts. Active smoking was highest in Datiya district 35% and least in Guna district 5%.Presence of Cigarette and bidi butts was highest in Datiya district 79% places and least in Gwalior district 22.5%. Presence of ads at Point of Sale and sale to tobacco to minors was highest in Sheopur, Morena,Bhind and Datia districts. Mandatory boards for section 6a were not available in any shops. Availability of tobacco shops near educational institutions was highest in Bhind 50% and Datiya districts 60% and least in Shivpuri (20%) and Sheopur (10%) districts.
Conclusions: Baseline Compliance assessment was useful in understanding the status of implementation of tobacco control act and to make need based interventions in different districts and using as a tool for advocacy at top level.

PS-19-711-01 Designated smoking area (DSA) violations weakening the smoke-free rules: is the exception necessary? A study from Chandigarh

OPK Gill,[1] [1]Generation Saviour Association, Tobacco Control, Mohali, India. e-mail: gsa338@gmail.com

Background: The National Legislation, Cigarette and Other Tobacco Products Act (COTPA) Section 4 Prohibits smoking at public places but gives an exception to make Designated Smoking Areas at Airports, Hotels and Restaurants. This is widely violated, hence a study was conducted to see if such DSA exception is really needed in the law.
Methods: Restaurants and hotels were randomly selected in UT Chandigarh and checked on the parameters of presence of DSAs and the DSAs were evaluated to check if they comply the specifications as mentioned in COTPA. All segments of restaurants were selected which have a capacity of 30 tables or more, on which the DSA exception applies.
Results: Out of the 50 randomly selected restaurants only 2 (4%) places had a DSA, out of which one was a five-star hotel and the other a Restaurant. The remaining 48 (96%) had made no separate provision for a DSA. Out of the 48 places 5 (10%) Hotels have made provision of smoking rooms in form of allowing smoking in few selected rooms, 14 (29%) had made the adjoining open seating spaces as smoking areas which is clear violation of the smoke-free laws and 29 (58% of the total sample) having no need to provide for any smoking area.
Conclusions: Through the study it can be clearly pointed out that is only 2% restaurant and hotel owners who own up to the law of exception need in the Smoke free laws and roughly 30% only violate the smoke free laws by covering them under the exception provided, whereas majority 58% find no need of this exception to the smoke free rules, hence it will be in interest of the public to forgo with this exception in the law.

PS-19-712-01 The role of media-led advocacy in advancing tobacco control initiatives: a case study from Jharkhand, India

DK Mishra,[1] A Pandey,[2] [1]Socio Economic and Educational Development Society (SEEDS), Tobacco Control, New Delhi, India, [2]International Union Against Tuberculosis & Lung Disease, Tobacco Control, New Delhi, India.
e-mail: seedsdelhi@gmail.com

Background and challenges to implementation: The state of Jharkhand is among the poorest states in India and has a high burden of tobacco use. Early efforts in advancing tobacco control had a limited effect. Since 2016, the efforts of civil society to create public awareness through mainstream and vernacular print media has proved as a successful yet cost-effective strategy to create awareness on harms of tobacco use and put pressure on enforcers to ensure the implementation of tobacco control policies and programmes. With limited resources, media-led advocacy can reach out to millions of people and advance tobacco control.
Intervention or response: In Jharkhand, as part of tobacco control programme a multi-pronged mass media strategy has been developed to create widespread awareness in the citizens of the state and to promote tobacco control policies.
Results and lessons learnt: Since December 2016, there were 245 earned media reports in national newspapers published locally, and regional papers. Of these 42.5% related were to enforcement of the law and provisions of the National Tobacco Control Programme. According to the readership survey, we estimate that these stories have reached to 13.5 million readers (or 80% of all adults in the state). The earned media in monetary terms translates to about INR 16921800 (=USD 252500).
The issues' reported, its' frequency of appearance in media and the timing when they appeared (for example just before important policy meetings) have advanced the tobacco control at the centre of discussion and ensured rapid acceptance of policies in the state.
Conclusions and key recommendations: Earned media advocacy needs to be made an integral strategy to reach citizens, community and pressure groups and policymakers. This can be done within a very short span of time to fill knowledge gaps about the provisions of the law and the tobacco control programme while creating a favorable policy environment for tobacco control.

PS-20-E1 Enhancing services and supporting care

PS-20-713-01 Implementing TB elimination mission through local self-government stewardship in Kerala, India

R Sadanandan,[1] K Kumar,[2] RL Saritha,[3] S Kumar,[3] S Balakrishnan,[4] PS Rakesh,[4] [1]Ministry of Health & Family Welfare, Government of Kerala, Thiruvananthapuram, India, [2]National Health Mission, Government of Kerala, Thiruvananthapuram, India, [3]Directorate of Health Services, Government of Kerala, Thiruvananthapuram, India, [4]WHO RNTCP Technical Assistance Project India, RNTCP, Thiruvananthapuram, India.
e-mail: sunilkumarm2000@gmail.com

Background and challenges to implementation: Incident TB notification is decreasing in Kerala against a backdrop of high case finding efforts. The state government has launched a Mission for TB Elimination in January 2018. Ensuring community ownership and social mobilization is essential for successful implementation.

Intervention or response: Local self-governance [LSG] is a form of democratic decentralisation. It implies transference of the power to rule to the lowest rungs of the political order. Rural LSGs cater to a population of 10000 to 25000 and urban bodies cater to 300000 to 100000. Kerala TB Elimination Mission is being implemented through the LSG Bodies with a theme "My TB free [name of LSG]". TB Elimination taskforces chaired by the head of the LSG are formed in all the 1034 LSG bodies. The LSG Task Force plans and implements local activities mobilizes resources, monitor self, adopts mid-course correction and reports to the district task force. Provisions are made from RNTCP budget for quarterly meetings of taskforce, mapping of TB vulnerabilities of all citizens under the LSG, ACSM, house-hold airborne infection control and active case finding. For social and nutritional support of patients, budgetary provisions are made from LSG bodies' own funds.
Results and lessons learnt: Of the 1034 LSG Heads, 1021 (98.7%) were sensitised on TB Elimination Mission. Among the LSG bodies, 951 (92%) formed TB Elimination Task Forces. Vulnerability mapping was done in 7428886 (87%) households. Nutritional support projects for TB patients worth INR27,25,711 was implemented from LSGs own fund. Treatment Support Groups were formed in 334 (36%) LSGs. TB messages reached 7428886 / 8560731 (87%) households in the state. Each LSG plans for TB Vulnerability reduction including tobacco cessation and indoor air pollution control.
Conclusions and key recommendations: Decentralising TB Elimination activities and empowering local self-governments for implementing them is a feasible and effective method for TB Elimination.

PS-20-714-01 Occupational lung diseases in mine workers in South Africa

B Kistnasamy,[1] [1]Compensation Commissioner for Occupational Diseases, Department of Health, Johannesburg, South Africa.
e-mail: barry@fnbconnect.co.za

Background and challenges to implementation: Overcoming the legacy of occupational lung diseases in mine workers in South Africa has required innovative service delivery programs. Occupational lung diseases other than Tuberculosis (TB) are often not diagnosed due to the latency period for development of symptoms and clinical signs, a lack of awareness and knowledge of occupational lung diseases among health professionals and the need for diagnostic tools. The Moscow Declaration to End TB and the United Nations Political Declaration on the Fight against TB have highlighted mine workers as a vulnerable population.
Intervention or response: Consensus was developed with mining companies, trade unions, ex-mine worker associations and government departments about appropriate interventions to find the ex-mine workers and assess them for occupational lung diseases. An electronic database was developed covering 200 000 mine worker claimants with provision of fixed and mobile clinics. Trained health professionals and administrative personnel assessed the mine workers for occupational lung diseases. Diagnostic services included chest X-rays, spirometry, audiometry and geneXpert.
Results and lessons learnt: Over the 3 year period of 2016 to 2018, approximately 46 000 current and ex-mine workers were assessed, 27 000 claims certified and 24 000 claimants paid $45m. An out of court class action settlement for mine workers with TB and silicosis in the gold mining sector amounting to $350m has provided increased impetus to track and trace ex-mine workers, provide the clinical assessments and ensure payment of compensation.
Conclusions and key recommendations: These service delivery innovations in South Africa and neighboring countries while not providing health care interventions did assist with poverty alleviation through cash transfers to individual mine workers with occupational lung diseases, enhanced their access to services and raised awareness among current and ex-mine workers about occupational lung diseases and compensation. The mining sector has made progress with decreasing hazardous dust exposures to current mine workers.

PS-20-715-01 Understanding who's home: a sociodemographic analysis of household contact investigations, Buffalo City Metro Health District, Eastern Cape Province, South Africa

D Bresenham,[1] C Bezuidenhout,[1] R Mawarire,[1] P Ngwepe,[1] A Medina-Marino,[1] [1]Foundation for Professional Development, Research Unit, Pretoria, South Africa. e-mail: danab@foundation.co.za

Background: Household contact investigations (HHCI) are integral to tuberculosis (TB) control programs, early case detection, and finding missing cases. However, HHCI strategies are often omitted or constrained due to limited resources. Knowing who to prioritize to optimize HHCIs and allocate adequate resources remains challenging. Consequently, we sought to define the most at-risk contacts and analyze the feasibility of ensuring their prioritization during investigations.
Methods: We conducted HHCIs among TB patients receiving care from six public health facilities in Duncan Village Informal Settlement, Eastern Cape Province, South Africa. Community health workers screened all contacts for TB in line with to South African national guidelines. Index patient and household contact data was captured and linked using a real-time electronic information platform. The primary purpose of this analysis was to describe the sociodemographics of household contacts who screened positive to better understand the composition of households and their needs.

Results: Among 279 TB index patients, we offered screening to 946 household contacts; 11 (1.2%) household contacts were already on TB treatment, 42/935 (4.4%) refused screening, and 894/935 (95.6%) agreed to be screened. Of those screened, 170/894 (19.0%) screened positive for at least one symptom. Household contacts listed as children (44/170; 25.9%) were most likely to screen positive, and spouses (17.6%) were mostly likely to present with the most severe symptoms (3-4 symptoms). Among 935 household contacts screened, 174/232 (75.0%) children and 50/71 (70.4%) spouses were reached on the first visit.
Conclusions: The findings highlight the great need for targeted screening of children and spouses. Having a better understanding of the overall household composition and their needs will allow local health departments to target household contacts at highest risk. Targeting of high-risk household contacts may minimize costs associated with trying to reach all individuals in a house for TB screening.

PS-20-716-01 Supporting TB patients through vocational training for their better livelihood

L Raibole,[1] N Mulackal,[2] S Robert,[2] [1]CBCI CARD, NGO, Jabalpur, India, [2]CBCI CARD, NGO, New Delhi, India. e-mail: jabalpur@cbcicard.org

Background and challenges to implementation: One of the social protection mechanisms for combating poverty and for sustainable social and economic development is vocational education and training. Families of the TB patient usually face economic barriers to Healthcare and other household activities especially if the TB patient is the sole bread earner for the family. These barriers can aggravate economic hardships. The main challenge of TB patient is to earn income while they suffer from TB.
Intervention or response: Tuberculosis patients & their family members are provided free training for livelihood upliftment with an aim to make the patients & their family members self - dependent on financial ground. The patients belonged to Gaur,Bargi, Barela& other nearby areas. The training was given in four areas that are Stitching & Tailoring, Electrician, Certificate in Computer Application & Driving.
Results and lessons learnt: A training had organized by CBCI CARD in which 21 participants were trained. Out of this 13 Trainees are now generating income for their basic needs through the training provided to them. For example there is a story of Mr. Suneel Prajapati who has done training in driving trade he has also purchased one second hand car and now is earning around eight thousand per month. With this example we can see that vocational training plays a very important role in a TB patient's life.
Conclusions and key recommendations: This vocational training was designed to create skilled manpower that in turn helps in the financial development and freedom of the TB patients and their families. For a TB free world the patients themselves and their families need to be empowered and it can be done through good education and vocational training.

PS-20-717-01 Economic development assistance (EDA) to help improve treatment outcomes

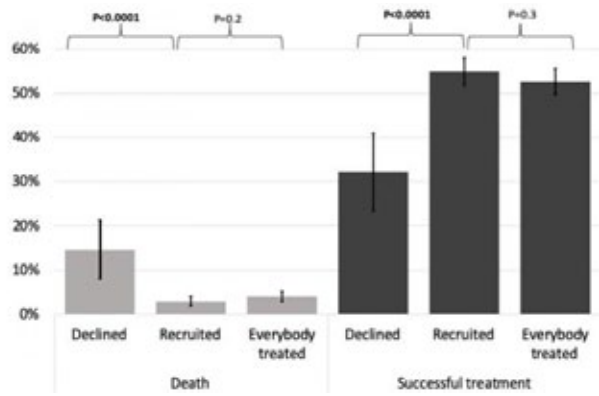
D Livingstone,[1] A Victor,[1] A Motupalli,[2] [1]World Vision India, Health, Chennai, India, [2]World Vision India, Health, Hyderabad, India. e-mail: david_livingstone@wvi.org

Background and challenges to implementation: The link between TB and poverty is an age old association. Long treatment regiments, out of pocket expenditures and lack of proper follow up results in patients not able to get back to work soon or drop out of treatment. The RNTCP DBT to assist TB patients with 500 INR for nutritional support is one way to address treatment adherence and ensure successful treatment outcomes.
Intervention or response: World Vision India Implemented Project Arubah from 2014 to 2018 in semi urban and rural areas near Achampet in Telangana. Treatment Adherence counselling and Economic development assistance (EDA) in the form of cash or kind ranging from 5000 INR to 20000 INR was provided to TB patients. The EDA provided beneficiaries were Goat, Cow, Sewing machine, Pushcart, Petty business, Educational assistances and Tea stalls. The beneficiaries also received training on how to run a business as a part of the program. Beneficiaries were chosen based on their economic backgrounds. EDA was provided to 289 families and EDA training provided to 463 family members. 66% of the beneficiary families were below poverty line (BPL) and the remaining 98 had income less than 5000 INR.
Results and lessons learnt: EDA has shown to have sustained livelihoods (e.g. tyre puncture business) and created employment. Some patients who had lost their jobs owing to stigma from TB were able to have a standing. EDA helped support continuation of education of 49 children. Beneficiaries reported income from 1000 to 15,000 per month as a result. The treatment success rate among those who received EDA was also high.
Conclusions and key recommendations: Treatment adherence support along with Providing EDA and training to TB patients can benefit both patients and their families by improving their financial status and also improving treatment outcomes. This can be a sustainable alternative to DBT and other incentives currently in place.

PS-20-718-01 Is there consent bias in the evidence generated from studies assessing socio-economic interventions to prevent TB?

L Quevedo Cruz,[1,2] R Montoya,[1,2] A Valencia,[3] J Picoy,[3] L Otero,[4] T Valencia,[1,2] MA Tovar,[1,2] M Saunders,[1,2,5] C Evans,[1,2,5] S Datta,[1,2,5] [1]Universidad Peruana Cayetano Heredia, IFHAD - Innovation for Health and Development LID 416, Lima, Peru, [2]Asociación Benéfica Prisma, IPSYD - Innovación por la Salud y el Desarrollo, Lima, Peru, [3]Diresa Callao, Equipo Técnico ESRPCTB, Lima, Peru, [4]Instituto de Medicina Tropical Alexander von Humboldt, Unidad de Tuberculosis, Lima, Peru, [5]Wellcome Trust Imperial College London Centre for Global Health Research, Infectious Diseases & Immunity, London, United Kingdom.
e-mail: luz.quevedo1108@gmail.com

Background: The World Health Organization (WHO) End TB Strategy emphasizes the importance of socio-economic support in Tuberculosis (TB) control, based on evidence from research studies. However, declined participation in these studies may cause consent bias to affect their conclusions. The objective of this study was to assess representativeness of patients with TB recruited into a socio-economic intervention study.
Methods: Patients starting TB treatment in 32 community health centres in Callao, Peru were invited to participate in the PREVENT TB cohort and CRESIPT study (http://www.isrctn.com/ISRCTN17820976) from June 2016 to June 2017. Demographic and treatment outcome data was extracted from the Peruvian National TB program treatment cards. Treatment outcome was as defined by the WHO.
Results: After ethical approval, 1103 people started TB treatment, of whom 99% (n=1093) were invited to participate. The median age was 31 years (interquartile range=22-46 years), and 66% were male. Within those who were invited, 90% (n=984) provided informed written consent and were recruited to the study. Comparing those who were recruited versus everyone who was treated, there was no difference in the proportion of patients who died during treatment, or had a successful treatment outcome (both p>0.2, see figure). However, those who declined participation (n=109) were 4.9-times more likely to die during treatment (11%, n=12) compared to recruited participants (2.5%, n=25, p< 0.0001, see figure), and 0.59-times, i.e. approximately half as likely to have a successful treatment outcome (p< 0.0001).
Conclusions: Consent bias is usually assessed by analysing whether the study population has similar characteristics to the source population, which in our study had almost indistinguishable characteristics. However, obtaining ethical approval to additionally compare TB treatment outcome, we discovered that consenting patients significantly under-represented high-risk patients with TB. Thus, the usual approach for assessing consent bias was misleading and consent bias may cause studies to underestimate the impact of socio-economic interventions.



[Figure. Analysis was with Student's T test]

PS-20-719-01 Enablers and barriers to self-management of older adults with tuberculosis

R Loa,[1] [1]University of Santo Tomas, College of Nursing, Manila, Philippines. e-mail: ritz_loa2000@yahoo.com

Background: Older adults with Tuberculosis (TB) in developing countries is becoming a public health challenge with the rapid ageing population. In the Philippines, TB ranked fourth in the leading causes of mortality for adults 60 years or older. TB is curable, however, self-management is essential in achieving treatment outcome. Self-management refers to treatment adherence, assessment of progress and problems, infection control, maintaining nutrition, and coping to psycho-social demands. Literature suggest that little has been known about self-management of older adults with TB due to their physical and cognitive decline. Therefore, the objective of this study is to describe the enablers and barriers to self-management of older adults with TB.
Methods: Twenty-two community-dwelling older adults aged 60 years old or older with pulmonary TB, and receiving treatment in different rural health units in the Philippine were purposively selected participated in the qualitative study. Data were collected by in-depth interview conducted at the homes of each participants. Qualitative data were analysed using content analysis. Respondent validation was done to established trustworthiness of the findings.
Results: The enablers of self-management of older adults with TB in the Philippines are willingness of the individual, individual awareness of their health condition, family and community support, supportive health care providers, availability of medicines, and spiritual belief of healing. On the contrary, lack of knowledge about their health condition, powerlessness, lack of financial resources are the barriers to self-management.
Conclusions: Self-management of older adults with TB are influenced by the individual, family, community, and health care providers. Older adults with strong support system, aware of their current health condition, actively

engage with their treatment and spiritual activities that promote healing, economically productive, and have access to affordable medicines in rural health units can achieve self-management with TB.

PS-20-720-01 Improved quality of life and greater patient satisfaction achieved with a drug-resistant tuberculosis supportive care package in Wuhan, China

Q Tang,[1] W Liu,[2] C Jia,[1] W Chen,[1] N Chen,[1] C Yang,[3] S Hou,[3] [1]Jinyintan Hospital, MDR-TB Division, Wuhan, China, [2]Jinyintan Hospital, Caring Division, Wuhan, China, [3]Hubei Provincial CDC, TB Division, Wuhan, China.
e-mail: 1210708862@qq.com

Background: Treatment of drug-resistant tuberculosis (DR-TB) is complicated and challenging. With support from the USAID Control and Prevention of Tuberculosis Project, we evaluated on patient DR-TB care satisfaction and quality of Care within and without implementation of a supportive care package at Jinyintan Hospital in Hubei provinces in China.
Methods: 60 MDR-TB patients diagnosed from January 2018 to May 2018 was selected as control group. 60 MDR-TB patients diagnosed from June 2018 to October 2018 was selected as experimental group. The control group received standard programmatic DR-TB care, while experimental group received care enhanced by the comprehensive supportive care package. We used World Health Organization Quality of Life 100 questionnaire and satisfaction survey on both experimental group and control group during hospitalization, to compare the difference of two care model. SPSS 20.0 was used for statistical analysis. Enumeration data was tested by chi square and measurement data was tested by Wilcoxon rank sum test.
Results: Complete surveys were obtained from 60 control group and 60 experimental group patients. Comparing two groups, respectively, they were similar in terms of overall demographics such as sex (37% vs. 43% female), age (47 years old vs. 43 years old on average).
Experimental group was higher than control group on overall satisfaction level with their TB care (95% vs. 80%, $p<0.05$), quality of life (median 94 vs. 81, $p<0.001$), re-checkup rate (97% vs. 80%, $p<0.01$) and sputum culture rate (88% vs. 65%, $p<0.01$).
Conclusions: DR-TB patients in Wuhan, China report higher levels of satisfaction and greater quality of life in their care with a supportive care package. Supportive care package was proved to be effective. Scale-up of this package should be considered at other sites in Hubei province, China and similar settings elsewhere.

PS-20-721-01 The impact of formalised community-based TB care on TB deaths and loss to follow-up

I Katjau,[1] N Ruswa,[2] A Thomas,[2] [1]Ministry of Health & Social Services, National TB & Leprosy Control Programme, Windhoek, Namibia, [2]Ministry of Health & Social Services, National TB & Leprosy Programme, Windhoek, Namibia.
e-mail: nkatjau@yahoo.com

Background and challenges to implementation: Successful treatment outcomes are essential tuberculosis (TB) elimination and prevention against drug resistance. Loss to follow up, death and treatment failure are the main causes of poor treatment outcome. To improve outcomes, community-based TB care (CBTBC) programmes were promoted in Namibia, a high TB burden country in Southern Africa. We present an assessment of the effects of introducing community TB programmes on loss to follow-up and death rates among TB patients in Namibian districts.
Intervention or response: After the first community-based TB care project in Namibia was introduced in Gobabis District in 2004, it inspired the introduction of other mainly NGO-driven projects for CBTBC between 2006 and 2014. Secondary data (annual district TB reports) was analysed to evaluate the treatment outcomes of TB patients between 2004 and 2017 against the presence of an officially-recognised CBTBC programme in each district.
Results and lessons learnt: By 2015, all 34 districts in Namibia had implemented an organised form of CBTBC, from none in 2003 and one in 2005. Data on treatment outcomes for all forms of TB from 178 district-years before introduction of CBTBC programmes and 246 district-years after introduction of CBTBC was available. The mean rate of loss to follow up decreased from 10.9% to 4.6%, a statistically significant difference ($p< 0.01$). The standard deviation and hence the variance also reduced drastically from 10.5% to 5.8% and 1.1% to 0.3% respectively. The mean death rate reduced from 11.2% to 7.8% ($p< 0.01$), with a corresponding reduction in standard deviation (10.2%-4.4% and variance (1.1-0.2).
Conclusions and key recommendations: Introduction of formalised community-based care projects is associated with positive treatment outcomes, in particular drastic reduction of loss to follow up and TB deaths. This is consistent with anecdotal and empirical findings elsewhere. Low and middle income countries such as Namibia should invest in and consolidate the work done through community TB care.

PS-20-722-01 Utilising community health advocates´ skills to promote TB rights and right to health in Kenya

L Ghati,[1,2] A Maleche,[1,3] T Saoyo,[1] N Monda,[1] [1]Kenya Legal and Ethical Issues Network on HIV & AIDS (KELIN), HIV & TB, Nairobi, Kenya, [2]National TB and Leprosy Program (NTLP), ACSM, Nairobi, Kenya, [3]Kenya Legal and Ethical Issues Network on HIV & AIDS (KELIN), Mangement, Nairobi, Kenya. e-mail: lghati@gmail.com

Background and challenges to implementation: To demonstrate that empowered Communities are change agents within their localities in championing realization of the right to health and ensuring implementation on rights based approaches to TB care.
Intervention or response: KELIN, with financial and technical support from CFCS grant- Stop TB partnership, has trained and engaged 178 Community Health Advocates (CHAs) from six informal settlements of Nairobi County, in Kenya to raise awareness on TB and human rights, identify, document and reports rights violations, enhance treatment literacy and demand for quality health care services. Being natives of their communities, the CHAs understand the social dynamics and needs of their localities and are thus able to provide objective counseling and education that helps to shape the opinions of the community with limited resistance and contribute to strengthening community and health facility linkages.
The CHAs document and report cases of health human rights violation ranging from HIV & TB related stigma and discrimination, breach of privacy and confidentiality, among others. They hold regular feedback meetings and conduct community outreaches by leveraging on existing community platforms including chiefs *barazas,* religious gatherings, and in health facilities. They receive technical support from KELIN, who has linked them to local partners working on TB, HIV and Human Rights.
Results and lessons learnt: Community health advocates, adequately trained, supported and motivated, are better champions of health rights in their respective communities. This kind of intervention has proved necessary, useful and easy to implement and can be replicated in other areas of similar and comparable settings to yield positive results.
Conclusions and key recommendations: The CHAs will continue with the community based outreaches to increase awareness, document and report TB rights and other health rights violations, and link the communities and healthcare facilities to ensure that communities enjoy their health rights.

PS-20-723-01 The ethics of tuberculosis research and care in indigenous groups

L Ruhl,[1] C Bourassa,[2] D Silva,[3] W Wobeser,[4] [1]Simon Fraser University, Faculty of Sociology and Anthropology, Burnaby, BC, Canada, [2]University of Saskatchewan, Faculty of Community Health and Epidemiology, Saskatoon, SK, Canada, [3]Simon Fraser University, Faculty of Health Science, Burnaby, BC, Canada, [4]Queen's University, Department of Biomedical and Molecular Science, Kingston, ON, Canada. e-mail: leo_ruhl@sfu.ca

Background: Globally, indigenous peoples suffer from Tuberculosis (TB) more than their non-indigenous counterparts, sparking increased care and research in and for indigenous communities. However, interactions with indigenous populations have historically resulted in many intended and unintended harms, including appropriation, misinterpretation, and inappropriate treatment. This study identifies several ethics principles and practices to guide ethical TB research and care with indigenous groups.
Methods: A literature review was conducted which gathered research ethics documents from Canada, the U.S.A., Australia, and New Zealand. Keywords were run through Pubmed and grey literature sites such as Google. Relevant ethics principles and practices related to research ethics were collected and coherent definitions of the principles were generated. *Principles* were defined as any concept or value that could guide an individual's conduct. *Common ethical practices* were defined as processes that were considered important, independent of any one ethical principle.
Results: We deduced thirteen principles from the literature and defined them. Examples include, Self-Determination, Ownership, Control, Access, Possession, Respect for Persons, Reciprocity, Trust, Transparency, Fairness, Responsibility and Accountability, Justice, and Benevolence. To make these principles relevant to researchers and healthcare practitioners, the authors suggested several ways that each principle could be applied. Likewise, important ethical practices were also defined and described, including informed consent, community collaboration and engagement, and the use of reflexivity by the researcher. Notable case studies were described which demonstrate how the principles and concepts interact together in practice. These include the Havasupai study in the U.S. and an indigenous-led TB program in Canada.
Conclusions: The principles and practices identified in this research provide tangible ways in which researchers and health workers may begin to ethically interact with indigenous groups. Although indigenous groups differ significantly in culture, language, and epistemology, this study identifies the mechanisms which health professionals and researchers can use to help navigate these differences.

PS-20-724-01 Empowering village administration for monitoring air pollution

AK Singh,[1] [1]YSP University of H& F, Nauni, Solan (HP), Environmental Science, Solan, India.
e-mail: ajaysingh7279@gmail.com

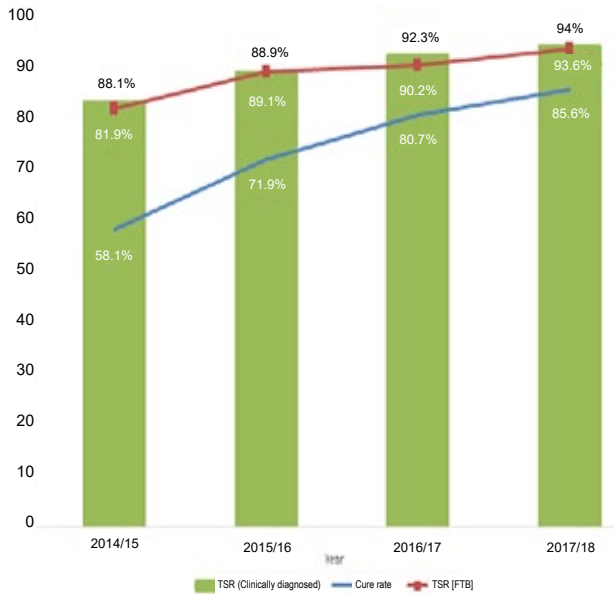
Background and challenges to implementation: Air pollution is the world's largest single environmental health risk. India, basically an agriculture and rural based economy is witnessing industrialization in rural region, as a part of government policy to reduce rural migration and uplift living standards of villagers. Laxity of norms, ease of land and labour availability has led to rampant unchecked industrial growth eventually polluting rural ambient environment and has now emerged as a public health challenge. An operational research was undertaken with the objective of strengthening the village administrative bodies called Panchayats, to become environmental monitors.
Intervention or response: Retrospective secondary health data analysis of Solan district, a fast industrializing area in northern India was undertaken. High burden chronic obstructive pulmonary disease regions were identified. Twelve environmental sanitation sensitization camps were organised for empowering the elected village leaders. Three Panchayats, administrating about 36 villages, opted to lead for the cause of checking the perceived air pollution in respective regions. Administrative resolutions on record were endorsed by the Panchayats to monitor air quality in four industries operating in the regions. Particulate matter (PM) 10 and 2.5, Nitrogen oxide (NO_2) and sulphur dioxide (SO_2) were assessed. Air quality index was calculated by adopting United States Environmental Protection Agency method and evaluated by adopting Central Pollution Control Board, India guidelines.
Results and lessons learnt: PM_{10}, $PM_{2.5}$, SO_2 and NO_2 were detected in the range of 61.57-98.42, 26.54-45.61, 22.08-39.74 and 10.98-20.03 $\mu g/m^3$ respectively. Air Quality Index (AQI) calculations evinced moderately polluted ambient air quality in two industries (AQI-55 and 58) and fairly clean air in other two industries (AQI- 43 and 45). Remedial actions for improving air quality were thereafter suggested.
Conclusions and key recommendations: The research inferred the existence of air pollution even in the rural areas and that Panchayats, if empowered administratively, can themselves play a crucial role in eco friendly environmental management.

PS-21-C2 Treatment outcomes: DS-TB

PS-21-725-01 Improved tuberculosis treatment outcomes in Tigray, Ethiopia

E Michael,[1] M Abraha,[1] A Werede,[1] H Sibagadis,[1] A Gebremedhin,[2] N Teklehaimanot,[3] S Niguse,[4] P Suarez,[5] [1]Management Sciences for Health (MSH), Health Program Group (HPG), Mekelle, Ethiopia, [2]Tigray Regional Health Bureau, Disease Prevention and Control, Mekelle, Ethiopia, [3]Tigray Regional Health Bureau, TB Program, Mekelle, Ethiopia, [4]Tigray Regional Health Bureau, Health Management Information System (HMIS) Unit, Mekelle, Ethiopia, [5]Management Sciences for Health (MSH), Infectious Diseases Cluster, Arlington, VA, United States of America. e-mail: eyabato@gmail.com

Background and challenges to implementation: TB is a major communicable disease with a significant impact on public health. Ethiopia is among the high-burden countries for TB. The Tigray Regional Health Bureau (TRHB), one of the regions in Ethiopia, in collaboration with USAID/Challenge TB, has supported the region to improve overall TB program performance since 2015. We describe the trend of the treatment outcomes of TB cases in the region.
Intervention or response: This is a TB program review based on aggregated quarterly data from the health information systems (HMIS) of 247 health facilities in the region from 2014/15 to 2017/18. We analyzed the results against the regional targets of 80% for cure rate and 90% for treatment success rate (TSR).With support from USAID/Challenge TB, the TRHB conducted need-based trainings, review meetings, and sensitization workshops to health care workers (HCWs), woreda experts, and primary health care unit (PHCU) directors.
Over three years, 418 HCWs received basic comprehensive TB training, 290 health information technology and HMIS officers were trained on TB M&E, and 231 PHCU directors were sensitized on TB/HIV. Routine quarterly joint supportive supervision was conducted by CTB/TRHB/woreda experts to 16 hospitals and 52 high-load health centers, and quarterly independent supportive supervision was done by woreda TB experts to low-load health centers.
Results and lessons learnt: For bacteriologically confirmed cases, the cure rate improved from 58.1% to 85.6% and the TSR improved from 81.9% to 93.6%. The TSR for all TB cases improved from 83.1% to 94% (figure 1). The region achieved the targets set for cure rate (80%) and TSR (90%).
Conclusions and key recommendations: The strong aligned coordination support through capacity building and onsite supportive supervision was proven to improve treatment outcomes of TB. Need-based capacity building and onsite support should be scaled up.



[Figure 1. TB treatment outcome in in Tigray Region, Ethiopia: 2014/15-2017/18]

PS-21-726-01 Improving TB treatment outcomes in a rural setting with difficult access in Papua New Guinea

L Sannino,[1] H Bogati,[2] T Marquardt,[3] P Blasco,[1]
[1]Médecins Sans Frontières (MSF), Medical, Paris, France, [2]Médecins Sans Frontières (MSF), Medical, Port Moresby, Papua New Guinea, [3]Médecins Sans Frontières (MSF), Operations, Tokyo, Japan.
e-mail: laura.sannino@paris.msf.org

Background and challenges to implementation: The Gulf Province in Papua New Guinea (PNG) is a rural area with a very dispersed population and geographical challenges which limit people's mobility and access to care. Médecins Sans Frontières (MSF) has supported the National TB program in Kerema, capital of Gulf Province, since 2014. One of the major challenges has been the high rate of lost-to-follow-up (LTFU) from TB treatment.
Intervention or response: This challenge has been addressed with a differentiated approach: improved TB diagnosis, proper usage of TB recording and reporting tools, such as treatment cards and TB register, establishment of a community-based treatment supporter network, implementation of missed appointment register and tracing system, dedicated lay counselors for patient education and counselling, provision of transport fees to patients and treatment supporters and training of staff to implement all of the above activities.
Results and lessons learnt: The 2014 TB cohort had a success rate of 43% for all TB cases and 44% for confirmed TB cases, with a LTFU rate respectively of 36% and 31%. The LTFU rate dropped to 25% for all TB cases and 19% for confirmed TB cases in 2017 cohort, while the success rate rose to 64% and 70%, respectively. Better reporting, patients' education and counselling and community awareness accounted for a significant share of this improvement. Treatment supporters' network posed some challenges regarding supervision and task definitions, but ultimately proved to be useful. Additionally, improved TB diagnosis decreased the number of patients stopping because of lack of improvement. Challenges remain to offer treatment as close as possible to the patient and to better respond to individual patients' needs. The outcomes are significantly improved, but still far from ideal.
Conclusions and key recommendations: A multi-sectoral approach is needed to improve TB treatment outcomes. In rural areas with poor access, WHO-recommended targets remain difficult to achieve even when significant investments are made.

PS-21-727-01 Factors associated with TB patients lost to follow-up: a case-control study in four health districts in Mali

Y Ballayira,[1] F Camara,[2] Y Toloba,[3] N Traoré,[1] B Konaté,[1] A Cissé,[2] CSC Merle,[4] M Savy,[5] M Dramé,[6]
[1]General Directorate of Health and Public Hygiene, National TB Program, Bamako, Mali, [2]National Institute of Research in Public Health, National Reference TB Lab, Bamako, Mali, [3]Univesity of Bamako, Pneumophtisiology, Bamako, Mali, [4]WHO, TDR WHO, Geneva, Switzerland, [5]WHO Benin, TDR WHO, Cotnou, Benin, [6]University of Reims Champagne-Ardenne, Faculty of Medicine, EA 3797, Reims University Hospital, Robert Debré Hospital, Research and Public Health Center, Reims, France. e-mail: ballayira@gmail.com

Background: According to WHO, TB patients lost to follow-up should be <5%. In Mali, this rate was 12% and 11% in the regions of Sikasso and Mopti in 2015. These lost to follow-up are sources of spread of tuberculosis, can develop drug resistance, more expensive to treat resulting in an increased risk of mortality. Thus we conducted this study at Sikasso and Mopti in 4 health districts. The objective was to identify factors associated with TB patients lost to follow-up.
Methods: We conducted a case-control study from November 2017 to February 2018. The population was tuberculosis patients registered from July 1, 2016 to June 30, 2017, aged 18 and over. A case was any TB patient who had not started treatment or was interrupted for two consecutive months or more. A control was the one who had correctly followed the treatment without interruption. The data were collected using an interview questionnaire. We analyzed the data using Epi Info7. Logistic regression was used to identify the significance factors at 0.05. Frequencies, proportions and 95% confidence interval (95% CI) were calculated.
Results: In total we had 66 cases and 133 controls. The mean ages were 43 and 41 years (p = 0.3070) respectively in cases and controls. In multivariate analysis distance to diagnosis and treatment center >15 km (OR 3.64, 95%

CI [1.63-8.14]), supervised treatment (OR 0.13, 95% CI [0.04-0.48]), feeling better on treatment (OR 2.36, 95% CI [1.18-4.73]) and early morning fasting treatment (OR 0.15, 95% CI [0.03-0.73]) were the factors independently associated with tuberculosis lost to follow-up.
Conclusions: Distance >15 km supervised treatment are important factors associated with lost to follow-up. We recommend bringing care closer to patients and restoring the treatment directly observed by the community and to sensitize patients feeling better under treatment.

PS-21-729-01 Identification of risk factors for unfavourable tuberculosis treatment outcomes among patients in Chingola District, Zambia

N Zimba,[1] R Kumar,[2] R Kabeya,[3] C Siluyele,[3] C Deyala,[3] J Bwembya,[2] M Makasa,[4] A Mwinga,[2] [1]Ministry of Health Zambia, Chingola District Health Office, Lusaka, Zambia, [2]Eradicate TB Zambia, Zambart, Lusaka, Zambia, [3]Ministry of Health Zambia, Chingola District Health Office, Chingola, Zambia, [4]University of Zambia, School of Public Health, Department of Community & Family Medicine, Lusaka, Zambia. e-mail: zimba.noel@yahoo.com

Background: In 2017, the mining district of Chingola, Zambia reported facility data which showed unfavorable TB treatment outcomes were exceeding national targets. This study sought to determine factors associated with TB treatment outcomes, as well as causes of death, and reasons for "not evaluated" treatment status.
Methods: This study was a cross-sectional survey of TB treatment registers in 8 treatment facilities. We extracted secondary data for adults (>15yrs) who initiated TB treatment in Chingola between January 1 and June 30, 2017. We calculated proportions of treatment outcomes and noted the recorded causes of death, or reasons for a "not evaluated" treatment status. We analysed associations between TB treatment outcomes and patients' age, gender, HIV status, and relapse status, clinical-diagnosis, relationship to a miner, and reported adjusted odds ratios (aOR) and 95% confidence intervals (95%CI).
Results: Of the 463 TB patients, 84 (18%) had unfavorable outcomes (died, lost to follow up, or not evaluated). The odds of unfavorable outcomes were higher among patients who were TB/HIV coinfected (aOR= 2.83; 95% CI:1.41-5.70), clinically diagnosed (aOR= 2.58; 95% CI:1.36-4.90), or relatives of a current/former miner (aOR=2.60; 95% CI:1.01-6.67). Of 40 patients who died, 31 (77.5%) were TB/HIV coinfected; of these, 14 (45%) were not recorded on antiretroviral therapy (ART). Of 20 "not evaluated" patients, (65%) were recorded as "transferred out of the facility," with no facility specified.
Conclusions: HIV coinfection, clinical diagnosis, and relation to a miner are significantly associated with unfavorable outcomes, and reasons for these outcomes are poorly recorded in registers. Facility staff should counsel all TB/HIV coinfected patients to initiate ART, perform confirmatory TB testing on clinically diagnosed patients, and assign TB treatment supporters to patients who are relatives of miners. All staff should be re-oriented on TB data-recording procedures and specify transfer facilities in order to ensure continuity of care.

PS-21-730-01 Epidemiological, clinical aspects and outcome of patients under anti-tuberculosis treatment: a retrospective cohort study in Parakou, Benin

CA Attinsounon,[1] L Behanzin,[2] S Adé,[3] A Alassani,[4] CA Dovonou,[4] [1]University of Parakou, Department of Infectious and Tropical Diseases, Parakou, Benin, [2]University of Parakou, Public Health School, Parakou, Benin, [3]University of Parakou, Department of Pneumology, Parakou, Benin, [4]University of Parakou, Department of Internal Medicine, Parakou, Benin.
e-mail: acosange@yahoo.fr

Background: With 4092 new cases in 2016, tuberculosis remains a major public health problem in Benin. This study aims to describe the epidemiological, clinical and outcome of tuberculosis cases followed in North Benin from 2009 to 2016.
Methods: This was a retrospective and descriptive cohort study. All cases of tuberculosis among adults' patients followed on the Parakou's centre of diagnosis and treatment of tuberculosis from 1 January 2009 to 31 March 2016 were included. Recruitment was exhaustive. Epidemiological, clinical, therapeutic and outcome data were collected from medical files. The data were analysed using Epi-info software 3.5.2.
Results: A total of 286 patients (173 men and 113 women) were treated for tuberculosis out of 7311 patients received during the study period or a prevalence at 3.91%. The average age was 39.5 ± 15,1 years and 209 patients (73.08%) lived in rural areas. There were 242 cases of pulmonary tuberculosis (84.62%), 21 cases of extrapulmonary tuberculosis (7.34%), 13 cases of multifocal tuberculosis (4.54%) and 10 cases of miliaria (3.50%). There were 266 new cases (93.01%), followed by 9 cases of relapse (3.15%), 6 cases of treatment failure (2.10%) and 5 cases of resumption of treatment (1,75%). According to the treatment outcome, there were 229 cases (80.07%) of healing and 57 cases (19.93%) of unfavourable outcome, including 34 deaths (11.89%), 9 treatment failures (3.15%), 11 lost to follow-up (3.85%) and 3 discontinued (1.05%). The HIV test was positive in 123 TB patients or a prevalence at 43.01% of TB-HIV co-infections.
Conclusions: This study shows the need to reinforce the follow-up of anti-tuberculosis treatment in patients coming from rural areas to improve the outcome of treatment in North Benin.
Key words: Tuberculosis, epidemiology, treatment outcome, Parakou, Benin

PS-21-731-01 Supporting adherence to treatment for tuberculosis (TB): a relational view

K Kielmann,[1] N Vidal,[1] A Karat,[1] H Stagg,[2] M Lipman,[3] on behalf of the IMPACT study group (NIHR 16/88/06) [1]Queen Margaret University, Institute for Global Health & Development, Edinburgh, United Kingdom, [2]University of Edinburgh, Usher Institute of Population Health Sciences and Informatics, Edinburgh, United Kingdom, [3]University College London, UCL Respiratory, London, United Kingdom.
e-mail: kkielmann@qmu.ac.uk

Background: Determinants of adherence to treatment for TB have been classified as personal, social, and structural, reflecting fragmented disciplinary assumptions about *when*, *why*, and *how* people take medicines. Most interventions focus on behaviour change; initiatives to address social and structural issues affecting adherence are limited.

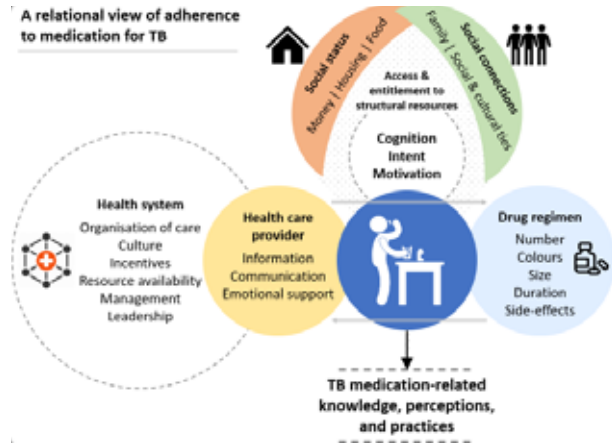
We aimed to critically synthesize qualitative evidence on determinants of adherence to treatment for TB and assess theories of change underlying interventions to support adherence to treatment.

Methods: We conducted a scoping review of qualitative studies following the Arksey and O'Malley methodology. CINAHL, MEDLINE, PsycINFO, and the Cochrane Library were searched for publications between January 2007 and December 2018 using qualitative methods to investigate reasons for non-adherence to treatment for TB and interventions to support adherence to treatment from the perspective of adult patients, care givers, and/or health care providers

Results: The search yielded 531 results, of which 138 were relevant. Qualitative research on adherence to treatment has steadily increased in the past decade yet is skewed towards high-burden settings and operational research assessing individual knowledge, attitudes, and practices (KAP). Gender, stigma, health literacy, and social connections emerged as multi-dimensional and cross-cutting constructs that impact on treatment adherence in different settings, yet we found limited evidence on how multiple determinants of adherence interact.

The few studies examining patient and provider experience of interventions to support treatment adherence are cross-sectional and do not capture changes in patterns and context of adherence over the course of treatment.

Conclusions: To date, interventions to support adherence to treatment for TB have mainly targeted gaps in patients' knowledge, 'misconceptions', or 'forgetfulness', reflecting a narrow focus on individual agency and choice in medicine-taking. We propose a relational view of adherence that acknowledges the importance of social roles, relationships, and context in enabling or hindering treatment literacy and adherence among individuals on treatment for TB.



[A relational view of adherence to medication for TB]

PS-21-733-01 Monitoring of patient treatment through eCompliance to ensure improved adherence resulting in favourable treatment outcomes in TB patients in urban Bhubaneswar, Orissa

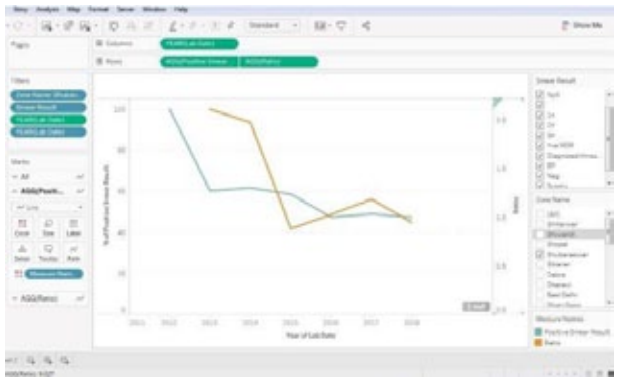
S Panigrahi,[1] S Batra,[2] S Ahuja,[3] M Bajiya,[4] S Batra,[5] [1]District Headquarter Hospital, TB & Infectious Diseases, Puri, India, [2]Operation ASHA, Medical Advisor & Chief of Fund Raising, New Delhi, India, [3]Operation ASHA, Operations, Partnerships & External Relations, New Delhi, India, [4]Operation ASHA, Operations, New Delhi, India, [5]Operation ASHA, Technology, New Delhi, India.
e-mail: satyarpanigrahi@gmail.com

Background: The Indian Revised National TB Control Program aims at achieving 85% or higher Treatment Success Rate. The hurdle in achieving this is the non-adherence of patients to TB Treatment. Poor adherence causes drug resistance and leads to failure of the TB control program.

Methods: Operation ASHA in collaboration with Microsoft Research designed a software application called eCompliance. All the TB patients are registered on this software application to track every dose through fingerprinting.

Results: In Bhubaneswar, Operation ASHA has 19 Operational centers with a staff of 11 people. A total of 2378 patients have been registered on eCompliance. The DOTS Providers give daily supervised medicines to TB patients and take fingerprint of the patient on every dose. There is real time information of every missed dose resulting in prompt action by Providers. This ensures adherence, reduces chances of lost to follow up, leading to good TSR. The TSR achieved in the given period was 85% for the DS-TB patients. The default rate was only 6%. Also, the supervised doses provided through eCompliance were 88.4% for Bhubaneswar. Operation ASHA also did an analysis with the help of a software provided by Tableau for free. This calculated the ratio of highly infectious patients (where sputum is 2+ or 3+) to

less infectious patients (where sputum is 1+ or scanty). The ratio has dropped drastically as accelerated Active Case Finding has led to identification of patients at early stage of the disease. The ratio has dropped from 2.2 to less than 1 with the efforts made by Operation ASHA.
Conclusions: Treatment adherence can be improved by close monitoring of the treatment of TB patient. Using eCompliance digital technology ensures transparency and authenticity of data recorded. Frequent interaction of patient and Provider gives patient an opportunity to get counselled during the treatment.



[Bhubaneswar_Sputum results graph]

PS-22-C1 Everything about TB infection

PS-22-735-01 Vitamin-D deficiency in latent tuberculosis predicts progression to active disease: a longitudinal study

B Patterson,[1,2] D Smith,[1] A Tana,[1] D Johnstone,[1] R Davidson,[1] A Martineau,[3] [1]Northwick Park Hospital, Infectious Disease Department, London, United Kingdom, [2]University of Amsterdam, Institute for Global Health and Development, Amsterdam, Netherlands, [3]Barts and The London School of Medicine and Dentistry, Queen Mary University of London, Blizard Institute, Centre for Immunobiology, London, United Kingdom.
e-mail: patterson.b@unic.ac.cy

Background: Low vitamin D levels have been associated with active tuberculosis (TB) disease and normal levels may be protective against progression to disease for those with latent infection by supporting innate and adaptive immune responses. We assessed the impact of baseline levels of vitamin D on incidence of active disease in latent TB patients in a low burden country.
Methods: Serum 25-hydroxyvitamin D (25(OH)D) levels were retrospectively linked to adults diagnosed with latent TB by tuberculin skin test (TST) or interferon gamma release assay (IGRA) between April 2010 and January 2019 in a hospital in London, UK. Individuals with subsequent progression to active TB were identified by matching this cohort with notifications to a London-wide TB register. We then constructed a logistic regression model to examine the relationship between baseline vitamin D deficiency and subsequent incidence of TB disease.
Results: 1323 latently infected individuals were matched to vitamin D levels at the time of latent TB diagnosis or within the year. There was a median of 4.0 (IQR: 2.2 to 5.1) years of follow-up representing 4826 patient-years. There were 13 (1%) instances of TB reactivation, all of which were at least three months following the latent TB diagnosis. 515 (39%) cases were identified as vitamin D deficient (serum 25-hydroxyvitamin D < 25 nmol/L). Vitamin D deficiency was strongly associated with progression to active TB disease (adjusted OR: 6.5 (95% CI: 1.9 to 30.2; p=0.008) after controlling for age, sex, patient weight and season at time of latency diagnosis, HIV status and administration of latent TB chemoprophylaxis (analysed as an intention to treat). No interaction between vitamin D status and chemoprophylaxis was seen.
Conclusions: Our results show a significant independent association between vitamin D deficiency and progression from latent TB infection to active disease.

PS-22-736-01 Serial QuantiFERON® TB-Gold in-tube testing after TB preventive therapy in a tuberculosis high-endemic country: a controlled study

Q Yang,[1] Q Ruan,[1] X Huang,[2] L Shao,[1] W Zhang,[1] [1]Huashan Hospital Affiliated to Fudan University, Infectious Diseases, Shanghai, China, [2]Wenling First People's Hospital, Infectious Diseases, Taizhou, China. e-mail: 10301010198@fudan.edu.cn

Background: T-cell interferon-γ (IFN-γ) responses to Mycobacterium tuberculosis specific antigens is currently used to diagnose latent tuberculosis. Whether the test can be used as an efficacy biomarker in tuberculosis preventive treatment in a high-endemic country is uncertain.
Methods: In this prospective, open-label, controlled study, 513 silica dust exposed individuals were randomly assigned to treatment with 3-month (12-dose) regimen of weekly rifapentine and isoniazid (3RPT/INH) preventive treatment or observation. QuantiFERON®-TB Gold In-Tube (QFT-GIT) assay was used to measure IFN-γ response to mycobacterial antigens at baseline (T0) and 6 months after completion of therapy(T1), 36 months after therapy completion(T2).
Results: A total of 222 subjects were included in final analysis, 106 in prevention group and 116 in observation group. The proportions of QFT-GIT reversion from baseline to T1 were similar in the prevention and observation groups(P=0.566).
However, reversion from baseline to T2 was more frequent in the prevention group (24.2%) compared with the observation group (6.3%), but no statistical signifi-

cance received (P= 0. 881). As for quantitative responses of QFT-GIT during the follow-up, there was no significant difference between two arms (P=0.648) with a slightly decline in concentration at T1.
However, in the subjects who were also evaluated at T2, significant arise in quantitative response were observed in both prevention arm (P< 0.001) and observation arm (P< 0.05) during T2, but no significant difference between two groups (P =0.918).
Conclusions: Serial QFT-GIT testing is probably not a useful biomarker for evaluating the efficacy of tuberculosis preventive treatment. QFT changes were found to be similar among individuals with and without preventive treatment.
Trial registration: www.clinicaltrials.gov (NCT02430259)

PS-22-737-01 Prevalence of tuberculosis infection and disease in adult household contacts

M Adjobimey,[1] S Ade,[2] P Wachinou,[2] F Kassa,[3] L Yaha,[3] W Bekou,[4] D Capochichi,[5] C Valiquette,[6] G Agodokpessi,[2] [1]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Prevention, Cotonou, Benin, [2]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Pneumologie, Cotonou, Benin, [3]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Recherche, Cotonou, Benin, [4]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Statistique, Cotonou, Benin, [5]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Clinique, Cotonou, Benin, [6]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada.
e-mail: menoladjobi@yahoo.fr

Background: Patient recruitment for a multicenter, open-label, randomized controlled trial (NCT00931736) comparing four-months of rifampicin (4RIF) with nine-months of isoniazid (9INH) was conducted between November 2009 and January 2015. We wished to determine the prevalence of latent tuberculosis infection (LTBI) and tuberculosis (TB) disease among adult household contacts (HHC) of pulmonary TB patients, screened as part of this trial in Benin.
Methods: All adult (≥18 years) HHC who agreed to voluntarily come for clinical TB assessment as part of this trial were included. Each HHC received a tuberculin skin test (TST; 0.1ml [2 tuberculin units]), which was read 48-72 hours after placement. HHCs with TST <5mm were asked about TB symptoms and contacts with TST ≥5mm were given a clinical examination and chest x-ray (CXR).
Those with TB symptoms and/or CXR abnormalities consistent with TB were assessed microbiologically. A TB diagnosis was made based on microbiological results or clinical assessment. HHCs without a TB diagnosis, but with a TST ≥5mm, were diagnosed with LTBI.
Results: A total of 1868 adult HHC received a TST and 1770 (94.7%) had their TST read. A TST ≥5mm was found in 1382 (78.1%). Among HHCs with a TST result, 27 (1.5%) cases of TB were identified for a TB prevalence of 1525 per 100,000. Among those diagnosed with TB, 25 (92.6%) had a TST ≥5mm. The mean (SD) age of the 27 TB cases was 32 (12) years, 12 (44.4%) were female, and 1 (3.7%) had HIV-coinfection. TB diagnosis was made based on acid-fast bacilli smear positivity in 15 (55.6%) cases and based on clinical assessment in 12 (44.4%) cases.
Conclusions: The prevalence of LTBI and TB disease was high among adult HHCs. These results emphasize the importance of including thorough contact investigations for LTBI and TB disease within the TB programme in Benin.

PS-22-738-01 Usefulness of interferon-gamma releasing assay in patients with hematologic malignancies

YW Huang,[1,2] WW Chen,[3] WC Huang,[4] [1]ChangHua Hospital, Ministry of Health and Welfare, Medical Affairs, Chang-Hua, Taiwan, [2]Chang Shan Medical University, Institute of Medicine, Taichung, Taiwan, [3]ChangHua Hospital, Ministry of Health and Welfare, Tuberculosis, Chang-Hua, Taiwan, [4]Taichung Veterans General Hospital, Chest Medicine, Taichung, Taiwan.
e-mail: sweefa818@gmail.com

Background: It is estimated that the Relative Risk of tuberculosis (TB) disease in patients with hematologic malignancies is 2 to 40 times that of the general population. Therefore, it is recommended to diagnose latent TB infection and consider preventive therapy that could avoid the progression from a latent state to active TB disease. The aim of our study was to investigate the usefulness of interferon-gamma releasing assay for predicting active TB in patients with hematologic malignancies.
Methods: We prospectively included patients with hematological malignancies at Taichung Veterans General Hospital, Taiwan between January 2012 and December 2013. The performance of QuantiFERON for predicting active TB was studied.
Results: A total of 89 patients were included in the final analysis, of whom 11.2% (10/89), 58.4% (52/89), and 30.3% (27/89) had positive, negative, and indeterminate results of QuantiFERON. Of those with positive results, none of 3 patients receiving isoniazid prophylaxis developed TB but 3 of the 7 patients without receiving isoniazid prophylaxis developed TB. Of those with indeterminate results, one patient developed active TB. The lymphocyte counts were significantly lower in patients with indeterminate QuantiFERON results compared to those with determinate QuantiFERON results. Further analysis found that the lower white blood count, the lower lymphocyte count, and the lower lymphocyte percentage, the higher percentage of indeterminate QuantiFERON results.

Conclusions: In patients with hematologic malignancies, QuantiFERON assay results can predict development of TB. QuantiFERON indeterminate results happened more frequently when the white blood count, lymphocyte count and lymphocyte percentage were lower.

PS-22-739-01 Association of latent TB infection in pregnancy with perinatal health outcomes in an Indian cohort

R Bhosale,[1,2] H Graham,[3] M Alexander,[2] A Kinikar,[4] S Khwaja,[2] N Patil,[5] A Gupta,[2,6] J Mathad,[2,7] R Shivakoti,[3,8] [1]B. J. Government Medical College, Dept of Obstetrics and Gynecology, Pune, India, [2]B. J. Government Medical College-Johns Hopkins University Clinical Research Site, Clinical Trial Unit, Pune, India, [3]Columbia University Mailman School of Public Health, Mailman School of Public Health, New York, NY, United States of America, [4]B.J. Government Medical College, Dept of Paediatrics, Pune, India, [5]B. J. Government Medical CollegeJohns Hopkins University Clinical Research Site, Clinical Trial Unit, Pune, India, [6]Johns Hopkins School of Medicine, Infectious Diseases, Baltimore, MD, United States of America, [7]Weill Cornell Medical College, Center for Global Health, New York, NY, United States of America, [8]Johns Hopkins School of Medicine, Medicine, Baltimore, MD, United States of America. e-mail: drrameshbhosale@yahoo.com

Background: Latent TB infection(LTBI) is common among pregnant women but it is unknown if LTBI affects perinatal health outcomes, similar to other latent infections. The objective of this study was to assess whether LTBI status during pregnancy is associated with adverse maternal and infant health outcomes during the perinatal period.
Methods: We conducted a longitudinal cohort study of HIV-infected and HIV-uninfected pregnant women. At enrollment, all women were tested for LTBI by interferon gamma release assay (IGRA). Maternal data such as preeclampsia, hemoglobin levels, membrane rupture timing, amniotic fluid findings, and delivery type, was collected at appropriate time points, enrollment, third trimester and delivery. Birth outcomes, infant IGRA+ status at 6 months and infant anthropometrics from birth through twelve months of age were also collected. Outcomes of women with and without LTBI and their infants were compared using t-tests and chi-squared tests.
Results: We enrolled 234 women: 165 (70%) with LTBI and 69 (30%) without LTBI. Participant median age was 23 years, 34% were HIV+, and 23% had primary school or less education. Infant birth weight (p=0.60) and gestational age at birth (p=0.27) were not different by maternal LTBI status. Infant weight was significantly lower at 12 months of age for children of LTBI+ women versus those without LTBI (7.86 kg vs 8.28 kg, p=0.04). A greater proportion of infants born to LTBI+ mother were also IGRA+ at 6 months (4.9% vs. 0%, p=0.13). LTBI status was not significantly associated with any maternal outcomes among the cohorts.
Conclusions: Infants born to LTBI+ women had lower weight at 12 months and were more likely to be IGRA+ at 6 months. This could reflect that maternal LTBI results in chronic inflammation and subsequent long-term modifications of infant growth trajectories. Future studies are needed to confirm these findings in other cohorts of pregnant women.

PS-22-740-01 The effectiveness of public health intervention upon screening for latent tuberculosis infection among household contacts in central Viet Nam

NB Tran,[1] VN Nguyen,[2,3] TA Nguyen,[1,4] BH Nguyen,[2,3] TA Nguyen,[2,3] C Valiquette,[5] OA Oxlade,[5] F Fregonese,[5] GJ Fox,[1,4] D Menzies,[5] [1]Woolcock Institute of Medical Research, Research, Hanoi, Viet Nam, [2]Vietnam National Tuberculosis Program, VICTORY, Hanoi, Viet Nam, [3]Vietnam National Lung Hospital, Programme, Hanoi, Viet Nam, [4]University of Sydney, Faculty of Medicine and Health, Sydney, NSW, Australia, [5]Research Institute of the McGill University Health Centre; McGill International TB Centre, Respiratory Medicine, Montreal, QC, Canada. e-mail: buu.tranngoc@sydney.edu.au

Background: Diagnosis and treatment of latent tuberculosis infection (LTBI) among household contacts (HHCs) is an important component of the End TB Strategy. However, implementation of HHCs investigation for tuberculosis (TB) in resource-limited settings may be challenging.
This study aimed to evaluate the effectiveness of a programme to implement latent TB screening and treatment in Vietnam.
Methods: A cluster randomized trial was performed in 11 district health centers in central Vietnam. Control sites delivered routine care, which involved a recommendation for staff to screen under five children and treat for LTBI. Sites randomized to the intervention group implemented a package of locally- chosen interventions to strengthen contact investigation, screening and treatment for LTBI. Intervention package included: brief health education session for index patients and their HHCs about the importance of TB/LTBI screening; training healthcare staff to perform tuberculin skin testing (TST); provision of tuberculin; support for HHCs travel expenses to visit clinic and for staff to performing TST. The national health insurance scheme covered other expenses. Outcomes included the number of HHCs identified and commencing LTBI treatment per 100 index cases (IC).
Results: In control sites, 125 index patients with bacteriologically confirmed pulmonary TB were registered for treatment and 31 of their HHCs were identified, of whom 14 under five (25 HHCs per 100 ICs). None were treated for LTBI. During the same 6 months, at intervention sites, 569 HHCs (51 under five) of 180 index patients were identified (320 HHCs per 100 ICs). Among these, 210 (117 per 100 ICs) started LTBI treatment,

including 32 under five. In intervention sites, identification and treatment commencement were 92% and 100% higher respectively.
Conclusions: A package of public health interventions was associated with a substantial higher in enrolment and treatment for LTBI. Further research is required to evaluate the cost-effectiveness of this approach.

PS-22-741-01 Postgraduate medical residents' perceptions of occupational tuberculosis and isoniazid preventive treatment

T Kadhiravan,[1] SA Rao,[1] RP Swaminathan,[1] [1]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Medicine, Puducherry, India.
e-mail: kadhir@jipmer.edu.in

Background: Anecdotal evidence suggests that healthcare workers (HCWs) often believe that they are immune to tuberculosis (TB), a phenomenon described as "TB-proof". We examined postgraduate medical residents' perceptions of occupational TB risk and isoniazid preventive treatment (IPT).
Methods: This is a secondary analysis of data from a previously published open cohort study on the risk of TB among 398 postgraduate residents from a medical school in southern India. The study questionnaires included 4 questions on the self-perceived risk of occupational TB, perceived efficacy of IPT in India, personal willingness to take IPT, and opinion about a Cochrane systematic review which found that IPT reduced the relative risk of TB disease by 60%. The responses were scored using a Likert-type scale. We describe the responses to these questions and how the responses varied across the 3 specialty-based risk strata.
Results: Overall, 85 (21%) of 398 residents perceived the risk of occupational TB as 'very low' (n=24) or 'low' (n=61); 54 of the 85 residents were working in intermediate-risk (n=40) or high-risk (n=14) specialties. While 120 (30%) of 396 residents believed that IPT is definitely beneficial, 23 residents believed that IPT is definitely not beneficial, and 253 were uncertain about the efficacy of IPT for TB prevention in India.
On the other hand, 286 (72%) residents responded that they would be willing to take IPT if they were diagnosed with latent TB infection; 49 residents responded as 'No'; and 61 residents were unsure. While 226 residents either strongly agreed (n=30) or agreed (n=196) with the findings of the Cochrane review, 14 residents disagreed or strongly disagreed; 12 of them were working in intermediate/high-risk specialties; 156 responded as "Don't know".
Conclusions: A considerable proportion of postgraduate medical residents believed that they were "TB-proof", and many of them were skeptical about the efficacy of IPT.

PS-22-742-01 Knowledge, attitude and practices on latent tuberculosis infection among general practitioners: a challenge for TB elimination in Havana, Cuba

A Martínez Rodríguez,[1] T Battaglioli,[2] CS Nuñez Mederos,[3] E González Ochoa,[1] P Van der Stuyft,[4] [1]Instituto de Medicina Tropical Pedro Kourí, Department of Epidemiological Research in Tuberculosis, Havana, Cuba, [2]Institute of Tropical Medicine Antwerp, Department of Public Health, Antwerp, Belgium, [3]Instituto de Medicina Tropical Pedro Kourí, Department of Epidemiology, Havana, Cuba, [4]Gent University, Department of Public Health and Family Medicine, Gent, Belgium.
e-mail: alina@ipk.sld.cu

Background: Tuberculosis (TB) preventive treatment in high-risk groups is a key, but generally poorly implemented TB elimination strategy. Understanding the barriers to completing the steps of the cascade of preventive care can inform improvement interventions. Cuba has a low TB incidence and aims at TB elimination. General practitioners (GPs) are responsible for identifying individuals at risk of latent TB infection (LTBI), referring for testing and following-up preventive treatment.
Methods: To explore GPs′ knowledge, attitude and practice on LTBI, a self-administered, semi-structured questionnaire was delivered to 62 randomly selected practitioners in a municipality of Havana. Questions addressed LTBI definition, diagnosis, treatment and referral mechanisms.
Results: The participants' median age was 33 years, duration of professional experience 9 years and of practice in the current post 1.5 years; 24% and 20% managed TB and LTBI cases in the past two years, respectively. Participants correctly recognized a median of 12 out of 19 essential knowledge items on the subject. 31% mentioned TB contacts among TB high-risk groups; most ascertained the definition of LTBI and 40% the associated probability of developing TB; 95% knew tuberculin skin testing (TST) and 76% where to refer for testing, but just 18% discerned what reaction is measured; only two GPs recognized all TST indications; 95% identified isoniazid as the drug used in Cuba for preventive treatment, but only 37% knew active TB is a contraindication for it.
Reasons mentioned for losses along the cascade of preventive care were health system-related (e.g. sub-optimal knowledge and compliance with national guidelines) and patient-related (e.g. non-compliance with prescriptions, low adherence).
Conclusions: During TB elimination, while incidence declines, keeping knowledge of and priority given to the disease up to standards pose challenges to the health system. Continuous and effective staff training must be implemented, alongside improving communication between the different levels of care and the TB program.

PS-22-743-01 Influence of isoniazid prevention treatment (IPT) on development of active tuberculosis among contact children in Georgia

E Kokhreidze,[1] N Tukvadze,[1] N Lomtadze,[2] N Jorjoliani,[3] M Avanashvili,[2] R Kempker,[4] [1]National Center for Tuberculosis and Lung Disease, Research Department, Tbilisi, Georgia, [2]National Center for Tuberculosis and Lung Disease, Strategic Planning and Development, Tbilisi, Georgia, [3]National Center for Tuberculosis and Lung Disease, Pediatric Department, Tbilisi, Georgia, [4]Emory University School of Medicine, Division of Infectious Diseases, Atlanta, GA, United States of America. e-mail: ekokhreidze@yahoo.com

Background: The utilization and uptake of LTBI treatment among children is an important measure to prevent active TB, but has not been well studied in low and middle-income countries (LMICs). Within the national guidelines of state Tuberculosis Control Program (NTP) in Georgia 6 months Isoniazid preventive treatment (IPT) should be administered in all investigated contact children aged 0-5 for disease prevention. We sought to evaluate the care cascade of LTBI treatment among children aged 0-5 years at NCTLD.
Methods: We performed the retrospective cohort-study among children aged 0-5 who visited NCTLD during 2012-2014 as a contact of active pulmonary TB cases to evaluate the care cascade and see how many patients had IPT recommended, how many started, how many completed and reasons for not completing. The secondary aim of the study was to determine the relation between 6 months of IPT and developing an active TB disease.
Results: Among all 175 contact children cases who visited NCTLD between 2012 and 2014, 98 (56%) were recommended to initiate IPT and 77 (44%) were not, including 40 (52%) children contacts of MDR-TB patients. Among children recommended to start IPT, 50 (51%) initiated treatment, 17 (33%) of whom completed a full course of treatment. Overall, 4 (4%) contacts developed an active TB during the 3-5 years of follow-up time. 1(2%) TB case in IPT group (treatment interruption at third month) compared to 3 (6%) in the non-IPT group (RR=0.33, 95%CI=0.03-2.97).
Conclusions: Our findings highlight very low rates of LTBI treatment recommendation, initiation and completion among children TB contacts in Georgia and hence the need for improved monitoring and treatment programs. However, study showed three times less risk of disease among IPT group. Based on study results and new WHO guidelines Georgia plans to implement 3HP weekly treatment above age 2.

PS-22-744-01 Role of contact investigation on isoniazid preventive therapy of children under five in Afghanistan

MN Samadi,[1] GQ Qader,[1] MK Rashidi,[1] MK Seddiq,[2] N Ahmadzadah,[2] M Melese,[3] [1]Management Sciences for Health (MSH), Challenge TB, Kabul, Afghanistan, [2]National Tuberculosis Control Program, National Tuberculosis Control Program, Kabul, Afghanistan, [3]Management Sciences for Health (MSH), Health Program Group, Arlington, WA, United States of America. e-mail: nazimsamadi@yahoo.com

Background and challenges to implementation: The National TB program (NTP) of Afghanistan implemented the strategy of active household contact screening of all bacteriologically confirmed TB index cases since 2014. The aim of this abstract is to share the experience of contact screening in a routine program set up.
Intervention or response: NTP implement the active contact screening countrywide, which included door to door screening of TB index case contacts. Those with sign and symptoms of TB were referred to DOTS centers for diagnosis. Children under five years of age without sign and symptoms of TB were started on Isoniazid Preventive Therapy (IPT).
Results and lessons learnt: From the total of 449,322 contacts screened for TB between 2014 and 2018 89561(20%) were children under five years of age and 79784(89.1%) were able to started on IPT. The contact screening volume increased progressively and the IPT coverage was also increased parallel (Table1). The average IPT completion rate was 75%.
Conclusions and key recommendations: The IPT coverage is very high for children and the completion rate is also high as compared to the global report. The active contact screening is good approach for IPT and IPT adherence.

Period	Total number of household (HH) contacts registered	Number of HH contacts under 5 years of age	% of under 5 among household contacts	Number of HH contacts under 5 years of age who started INH preventive therapy (IPT)	% of under 5 started INH preventive therapy	% of IPT completion
2014	53189	11919	22%	8792	74%	69%
2015	61678	11799	19%	10164	86%	70%
2016	85755	17215	20%	15417	90%	74%
2017	125467	24692	20%	22959	93%	79%
2018	123233	23936	19%	22452	94%	85%

[Isoniazid Preventive Therapy of children less than 5 years in Afghanistan (2014-2018)]

PS-22-745-01 Can isoniazid preventive therapy be given to people living with HIV without pyridoxine supplementation?: experience from one antiretroviral therapy centre of Andhra Pradesh, India

S Achanta,[1] M Gorla,[1] S Mase,[1] J Peravali Carel,[1] N Vasundhara,[2] S Chandra Reddy,[3] R Tekumalla,[4] R Rao,[5] KS Sachdeva,[5] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]Government of Andhra Pradesh, District TB Centre, Department of Health & Family Welfare, Visakhapatnam, India, [3]Government of Andhra Pradesh, State AIDS Control Society, Department of Health & Family Welfare, Visakhapatnam, India, [4]Government of Andhra Pradesh, State TB Cell, Department of Health & Family Welfare, Vijayawada, India, [5]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: achantas@rntcp.org

Background: Isoniazid Preventive Therapy (IPT) is an important intervention recommended by WHO for preventing progression to tuberculosis (TB) disease in people living with HIV(PLHIV). Peripheral neuropathy from Isoniazid, rare side effect of IPT, is considered preventable with co-administration of Pyridoxine (50 milligrams/day). However, non-availability of Pyridoxine has led to less uptake of IPT among PLHIV under the National TB Control Programme, India. Limiting IPT initiation due to non-availability of Pyridoxine can lead to more TB disease among PLHIV. We therefore explored feasibility of IPT initiation without Pyridoxine supplementation in one Antiretroviral Therapy (ART) Center in Andhra Pradesh (AP), India.

Methods: All PLHIV attending ART Center from March 2017-December 2018 were screened at every visit (generally monthly) for TB-symptoms, alcohol and tobacco use, diabetes, hypertension and tested for hemoglobin, SGOPT-SGPT and serum-creatinine. Those without TB-symptoms and clinically eligible were initiated on IPT for 6-9 months without Pyridoxine supplementation. Patients were monitored every month for ART, INH adherence and adverse events. Data was collected retrospectively.

Results: A total of 3334 PLHIV were screened, of which 1669 (50%) were started on IPT. Of these, 1572(**94.18%**) successfully completed prophylaxis, **79**(**4.73%**) are still on treatment, **5** (**0.29%**) lost to follow-up and **13**(**0.78%**) reported adverse events of peripheral neuropathy (8), hepatitis (3), rash (1) and epilepsy (1). Among those on IPT, 105(6%) had diabetes, 131(8%) had hypertension and 308(18%) had history of alcohol intake.

Of 1665 not started on IPT; 22.5%(*n*=751) with initial TB-symptoms were evaluated further and excluded from this analysis, 2%(*n*=60) were < 14yrs, and 26% (*n*=854) were clinically ineligible with abnormal SGOT/SGPT/creatinine values.

Conclusions: It is feasible to initiate and successfully complete IPT without Pyridoxine supplementation among eligible PLHIV. Policy makers must adopt this strategy and expand TB prophylactic services. Prospective studies in more ART Centers could strengthen evidence.

	Characteristic	Screened for TB Symptoms N (%)	Initiated on IPT N (%)	Completing IPT N (%)	Not Initiated on IPT N(%)
	Total	3334	1669(50%)	1572(94.1%)	1665(50%)
Age	<25yrs	300 (8.99%)	149 (49.7%)	137 (91.94%)	**751 (22.5%)** had one/more TB symptoms on initial screening, were evaluated further and were excluded from this analysis. **60 (2%)** were children **450 (13.5%)** had abnormal SGOT/SGPT Levels **404 (12%)** had abnormal Serum creatinine levels
	25-50yrs	2776 (83.26%)	1408 (50.7%)	1326 (94.17%)	
	>50yrs	258 (7.73%)	112 (43.4%)	109 (97.32%)	
Gender	Male	1744 (52.3%)	801 (45.9%)	756 (94.4%)	
	Female	1582(47.45%)	864(54.6%)	812(94.0 %)	
	Transgender	8 (0.02%)	4 (50.0%)	4 (100%)	
CD4 Count	<100	316 (9.47%)	24 (7.6%)	23 (95.8%)	
	101-300	638 (19.13%)	167 (26.18%)	155 (92.81%)	
	301-500	697(20.90)	348(49.9%)	326(93.67%)	
	>500	1683 (50.48%	1130 (67.1%)	1068 (91.36%)	
Associated Co-Morbidity	Diabetes	150 (4.49%)	105 (70%)	104 (99.11%)	
	Hypertension	175 (5.25%)	131 (74.9%)	126 (96.2%)	
	Alcohol	336 (10.07%)	336 (100 %)	336 (100%)	

PLHIV -People Living with HIV; IPT - INH Prophylaxis Therapy; ART- Anti Retroviral Therapy, TB; Tuberculosis, IPT; INH Prophylaxis Therapy, Diabetes; Random Blood Sugar > 126 mg/dl, Hypertension; >140/90 mm Hg

[Characersitics of PLHIV who have successfully completed IPT in one ART Centre, Andhra Pradesh, India during March 2017 - December 2018]

PS-23-C8 Let's talk about contact management and active TB case finding

PS-23-746-01 Did adjusted guidelines for tuberculosis contact investigations lead to improved efficiency?

S van de Berg,[1] M Borgdorff,[1] C Erkens,[1] C Mulder,[1] [1]KNCV Tuberculosis Foundation, Technical Division, The Hague, Netherlands. e-mail: sarah.vandeberg@kncvtbc.org

Background: In low tuberculosis (TB) incidence countries,TB contact investigation (TCI) is a balancing act between not missing contacts with TB and making optimal use of resources by not unnecessarily evaluating non-infected contacts.The objective of this study was to assess if updated guidelines reiterating the importance of adhering to the stone-in-the-pond principle improved efficiency of TCI in the Netherlands.

Methods: In this retrospective study,surveillance data was used to compare TCI outcomes before (2011-2013) and after (2014-2016) the guideline-update.Negative binomial regression,logistic regression and linear regression were used to compare:a) the number of contacts invited per index patient;b) the TB testing coverage per index patient,and c) the number needed to screen (NNS) to identify one contact with active TB per index patient,respectively.

Results: In total,3,192 index patients were included in the analyses:1,703 from 2011-2013 and 1,489 from 2014-2016. In the two periods 27,187 and 21,056 contacts

were eligible for TCI,86% and 89% were tested for TB and 0.70% and 0.73 % were identified with active TB, respectively. The average number of contacts invited per index patient tended to change only for non-Dutch smear-positive PTB index patients and Dutch non-bacteriologically confirmed PTB index patients, decreasing from 26 to 23 (Rate Ratio (RR)=0.87[95%CI:0.75-1.01], p=0.06) and 15 to 5 (RR=0.31[95%CI:0.18-0.53], p<0.01), respectively. The TB testing coverage remained similar among extrapulmonary TB and smear-negative PTB index patients but improved among smear-positive (OR=1.42[95%CI:1.12-1.81], p<0.01) and non-bacteriologically confirmed PTB (OR=2.11[95%CI:1.06-4.20], p=0.03) index patients.Only for non-Dutch smear-positive PTB index patients the average NNS per index patient tended to change: the mean decreased from 29 to 26 (RR=0.74[95%CI:0.54-1.02], p=0.06).

Conclusions: For non-Dutch smear-positive PTB index patients,the NNS decreased marginally, suggesting that the guideline-update possibly increased TCI efficiency. An evaluation of a longer observation period including more contacts with TB is required to confirm this finding.

PS-23-747-01 Acceptability of active case finding with a seed-and-recruit model to improve tuberculosis case detection and linkage to treatment in Cambodia: a qualitative study

S Tuot,[1,2] AKJ Teo,[3] D Cazabon,[4] S Sok,[2] M Ung,[5] SC Choub,[1] S Ly,[1] S Yi,[1,3,6] M Smelyanskaya,[7] [1]KHANA, Center for Population Health Research, Phnom Penh, Cambodia, [2]Royal University of Phnom Penh, Social Sciences and Humanity, Phnom Penh, Cambodia, [3]National University of Singapore and National University Health System, Saw Swee Hock School of Public Health, Singapore, Singapore, [4]McGill University Health Centre, McGill International TB Centre, Montréal, QC, Canada, [5]Nanyang Technology University, Humanities and Social Studies Education Academic Group, National Institute of Education, Singapore, Singapore, [6]Touro University California, Center for Global Health Research, Vallejo, CA, United States of America, [7]Stop TB Partnership, Stop TB Partnership, Geneva, Switzerland.
e-mail: tsovannary@khana.org.kh

Background: Globally, it is estimated that 36% of TB cases were undiagnosed in 2017, and a similar proportion is observed in Cambodia. KHANA implemented tuberculosis (TB) active case finding using a seed-and-recruit model - previously untested in TB interventions - to engage TB survivors and increase TB case detection in Cambodia. Community screeners (seeds) recruited people with presumptive TB in their social networks, verbally screened them and provided linkage to treatment. Our study aimed to explore the acceptability of the intervention by key stakeholders and determine the characteristics of successful seeds.

Methods: This study was conducted in four of Cambodia's 25 provinces (Banteay Meanchey, Kampong Chhnang, Siem Reap, and Takeo) in 2017. Fifty-six in-depth interviews with health providers, project staff, village health support groups and community volunteers, and 10 focus group discussions with key populations for TB (64 participants) were conducted. Transcripts were coded, and content analyses were performed using Nvivo11.

Results: The seed-and-recruit model was generally well-received by the study participants. They saw the benefits of engaging TB survivors and utilizing their social networks to find people with TB in the community. The social embeddedness of the model within the local community was one of the major strengths. The success of the model also hinged on the integration with existing health facilities.

Being motivated, having an extensive social network, and being knowledgeable about TB were important characteristics of successful seeds. Seeds and field staff reported challenges in motivating presumptive TB for screening, lacked sufficent training, and high workload during implementation. However, there was a consensus that the model ought to be expanded.

Conclusions: These findings indicate that the seed-and-recruit model for TB case finding is well-accepted by the key stakeholders. Further studies are needed to evaluate the impacts and cost-effectiveness of this model for finding people with TB in Cambodia.

PS-23-748-01 Contribution of retrospective contact investigation of index TB cases in finding missed TB cases: experience from Tigray region

M Abraha,[1] E Michael,[1] H Sebagadis,[1] A Werede,[1] T Gebrehiwot,[1] A Gebremedhin,[2] T Tsegay,[2] D Gemechu,[3] P Suarez,[4] [1]Management Sciences for Health (MSH), Health Programs Group (HPG), Mekelle, Ethiopia, [2]Tigray Regional Health Bureau, Health Promotion, Disease Prevention and Control Cor-Process, Mekelle, Ethiopia, [3]Management Sciences for Health (MSH), Health Programs Group (HPG), Addis Ababa, Ethiopia, [4]Management Sciences for Health (MSH), Health Programs Group (HPG), Arlington, VA, United States of America. e-mail: mabraha@msh.org

Background and challenges to implementation: Contact investigation is a systematic screening of contacts of index TB cases done prospectively of retrospectively in time. Retrospective contact investigation (CI) is implemented to trace contacts who were exposed to adult pulmonary TB index cases or extrapulmonary TB. The Tigray Regional Health Bureau, in collaboration with the USAID/Challenge TB project, implemented retrospective CI since January 2017 to clear the backlog of untraced contacts and find missed TB cases. We report the yield and document lessons learned from retrospective CI implementation in Tigray region, Ethiopia.

Intervention or response: Training was provided to 254 health facility TB focal persons, 231 supervisors of health extension workers, and 52 woreda TB experts. During the session, participants received practical training and were provided with adequate tracking and reporting tools to be used at regional health posts. Retrospective CI was done for index cases that were diagnosed and treated from January 2016 to January 2018.
Results and lessons learnt: during the same period, 9,599 index TB cases (all forms) were registered. Of these, 45.2% (4,339) had at least one contact screened for TB. Among the contacts, 79.4% (14,696/18,514) were screened for TB and 4.4% (640) of those were found to be presumptive TB cases. Among contacts, 86 TB cases were diagnosed for a case notification rate (CNR) of 585/100,000.
Conclusions and key recommendations: The retrospective CI was found to be a high impact intervention to find missed TB cases, as the CNR was three times higher than for the general population and contributed to 1.36% (86 of 6,424) of all forms of TB cases notified in the region in 2017/18. This approach could be used to properly implement prospective CI.

Indicators	Total	%/Remarks
Number of index TB cases (all forms) registered	9599	
Number of index cases whose contacts were screened	4339	45.2%
Number of contacts registered	18514	
Number of contacts screened for TB disease	14696	79.4%
Number of presumptive TB cases identified	640	4.4%
Number of TB cases detected among contacts	86	CNR: 585/100,000
Number diagnosed by AFB	43	50%
Number diagnosed by GeneXpert	15	17%
Number diagnosed by clinical exam	28	33%

[Yield of Retrospective CI in Tigray Region, January-July 2018]

PS-23-749-01 Role of active house-to-house screening in community-based interventions to find the missing people with TB in Mozambique

L Colaco,[1] J Conjera,[1] A Soto,[1] R Makombe,[2] L Bader,[3] I Manhica,[4] [1]FHI 360 Challenge TB Mozambique, Programs, Maputo, Mozambique, [2]FHI 360 Challenge TB Mozambique, Programs, Pretoria, South Africa, [3]FHI 360, Program, Pretoria, South Africa, [4]Ministry of Health, Program, Maputo, Mozambique.
e-mail: lcolaco@fhi360.org

Background and challenges to implementation: Mozambique is ranked 14th among TB high-burden countries (INE 2017) Historically, screening for TB has been done at the health facility level, but this approach misses many people due to the fact that few health professionals receive training on TB, high rotation of clinical staff and from the user side, the distance to the HF is a barrier to access TB service. In 2007, the Mozambique National Tuberculosis Program leveraged CHWs to introduce community-based directly observed treatment (CB-DOTS), including house-to-house case finding as part of a larger initiative to bring health services closer to the community.
Intervention or response: The Challenge TB (CTB) project is working with community-based organizations and CHWs to implement community-based case finding and treatment support, including monthly cough days, active house-to-house case finding and index contact referral. CHWs are responsible for identifying people with presumptive TB, giving referrals, contact tracing, and providing treatment follow-up and support. CB-DOTS was implemented in 68 districts across four provinces between 2015 to 2018;
Results and lessons learnt: Provinces supported by CTB's CB-DOTS intervention contributed 51% and 53% in 2017 and 2018 respectively to national TB Notification. House-to-house screening contributed 71% and 75% of all TB cases notified through community efforts in 2017 and 2018 in CTB areas, followed by monthly cough days and contact investigation.
Conclusions and key recommendations: CB-DOTS is an essential component of NTP's efforts to find missing people with TB in the community. Exploring and expanding on community innovative approaches that have shown results such house to house active search will contribute towards increasing the number of people diagnosed and treated for TB in Mozambique.

PS-23-750-01 Comparative analysis of TB case yield from three active TB case finding strategies: results from a TB REACH Project in Nigeria, 2019

V Obot,[1] E Aniwada,[2] O Onyedinachi,[1] A Eyo,[1] F Beulah,[1] U Ette,[1] D Uju,[1] [1]Excellence Community Education Welfare Scheme, Clinical Services and Programs, Uyo, Nigeria, [2]University of Nigeria College of Medicine, Community Medicine, Enugu, Nigeria.
e-mail: valerie@ecews.org

Background and challenges to implementation: Nigeria has the highest TB burden in Africa and with 24% TB case detection rate, accounts for 8% of the global gap in TB case detection. To improve TB case finding, the National TB program adopted the implementation of active TB case finding (ATCF) strategies. The ECEWS TB Reach project implements a mixed model of ATCF strategies among riverine and hard to reach population in 6 LGAs across 2 states within the Niger Delta region, Nigeria.
Intervention or response: Starting from October 2018 to February 2019, we implemented ATCF strategies working with volunteers for targeted community outreach (CO), house to house (H2H) case search and house hold

contact investigation (HCI). The project collaborated with patent medicine vendors, community pharmacists, Community volunteers, DOTS centers and private hospitals to identify presumptive TB and stand-alone laboratories to facilitate sputum referral for GeneXpert diagnosis and linkage to TB treatment. Index TB cases diagnosed in the past year within the collaborating DOTS centers were line-listed for contact investigation.

Results and lessons learnt: Out of the 104,503 clients investigated, the least number (2.5%) were through HCI. The TB case yield were 6.6%, 5.3% and 2.1% from targeted CO, H2H case search and HCI respectively. We found that there were no statistically significant association between the number of persons diagnosed with TB and intervention (p = 0.331) and likewise gender (p = 0.962). The number needed to screen (NNS) to detect one case of TB was least (332) for HCI and highest (498) for H2H case search (Table 1).

Conclusions and key recommendations: Tracking contacts of index TB cases through HCI is known to be a high yield active TB case finding strategy. We were limited in our HCI intervention in tracking the index TB cases for contact investigation. To surmount this challenge, valid client's address is a critical success factor especially in the more rural and underdeveloped communities.

Variable	TB Status Positive (%)	TB Status Negative (%)	χ^2 test; p value	Yield; NNS
Intervention				
Targeted CI	85 (0.2)	36,063 (99.8)		5.3 ; 426
H2H Case search	132 (0.2)	65,573 (99.8)	2.210; 0.331	6.6; 498
HCI	8 (0.3)	2,642 (99.7)		2.1; 332
Gender				
Male	109 (0.2)	50,682 (99.8)	0.002 ; 0.962	6.2 ; 475
Female	116 (0.2)	53,596 (99.8)		5.2 ; 493

NNS: Number needed to screen

[Relationship between TB case yield and Active TB case Finding interventions]

PS-23-751-01 Role of patient GIS in active case finding

A Imran,[1] N Kak,[2] P Daru,[1] R Garcia,[1] N Yacat,[1]
[1]University Research Co., LLC (URC), TB/Infectious Diseases, Manila, Philippines, [2]University Research Co., LLC (URC), Center for Innovation and Technology, Maryland, MD, United States of America. e-mail: aalimran@ic.urc-chs.com

Background and challenges to implementation: A prototype of ConnecTB, a mHealth application was piloted in Philippines for mapping TB patients under community-based TB treatment. Smartphone module of the mHealth application guides the provider to record the patient's treatment history including any side effects caused by TB regimen. The Geo tagging mechanism allows program supervisors to verify when and where each DOT session was recorded. Furthermore, this application allows to create patient GIS to locate patients under treatment on map and to visualize clusters to identify the high-risk areas.

Intervention or response: The objective of the survey was to collect patient information along with geo coordinates as a part of piloting the prototype of ConnecTB platform. Geo-mapping exercises have been performed to capture geo coordinates and some information related to TB treatment and household of identified DR-TB patients in Olongapo City and the municipality of Subic in Zambales (Region III) in December 2019. A total of 7 patients have been surveyed during the data collection process. Information collected during survey were plotted on the map based on the geo coordinates and multiple patients found within a short distance in Subic municipality. Based on the patient cluster, an outreach activity to screen Presumptive TB cases has been conducted in Subic municipality.

Results and lessons learnt: During the outreach campaign a total of 567 participants including 268 symptomatic have been tested for TB by Xray, Xpert and DSSM. 138 among the total number of participants were presumptive based on Xray (wet reading), 186 were tested by DSSM and 101 sputum samples were tested using GeneXpert. 16 patients were diagnosed positive, 8 of them are bacteriologically confirmed and 8 of them were clinically diagnosed.

Conclusions and key recommendations: Patient GIS can play a vital role to identify hotspots for active screening and eventually to increase TB case detection.

PS-23-752-01 Finding undiagnosed TB patients by using contact tracing in peri-mining districts in South Africa

Y Tsibolane,[1] E Ramarumo,[1] [1]Government of South Africa, Health, Pretoria, South Africa.
e-mail: yolisa.tsibolane@health.gov.za

Background and challenges to implementation: South Africa (SA) is ranked amongst top 5 countries accounting for 80% of the global TB burden. SA estimates that a total of 160 000 TB patients were not diagnosed, or never enrolled in the TB treatment programme in 2017. These "Missing TB patients" includes patients in the community not accessing services and those attending a health facility who may have TB but were never screened nor tested. Perimining communities are identified as being at high risk of having undiagnosed TB patients due to the living and working conditions characterizing these communities. TB infection rates in SA mines is the highest in the world and estimated at 3000 - 7000 per 100 000 populations.

Intervention or response: The National Ministry of Health launched a campaign trace contacts of index cases in their households, screen and test them and ensure

that those diagnosed positive are linked to TB treatment in 6 peri-mining districts. Community Health Workers (CHW) were assigned to screen and collect onsite sputa for testing in Mobile Gene Xpert trucks. Line lists of index patients were obtained from health facilities and a standardized TB screening tool was used. Symptomatic patients were entered in the TB identification register and those diagnosed positive were followed up, linked to treatment and entered in facility TB registers.
Results and lessons learnt: From April 2016 until March 2019, 10 306 TB index patients were identified, 395 037 contacts were screened ,66 002 (16,7%) were symptomatic, 65 212 had sputa tested of which 1 438 (2,2%) were diagnosed TB positive. 1 398 (97,2%) were started on TB treatment. The screening yield was 0,36%.High patient mobility affected linkage to care.
Conclusions and key recommendations: Contact tracing and screening is an effective way of finding undiagnosed TB patients. Follow up of patients initially lost to follow up needs strengthening.

PS-23-753-01 Systematic contact investigation to find missing cases and increase treatment adherence and success for MDR-TB patients in rural Morrumbala District, Zambezia Province, Mozambique

MJ Pires Machai,[1] [1]Family Health International, Challenge TB, Maputo, Mozambique. e-mail: mmachai@fhi360.org

Background and challenges to implementation: In Mozambique, MDR-TB prevalence is approximately 3,7% for new TB cases and 20% for retreatment cases. However, 77% (3157/4100) of the estimated cases remain undiagnosed. 65% of the country's population is rural and 50% of residents in rural areas live at about 8 kilometers from the closest health facility. The distance TB/MDR-TB patients must travel to access a health facility increases the risk of missed cases and non-adherence to treatment among patients that are diagnosed. This leads to delayed treatment seeking and culture conversion, treatment failure, relapse, and increased transmission of drug resistance.
Intervention or response: The National Tuberculosis Program organized systematic contact investigation for MDR-TB patients being treated at 12 peripheral health facilities in Morrumbala District that reported the highest number of MDR-TB patients in 2018. Community Health Workers screened contacts of MDR-TB patients using a structured questionnaire to identify risk factors, including those related to the increase of MDR-TB in this particular district. Laboratory technicians were on hand to collect, package and referred specimens to the closest health facility with GeneXpert technology to guaranty that the samples are immediately processed.
Results and lessons learnt: HCWs visited 30 patient households in the 12 selected areas and screened 1,160 patient contacts. 226 presumptive TB cases were identified, and 226 samples were collected for GeneXpert testing. From those tested, 18 drug-susceptible (DS) TB patients and 5 MDR-TB patients were confirmed. All of them were put on treatment.
Conclusions and key recommendations: Contact investigation in rural areas can increase the number of DS- and MDR-TB patients identified, treated, and cured. However additional interventions, such as DOTS Plus, would help increase early diagnosis and treatment success rates for MDR-TB, and reduce the transmission within the community.

PS-23-754-01 Using community-based population and family planning volunteers to conduct household contact investigations in four districts of Hai Phong, Viet Nam

TTT Dong,[1] HV Le,[2] HV Pham,[3] TV Pham,[3] RJ Forse,[4] AJ Codlin,[5] LNQ Vo,[6,7] [1]Friends for International TB Relief, Operations, Hanoi, Viet Nam, [2]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [3]Hai Phong University of Medicine and Phamarcy, Public Health Department, Hai Phong, Viet Nam, [4]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [5]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [6]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [7]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam.
e-mail: thuy.dong@tbhelp.org

Background and challenges to implementation: In Viet Nam there are 124,000 new tuberculosis (TB) cases and 12,000 deaths caused by TB annually. Household contacts (HHCs) are at high risk for TB, but programmatic implementation of HHC investigation has been limited.
Intervention or response: A cross-sectional study was conducted as part of the TB REACH-funded Zero TB Viet Nam project in Hai Phong in Northern Viet Nam during 2018 to measure the rate of active TB disease and associated risk factors among HHCs of index TB patients. A secondary goal was to assess the feasibility of engaging community networks such as the network of population and family planning collaborators to provide TB-related services. HHCs were verbally screened for TB symptoms and surveyed using a bespoke risk factor questionnaire. They were then referred for chest X-ray (CXR) screening. HHCs with an abnormal CXR were indicated for testing using the Xpert MTB/RIF assay. Risk factors were assessed using multivariate logistic regression.
Results and lessons learnt: 1,421 HHC screening in four districts yielded an active TB prevalence of 2,500/100,000. Three factors were associated with increased risk of active TB: living in a low-income household (aOR=4.72, 95% CI: 1.92-11.61, p=0.001), working >40 hours/week (aOR=5.40, 95% CI: 2.69-10.84, p< 0.001), and exposure to an index case with poor adherence to TB treatment (aOR=4.26, 95% CI: 1.89-9.60,

p< 0.001). Poor adherence was defined as index patients who were lost to follow-up or who missed at least one follow-up appointment.
Conclusions and key recommendations: TB prevalence among HHCs was 9 times higher than that of the general population in Viet Nam (289/100,000 population). The results of this study are concordant with existing literature and provide further evidence for HHC screening and addressing poverty to prevent the development of TB. Screening HHCs of TB patients is feasible and effective by training and engaging existing community networks, even those outside of the traditional TB care network.

PS-23-755-01 The yield of screening symptomatic contacts of drug-resistant tuberculosis cases in 25 states in Nigeria

CA Ohikhuai,[1] F Murtala-Ibrahim,[1] VC Ibeziako,[2] C Mgbemena,[3] A Agbaje,[2] [1]Institute of Human Virology Nigeria, Strategic Information, Abuja, Nigeria, [2]Institute of Human Virology Nigeria, Office of the CEO, Abuja, Nigeria, [3]Institute of Human Virology Nigeria, Clinical, Abuja, Nigeria. e-mail: cohikhuai@ihvnigeria.org

Background and challenges to implementation: There were over 300,000 Tuberculosis (TB) cases including 21,000 Drug-Resistant Tuberculosis (DR-TB) cases undetected in Nigeria in 2017. Finding and investigating contacts of DR-TB patients is a strategy that could help to find undetected TB cases. Contact tracing among DR-TB patients in Nigeria has not gained prominence.
Intervention or response: Community-Based Organization (CBO) staff were recruited and trained on contact tracing including patient confidentiality. They obtained a list of diagnosed DR-TB patients and reached out to them to set up a home visit. Patient's contacts were evaluated, and those symptomatic were either followed up by the CBO staff to ensure they visit the DOTS facility for further investigations or their sputum samples collected and sent to the facility if the CBO staff is a health officer. Results are sent back to the contacts, and those diagnosed with TB were linked with DOTS facility for appropriate treatment regimen. Outcomes of the home visit are documented in the National TB Programme forms and registers from which results are summarized and transmitted to the national database.
Results and lessons learnt: A total of 1,387 index DR-TB patients had their contacts traced, and 6,121 household contacts were screened for tuberculosis. A total of 1,827 (29.8%) presumptive TB cases were identified; 1,607 (88.0%) were tested with Xpert MTB/Rif assay and 220 (12.0%) had X-ray with clinical diagnosis for active TB. Out of the presumptive cases 52 (2.8%) were diagnosed with drug-susceptible tuberculosis with 49 (94.2%) started on anti-TB 1st line treatment and 28 (1.5%) diagnosed with DR-TB, but 16 (57.1%) started on 2nd line anti TB treatment.
Conclusions and key recommendations: Tracing the symptomatic contacts of DR-TB patients is an intervention that has shown the potential of being able to increase the yield in TB case finding in Nigeria. This intervention should be scaled up nationwide, and more diagnostic facilities should be activated.

PS-23-756-01 Active community surveillance for early TB notification through contact tracing and engaging rural healthcare providers in 128 districts across 14 states of India

A Sahu,[1] J Tonsing,[1] S Mohanty,[1] S Pandurangan,[1] BM Prasad,[1] A Das,[1] R Babu,[1] [1]International Union Against Tuberculosis and Lung Disease (The Union), Tuberculosis and Chest Diseases, New Delhi, India. e-mail: amit.sahu@theunion.org

Background: To establish active community surveillance system through network of local volunteers for early TB notification and linking the diagnosed TB patients to National TB Programme (NTP) for treatment initiation and completion.
Methods: The study has been implemented in 128 districts across 14 states. The community volunteers created awareness about TB, actively identified presumptive TB patients (PTBPs) through contact tracing, engaging rural health care providers and local community health workers. The identified presumptive TB patients were linked to diagnostic services through sample collection and transportation and accompanied referrals. Smear negative presumptive TB patients were linked to chest X-ray facility for screening for diagnosis. Diagnosed TB patients were linked to treatment under NTP identified treatment centres. The eligible contacts of TB patients were linked to NTP for TB preventive therapy (TPT).
Results: Within 12 months of implementation, 49956 presumptive TB patients were identified, of which 44181 (88%) were provided sample collection and transportation, 2593 (5%) were accompanied to the NTP identified labs for diagnostic services. Total 6685 TB patients were diagnosed, among which 5388(81%) Smear positive and 1297 (19%) clinically diagnosed. Among the TB patients diagnosed, 6378 (95%) were put on appropriate treatment regimen. The eligible contacts of TB patients were linked to NTP for TB preventive therapy (TPT).
Conclusions: These results indicate that active surveillance in the community yields early notification of TB patients and strengthening sample collection and transportation system minimizes loss of presumptive TB patients and yields in early diagnosis resulting in break in chain of transmission. Preventive treatment to eligible contacts of TB patients is essential for TB elimination.

PS-23-757-01 Yield of screening household and close contacts of tuberculosis cases treated in the last five years integrated into the routine programme in Southern Ethiopia

C Ruda,[1] M Yasin,[2] N Germamo,[2] A Bedru,[3] P Reji,[2] L Ketema,[3] [1]KNCV Tuberculosis Foundation, Challenge TB, Addis Ababa, Ethiopia, [2]KNCV Foundation, Challenge TB, Hawassa, Ethiopia, [3]KNCV Foundation, Challenge TB, Addis Ababa, Ethiopia.
e-mail: challanegeri2000@gmail.com

Background and challenges to implementation: Household contacts (HHCs) and close contacts (CCs) of patients with tuberculosis (TB) have a higher risk of developing TB. In this study, we present large scale implementation of contact screening for HHCs and CCs of index TB patients that were treated for TB in the last five years.
Intervention or response: Community level index case-based contact screening for HHCs and CCs was conducted to identify missing cases in 84 catchment kebeles of 10 selected health facilities in Wolaita Zone from July to September 2018. Index TB cases currently receiving treatment and those from the past five years were identified from selected health facilities. One day orientation was provided to Woreda TB and HMIS officers, health facility TB focal and two lab professionals from each health facility. Zonal health department and Woreda Health offices agreed to monitor the activities and allocated transportation means and supplies including sputum cup and triple package for sample transportation. A team visited an average of five index cases along with their HHCs and four CCs per each index case per a day (a total of 25 HHs).
Results and lessons learnt: A total of 518 index TB case households and 5,535 CCs were screened for TB. Index TB cases that have completed their treatment and were alive were also screened for TB. 726 (12%, 726/6053) presumptive TB cases were identified of whom 113 (16%) TB cases were identified. 69 (58%), 24 (20%) and 27 (23%) cases were P/Pos, P/Neg and EPTB cases respectively and, 7 (6%), 33 (29%), 50 (44%) and 23 (20%) cases were identified among index cases, HHCs, CCs and incidental cases respectively. Corresponding case notification was 1,867 per 100,000 populations.
Conclusions and key recommendations: Implementing contact investigation-based community level case finding is helpful to identify missed cases by the routine TB program including relapses among index cases.

PS-24-D1 Trends in TB epidemics across the world

PS-24-758-01 Final results of the second national tuberculosis prevalence survey in Viet Nam, 2017-2018

H Nguyen Viet,[1] N Nguyen Viet,[2] H Nguyen Binh,[2] H Nguyen Van,[3] P Nguyen Do,[2] N Khieu Thi Thuy,[3] P Glaziou,[4] A Finlay,[5] V Mirtskhulava,[6] E Tiemersma,[6] [1]National Tuberculosis Program, Vietnam Integrated Centre for Tuberculosis and Respirology Research, Hanoi, Viet Nam, [2]National Tuberculosis Program, National Lung Hospital, Hanoi, Viet Nam, [3]National Tuberculosis Program, National Tuberculosis Reference Laboratory, Hanoi, Viet Nam, [4]World Health Organisation, Tuberculosis Monitoring and Evaluation, Geneva, Switzerland, [5]Centers for Disease Control and Prevention, (CDC), Hanoi, Viet Nam, [6]KNCV Tuberculosis Foundation, Technical Division, Den Haag, Netherlands.
e-mail: hai.nguyen@kncvtbc.org

Background: Tuberculosis (TB) remains a significant cause of morbidity and mortality in Viet Nam. The first national TB prevalence survey was conducted in 2006/7 to evaluate the situation of TB in the country. To assess the current burden of TB disease and trends of TB prevalence over time, we conducted the second national TB prevalence survey in 2017/8.
Methods: In 82 clusters selected proportional to population size throughout the country, 87,207 residents aged ≥15 years were enumerated. Among them, 61,763 (70.8%) participated in the survey and were screened by questionnaire and/or chest radiography. Those who reported TB treatment history in the two years preceding the survey, and/or had cough for ≥2 weeks, and/or had abnormal chest radiography, submitted two sputum samples. The first (spot) sample was tested with the Xpert MTB/Rif assay and the next-day morning sample using liquid culture (BACTEC MGIT-960) and speciation. An expert panel reviewed all participants with laboratory samples positive for *Mycobacterium tuberculosis* for final case classification. We applied inverse probability weighting and missing value imputation to adjust for non-participation or partial participation bias.
Results: Among the survey participants, 4,747 (7.7%) were eligible for sputum examination. Of 221 definite TB cases, 43 were Xpert-positive only, 48 culture-positive only, and 130 were positive on both tests; 116 (52.5%) reported no cough in the screening interview. The prevalence of pulmonary TB among adults was 319 (95% confidence interval, 257-396). TB prevalence increased with age and the male-to-female ratio was 4.0 (2.9-5.6). Urban areas and the south of Vietnam had the highest prevalence of TB ($p>0.05$).
Conclusions: Using highly sensitive diagnostics during the 2018 survey, we found that the burden of TB in Viet Nam is still significant. Continued political commit-

ment, innovations and an enhanced multi-sectoral approach are needed in order to achieve End TB targets in Viet Nam by 2035.

PS-24-759-01 Prevalence and drug resistance of Mycobacterium tuberculosis Beijing genotype in northwestern Russia

A Vyazovaya,[1] I Mokrousov,[1] A Gerasimova,[1] N Solovieva,[2] I Avadenii,[2] O Kulikova,[2] V Zhuravlev,[3] O Narvskaya,[1] [1]St. Petersburg Pasteur Institute, Laboratory of Molecular Epidemiology and Evolutionary Genetics, St. Petersburg, Russian Federation, [2]St. Petersburg Research Institute of Phthisiopulmonology, Bacteriology Laboratory, St. Petersburg, Russian Federation, [3]St. Petersburg Research Institute of Phthisiopulmonology, Etiological Diagnostics, St. Petersburg, Russian Federation.
e-mail: annavyazovaya@gmail.com

Background: The high prevalence of the multidrug-resistant (MDR) *Mycobacterium tuberculosis* in Russia negatively impacts tuberculosis control program both in Russia and in the neighboring countries. We studied population structure of the epidemiologically significant *M. tuberculosis* Beijing genotype in 5 provinces of northwestern Russia that are bordering European Union.
Methods: A total of 433 *M. tuberculosis* isolates were recovered from newly diagnosed patients with pulmonary TB, permanent Russian residents. Drug susceptibility testing was performed using method of absolute concentrations and BACTEC MGIT 960. The isolates were assigned to the Beijing genotype, Beijing B0/W148-cluster and Beijing 94-32-cluster based on analysis of the specific markers: *dnaA-dna*::IS*6110*, *Rv2664-Rv2665*::IS*6110* and *sigE98* SNP, respectively. The Beijing genotype strains were also discriminated into modern and ancient sublineages based on the NTF locus analysis.
Results: Evaluation of drug susceptibility to anti-TB drugs showed that 50.6% of the strains were sensitive, and 34.3% were MDR. Beijing genotype was detected in 53.4% isolates. Clusters Beijing B0/W148 and Beijing 94-32 included 14.4% and 30.5% of all *M. tuberculosis* isolates, respectively. MDR was detected in 87.5% of the Beijing B0/W148 isolates and 32.8% of Beijing 94-32 isolates. The strains of the ancient Beijing sublineage were identified only in 2.5% of all collection but 81.8% of them were MDR.
Conclusions: In the provinces of the North-West of Russia, the proportion of the Beijing strains in the population structure of M. tuberculosis was 53.4%. Beijing 94-32 and B0/W148 clusters were predominant.
The prevalence of the ancient Beijing sublineage remains low compared to the situation 20 years ago but these strains were also marked with high MDR rate, that was unexpectedly similar to the high MDR rate in epidemic Beijing B0/W148-cluster.

We thank colleagues from the regional TB dispensaries for providing bacterial strains. We acknowledge partial support from Russian Science Foundation (grant 19-14-00013).

PS-24-760-01 Characteristics of tuberculosis in patients with chronic kidney disease in Shenzhen City

P Zhang,[1] T Ye,[2] L Fu,[2] Y Wan,[1] G Deng,[1] [1]Third People's Hospital of Shenzhen, Pulmonary Department 2, Shenzhen, China, [2]Third People's Hospital of Shenzhen, Department of Pulmonary Disease, Shenzhen, China.
e-mail: jxxk1035@yeah.net

Background: The incidence of tuberculosis in patients with chronic kidney disease (CKD) and end-stage renal disease(ESDR) is significantly higher than that of the general population.we study the prevalence and characteristic and prognosis of tuberculosis in patients with CKD and ESDR from 4 hospitals in Shenzhen City.
Methods: Patients with CKD and patients with ESDR and accepted dialysis at the department of nephrology and blood purification center in four hospitals in Shenzhen city during January 2013 to December 2017 were enrolled. The prevalence and clinical characteristics of tuberculosis were retrospectively analyzed.
Results: 1169 patients and 3062 patients were enrolled in ESRD and CKD groups, respectively. 57 (57/1169,4.9%) patients were confirmed active tuberculosis in ESRD group, of them 36(36/57, 63.2%) were pulmonary tuberculosis, 14 (14/57,24.6%) were extrapulmonary tuberculosis and 7 (7/57, 12.3%) were both. The mortality in ESDR group was 8.8% (5/57, 8.8%). While 69 (69/3062,2.3%) patients in the CKD group were confirmed active tuberculosis, of them 47 (47/69, 68.1%) were pulmonary tuberculosis, 16 (16/69, 23.2%) were extrapulmonary tuberculosis and 6 (6/69, 8.7%) were both. The mortality in CKD group was 2.9% (2/69, 2.9%). There was a statistically significant difference of the incidence rate between the two groups (X^2=20.138, P< 0.001). There was no difference of mortality between the two groups (X^2=0.243, P=0.152).
Conclusions: The incidence and morbidity of active tuberculosis was high in patients with ESDR and CKD. Screening tuberculosis was urgent needed in patients with ESDR.

PS-24-761-01 Defining the TB emergence in resource poor rural Papua New Guinea: a district programme

J Warner,[1] C Rush,[1] T Diefenbach-Elstob,[1] V Guernier,[1] R Dowi,[2] D Pelowa,[3] B Gula,[2] E McBryde,[1] [1]James Cook University, Australian Institute of Tropical Health and Medicine, Townsville, QLD, Australia, [2]Balimo District Hospital, Clinical Services, Balimo, Papua New Guinea, [3]Balimo District Hospital, Laboratory, Balimo, Papua New Guinea. e-mail: jeffrey.warner@jcu.edu.au

Background: Papua New Guinea (PNG) is a diverse country with >800 societies in a population of ~6 million with high burdens of tuberculosis (TB) and multi-drug-resistant TB. Logistical issues and limited resources are significant challenges for national and provincial TB control programs. The Balimo District Hospital (BDH) serves the Balimo region of The Middle Fly District, Western Province and is staffed by nurses and Health Extension Officers; the backbone of healthcare delivery in PNG. The present study described the features of the Balimo TB epidemic: clinical presentation, incidence, geospatial analysis, drug resistance and molecular epidemiology.

Methods: District and national approvals were obtained. Demographic, clinical and laboratory features of TB were sourced from TB registers at BDH. Molecular assays were used to assess drug resistance and MTB lineage. Evidence of TB exposure in the community was determined using IGRA. Interviews of TB treatment experiences were analysed. Data analyses included axial coding and Stata/EpiTools.

Results: The incidence of TB was 727 cases/100,000 per year, 25% were < 14 years and 77.1% presented as EP-TB, including 97% of all children. Villages with the highest TB rates were closer to diagnostic access and treatment failure was associated with poor access, food insecurity and traditional health-seeking behaviours which delayed treatment. The study identified diverse personal, systems, and sociocultural factors that influence TB treatment adherence. The rate of DR-TB was 10% (95% CI 4.4-21.4). DNA spoligotyping of archived sputum smears revealed mostly MTB Lineages 2 and 4, but also evidence of multi-lineage infection.

Conclusions: Rates of TB and DR-TB are high in this remote community, access to health diagnosis and treatment is challenging and associated with treatment failure and dynamic transmission as evidenced by high childhood TB and potentially multi lineage infection. This work lays the foundation for an evidence based, directed culturally and socially inclusive TB control program.

PS-24-762-01 Is sub-Saharan Africa on track towards ending TB by 2030?

H Lago,[1] F Mavhunga,[1] JDD Iragena,[1] M Gasana,[1] R Mbumba Ngimbi,[2] A Ndongosieme,[3] W Nkhoma,[4] [1]World Health Organisation, African Regional Office, Brazzaville, Congo, [2]World Health Organisation, African Regional Office / Intercountry Support Team Central Africa, Libreville, Gabon, [3]World Health Organisation, African Regional Office - Inter Country Support Team West Africa, Ouagadougou, Burkina Faso, [4]World Health Organisation, African Regional Office / Intercountry Support Team East and Southern Africa, Harare, Zimbabwe. e-mail: lagoh@who.int

Background: To end TB by 2030, targets have been set in terms reduction in TB deaths and TB incidence rates in addition to and 0% catastrophic costs as a result of TB disease, compared to 2015. Progress towards these targets will be monitored through milestones for 2020 and 2025. One year before 2020, it is important to assess whether sub-Saharan Africa, home of highest number TB cases per capita, is on track towards End TB strategy milestones for 2020 and call for corrective actions if need be.

Methods: We focused on the 16 African countries among the 30 TB high burden countries globally. We compared the actual trends of TB mortality and incidence since 2015 with the trajectories of these indicators that are required to reach the milestones and targets of the End TB strategy. We did not work on catastrophic costs.

Results: Of the 16 focus countries, 5 (Lesotho, Namibia, South Africa, Zambia and Zimbabwe) have decreasing incidence trend in line with the required trajectories to achieve the End TB Strategy milestones for 2020. Four countries have decreasing trends, but not stepped enough. Unlike the previous, 7 countries (Angola, Congo, DRC, Liberia, Mozambique, Nigeria and Sierra Leone) have trends that are completely in the opposite direction to what is required, putting them at risk regarding 2020 milestones.

As to TB mortality, we noticed increasing trends with the same 7 countries above. The remaining 9 countries had either plateauing or decreasing trends, but none was in line with what was required by the End TB strategy.

Conclusions: Increased effort is needed for the countries in Sub-Saharan Africa to be on track towards End TB strategy. For 7 countries a special attention is essential, in terms of an emergency catch-up plan, to bring them back on track.

PS-24-763-01 TB prevalence in Tibet, China: results of the most recent survey from 2014

X Zhang,[1] X Wei,[2] J Hu,[3] [1]Shandong Chest Hospital, Strategic Planning, Jinan, China, [2]University of Toronto, Dalla Lana School of Public Health, Toronto, ON, Canada, [3]Shigatse Centre for Disease Control and Prevention, General, Shitgase, China.
e-mail: zhangxiulei0531@126.com

Background: The paper reports a population-based, cross-sectional survey of pulmonary tuberculosis among local residents and migrants aged 15 or above in Tibet Autonomous Region, China in 2014.
Methods: We conducted a population based, cross-sectional survey using multi-stage random cluster sampling. Twenty clusters (8 urban and 12 rural) were randomly selected. In each cluster, a door-to-door survey was conducted, followed by a screening interview and a chest X-ray. Those having symptoms of tuberculosis and/or with abnormal chest X-ray had sputum microscopy tests and culture on Löwenstein-Jensen medium.
Results: A total of 30113 (95.5%) of 31527 residents participated in the survey, of whom 215 active TB cases were identified. Among the active cases, 49 (22.8%) were known cases, 24 (11.2%) were smear positive cases, 39 (18.1%) were culture positive cases, and 176 (81.9%) were bacteriologically negative cases. Adjusted prevalence of smear positive, bacteriologically positive, and all pulmonary cases were 85 (95% CI: 62-97), 144 (95% CI: 107-152) and 758 (95% CI: 662-766) per 100 000, respectively. This represented 37% decline of prevalence rates in active cases, and 21.3% decline in smear positive cases when compared with raw results of the 1990 survey. About 51.3% of bacteriologically positive TB patients in Tibet showed no symptoms in 2014 survey.
Conclusions: We observed a sharp decline of TB prevalence in Tibet. As well, there is a low proportion of bacteriologically positive cases among all active patients, and over 50% of TB patients had no symptoms. The low proportion of known cases in the survey reflected possible under-detection in the National TB Program.

PS-24-764-01 Multidrug-resistant tuberculosis in the most populous city in Viet Nam, 2011-2015

LH Van,[1] PT Phu,[1] VT Son,[1] NT Hanh,[1] DN Vinh,[1] D Ha,[2] N Trang,[3] NT Thuong Thuong,[1] GE Thwaites,[1] [1]Oxford University Clinical Research Unit, TB Group, Ho Chi Minh, Viet Nam, [2]Pham Ngoc Thach Hospital, General Planning Department, Ho Chi Minh, Viet Nam, [3]Pham Ngoc Thach Hospital, Administrative Department, Ho Chi Minh, Viet Nam. e-mail: vanlh@oucru.org

Background: Vietnam is among the 30 countries with high burden of multidrug resistant tuberculosis (MDR-TB), one of the major threats to global public health. Ho Chi Minh City (HCMC), the most populous city in Vietnam, provided treatment for 81% of Vietnamese MDR-TB patients in 2010. The study aims to describe demographic characteristics and to identify risk factors for poor outcome of MDR-TB in HCMC.
Methods: This retrospective study included all patients who initiated MDR-TB treatment from 2011 to 2015 in HCMC. Multivariate multiple imputation logistic regression models were used to examine the associations between patient baseline characteristics and treatment outcomes.
Results: Number of MDR-TB cases increased 1.4 folds from 2011 to 2015. Of 2,267 eligible cases recruited, median age was 43 years, 75.7% were male, 5.6% were new TB patients, 60.2% were failure of category I or II regimen, 57.7% were underweight, 30.2% had diabetes mellitus and 9.6% were HIV positive. Treatment success rate was 73.3% while 10.1% died and 11.6% lost to follow up. Risk factors for poor treatment outcome included HIV co-infection (adjusted odds ratio (aOR): 2.92, 95% confidence interval (CI): 2.06-4.14), advanced age (aOR: 1.47 for every increase of 5 years for patients older than 60, 95% CI: 1.19-1.80), previous history of MDR-TB treatment (aOR: 5.65, 95% CI: 2.93-10.93), AFB positive (aOR: 1.48, 95% CI: 1.08-2.03 for low smear grade, and aOR: 2.07, 95% CI: 1.49-2.89 for high smear grade), low BMI (aOR: 0.84 for every increase of 1kg/m^2 for patients with BMI< 21, 95% CI: 0.79-0.89).
Conclusions: High rates of new and failure of category I regimen posed a need to screen for MDR-TB in all TB patients regardless of their previous TB history. Patients with risk factors for poor treatment outcome such as HIV co-infection, high smear grade and history of previous MDR-TB treatment should receive additional medical care.

PS-24-765-01 Trends of TB rates in Mexico: analysis of the National Tuberculosis Registry, 2000-2017

N Mongua-Rodríguez,[1] F López-Luna,[2] E Ferreira-Guerrero,[1] R López-Ridaura,[3] E Jiménez-Corona,[4] H López-Gatell,[5] A Ponce-de-León,[6] J Sifuentes-Osornio,[7] L Garcia-Garcia,[8,9] [1]Instituto Nacional de Salud Publica, Centro de Investigacion Sobre Enfermedades Infecciosas, Cuernavaca, Mexico, [2]Centro Nacional de Programas Preventivos y Control de Enfermedades, Direccion de Micobacteriosis, Mexico City, Mexico, [3]Secretaria de Salud, Centro Nacional de Programas Preventivos y Control de Enfermedades, Mexico City, Mexico, [4]Secretaría de Salud, Dirección General de Epidemiología, Mexico City, Mexico, [5]Secretaría de Salud, Subsecretaría de Prevención y Promoción de la Salud, Mexico City, Mexico, [6]Instituto Nacional de Ciencias Médicas y de Nutrición 'Salvador Zubirán', Laboratorio de Microbiología, Mexico City, Mexico, [7]Instituto Nacional de Ciencias Médicas y de Nutrición 'Salvador Zubirán', Dirección Médica, Mexico City, Mexico, [8]Instituto Nacional de Salud Pública, Centro de Investigacion Sobre Enfermedades Infecciosas, Cuernavaca, Mexico, [9]Universidad Nacional Autonoma de Mexico, Mexico, Mexico. e-mail: garcigarml@gmail.com

Background: Tuberculosis (TB) remains a public health problem in Mexico. The present study had the purpose of describing the trends of TB rates between 2000 and 2017.

Methods: We analyzed the National Tuberculosis Registry from 2000 to 2017 including all notified cases countrywide. We estimated overall annual rates and according to prior anti-tuberculosis treatment, association with diabetes mellitus and drug resistance (isoniazid, ethambutol, rifampin, streptomycin). We used percent changes and performed the x2 test for trends to detect significant annual changes.

Results: In Mexico from 2000 to 2017, rates increased from 14.89 to 22.92 per 100,000 inhabitants. Drug tests were performed for 4.38% cases in 2000 and for 5.27% cases in 2017. Annual rates of overall, prior anti-tuberculosis treated, associated with diabetes and drug-resistant to at least one drug TB significantly increased as shown in the table.

Conclusions: Our data indicate that Mexico faces critical challenges to achieve the goals of the End TB Strategy. Efforts should include multidisciplinary and multisectoral approaches to control the association of TB and diabetes and to accelerate diagnosis and treatment of drug-resistant cases.

Cases/Year	2000	2017	% change	p value
All TB	14.89	22.92	53.96	<0.001
Prior treatment	1.70	1.85	8.53	<0.001
Associated to diabetes mellitus	1.60	5.87	266.40	<0.001
Resistance to at least one drug	0.20	0.33	60.95	<0.01

[TB rates per 100,000 inhabitants between 2000 and 2017. Source: National Tuberculosis Registry]

PS-24-766-01 A significant decline in tuberculosis prevalence between 2007 and 2018: results from a repeat national tuberculosis prevalence survey in Viet Nam

H Nguyen Viet,[1] H Nguyen Binh,[2] N Nguyen Viet,[2] H Nguyen Van,[3] P Nguyen Do,[2] N Khieu Thi Thuy,[3] P Glaziou,[4] A Finlay,[5] V Mirtskhulava,[6] E Tiemersma,[6] [1]National Tuberculosis Program, Vietnam Integrated Centre for Tuberculosis and Respirology Research, Hanoi, Viet Nam, [2]National Tuberculosis Program, National Lung Hospital, Hanoi, Viet Nam, [3]National Tuberculosis Program, National Tuberculosis Reference Laboratory, Hanoi, Viet Nam, [4]World Health Organisation, Tuberculosis Monitoring and Evaluation, Geneva, Switzerland, [5]Centers for Disease Control and Prevention (CDC), Vietnam, Hanoi, Viet Nam, [6]KNCV Tuberculosis Foundation, Technical Division, Den Haag, Netherlands. e-mail: hai.nguyen@kncvtbc.org

Background: The 2007 Vietnam national tuberculosis (TB) prevalence survey measured a prevalence 1.6 times higher than that estimated by the World Health Organization at the time. Since then, the National TB Program of Viet Nam (NTP) introduced a range of interventions to reduce the burden of TB, including: household contact investigations, TB preventive treatment, new TB drugs and diagnostics, and active case finding along with strengthening routine TB care and treatment. To assess the effect of interventions and guide future actions we conducted the second national TB prevalence survey in 2017.

Methods: The first survey enumerated 103,809 adult (≥15 years) residents in 70 clusters selected proportional to population size (PPS), of whom 94,197 (90.7%) participated. The second survey enumerated 87,207 adult residents in 82 clusters selected PPS with 61,763 (70.8 %) participating. Both surveys identified a subset of participants eligible for sputum collection with a productive cough for ≥2 weeks, and/or history of TB in the two years preceding the survey, and/or chest radiograph abnormalities. To compare results between surveys we conducted a restricted analysis by estimating sputum smear positive (SSM-positive) and bacteriologically confirmed TB among participants based on Ziehl-Neelsen microscopy and Löwenstein-Jensen solid culture results respectively. Analysis included missing value imputation and inverse probability weighting per recommended methods.

Results: The prevalence of bacteriologically confirmed TB decreased by 30%, from 324/100,000 population (95% confidence interval, (274-384) in 2007 to 240 (189-306) per 100,000 population in 2017. The prevalence of SSM-positive among culture-positive TB participants decreased by 61%, from 110 (86-142) in 2007 to 60 (37-99) in 2017.

Conclusions: TB prevalence in Vietnam has declined substantially over the past ten years with a marked reduction in more severe, smear positive disease. However, to achieve End TB targets by 2035, rigorous innovative interventions and a multi-sectoral approach will be needed.

PS-24-767-01 Drug-sensitive testing reporting for positive sputum cultures in the UK pre-entry tuberculosis screening programme, 2007-2017

M Muzyamba,[1] D Zenner,[1,2,3] [1]Public Health England, TARGET, London, United Kingdom, [2]University College London, Centre for Infectious Disease Epidemiology, London, United Kingdom, [3]International Organisation for Migration, Regional Office for the European Economic Area, Brussels, Belgium.
e-mail: morris.muzyamba@phe.gov.uk

Background: The UK has been carrying out pre-entry tuberculosis (TB) screening for all long-term migration visa applicants in 15 pilot countries since October 2005. Screening was subsequently rolled out to visa applicants in 101 high TB incidence (>40/100 000 population) countries. Sputum smear cultures and drug sensitivity testing (DST) were introduced in 2007 and are mandatory for all cases of pulmonary TB. This study determines the DST reporting patterns among sputum culture positive TB cases detected by the programme.
Methods: Our study used a cohort of migrants from all 101high incidence countries screened for TB pre-entry by the panel physicians between January 2007 and December 2017. The data was cleaned and checked for consistency prior to analysis. Univariate and multivariable analyses were performed to identify factors associated with having drug sensitivity testing reported on positive cultures.
Results: The cohort consisted of 1,680,356 migrants screened by the programme. A total of 997 culture positive TB cases were detected by the programme during the study period of which 70% (702/997) had DST reports. Most cultures were sensitive to all drugs (83.5%; 586/702) but 116 (16.5%) were resistant to at least one and 22 (3.1%) had multiple drug resistance and 1 (0.1%) culture had extreme drug resistance.
After adjusting for age and sex, multivariate analysis demonstrated that DST reporting was strongly associated region (OR 1.47; 95% CI 1.15-1.90 Indian subcontinent versus Africa and OR 2.51; 95% CI 1.94-3.24 South East Asia versus Africa), age group (OR 1.5; 95% CI 1.4-1.6) and examination year (0.97; 95% CI 0.94-0.99).
Conclusions: Our results show that DST reporting was strongly associated with the region of screening, age group, sex and that the likelihood of having DST reported decreased with time. This study allows us to better target underperforming regions to improve DST reporting so that migrants can receive appropriate treatment.

PS-24-768-01 Dynamics of tuberculosis in metro and non-metro regions of India: evidence from India Human Development Survey, 2011-12

S Sriavstava,[1] [1]International Institute for Population Sciences, Population Studies, Mumbai, India.
e-mail: shobhitsrivastava889@gmail.com

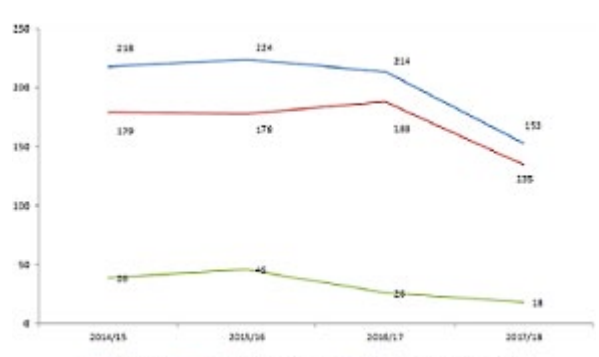
Background: Tuberculosis is the major public health concern in India. There are more than 850,000 cases of tuberculosis each year in India that are either undetected and untreated or diagnosed and treated by private healthcare providers with potentially substandard drugs and treatment regimens. Poverty is a powerful determinant of tuberculosis. Crowded and poorly ventilated living and working environments often associated with poverty constitute direct risk factors for tuberculosis transmission. Therefore the study aims to investigate the factors contributing to difference of tuberculosis prevalence between metro and non-metro regions of India.
Methods: Data from India Human Development Survey (IHDS) 2011-12 has been taken for analysis. Bivariate analysis, logistic regression and fairlie decomposition technique has been used to assess the results. Mumbai, Delhi, Kolkata, Chennai, Hyderabad and Bangalore were clubbed as metro regions. Sample for metro and non-metro region was 20,568 and 184,000 respectively. Regions were divided as low performing states and high performing states. Individual level analysis was done to generalize the results at national level.
Results: Prevalence of tuberculosis was 320/lakh in 2012. In non-metro region the prevalence was 340/lakh where as in metro region the prevalence was 110/lakh. Non-metro regions low socio-economic status (illiteracy and poor economic status), cooking in living area, less developed regions, tobacco and alcohol consumption are found to be significant predictors of tuberculosis. Through Fairlie decomposition analysis it was found that in 2014 regional status (70%), educational status (26%), wealth (13%) and tobacco consumption (11%) positively contributed towards the difference of tuberculosis prevalence in metro and non-metro regions of India.
Conclusions: Lower socio-economic status and tobacco consumption contributed most towards differences in tuberculosis prevalence in metro and non-metro regions of India. Increase in socio-economic status of people will lower the risk of tuberculosis and also infrastructural development will positively contribute towards decrement of tuberculosis cases in India.

PS-25-D8 Financing advocacy, modelling, and reporting improvements to end the TB epidemics

PS-25-770-01 High urban TB case notification rates can be deceptive: evidence from a major urban setting in Ethiopia

D Datiko,[1] S Negash,[1] A Hadgu,[1] D Jerene,[1,2] P Suarez,[3] [1]Management Sciences for Health (MSH), Health Programs Group, Addis Ababa, Ethiopia, [2]KNCV Tuberculosis Foundation, Team Evidence, The Hague, Netherlands, [3]Management Sciences for Health (MSH), Health Programs Group, Arlington, VA, United States of America. e-mail: dgemechu@msh.org

Background: Tuberculosis (TB) is a disease deeply rooted in social fabrics that requires a biomedical social response. Compared to rural areas, urban cities have higher TB case notification rates (CNR). The aim of the study was to describe the actual urban case notification in Adama city in Oromia region of Ethiopia.
Methods: Adama is one of the urban cities in the Oromia region of Ethiopia, with a population of about 386, 000; health service coverage has reached 95% of the cities' population. TB case finding and treatment outcome data were collected from 2014 - 2018 from which the case notification rate (CNR) and treatment success rate (TSR) were calculated.
Results: A total of 2,892 TB cases were registered in Adama city. . Of these, 2,432 (84%) were from Adama city while 460 (16%) were from other sites. The total TB CNR, was in the range of 153 to 218 per 100, 000 population. However, the adjusted TB CNR, which included cases of Adama city only) extended from 135 to 179 per 100,000 population. About 16% TB cases notified in Adama city were from other sites (figure 1).
Conclusions: The TB CNR in Adama city was reported as higher, however, a fifth of TB cases were not from Adama city. This overstates the urban CNR and underestimates the CNR of the rural Oromia region. NTPs should analyze urban TB data by disaggregating by place of residence to identify the gaps in case findings and strengthen urban case finding intervention.



[Figure 1: The trend of TB case notification from in Adama city, Ethiopia 2013 - 2018]

PS-25-771-01 Assessment of tuberculosis under-reporting through inventory studies in six European Union countries

M Straetemans,[1] PH Andersen,[2] H Schimmel,[3] A Simunovic,[4] P Svetina,[5] C Carvalho,[6,7] O Lyytikäinen,[8] RJ Harris,[9] C Ködmön,[10] R van Hest,[11,12] European Union Inventory Study / Capture Recapture Study Group [1]KIT Royal Tropical Institute, Health Unit, Amsterdam, Netherlands, [2]Statens Serum Institute, Department of Infectious Disease Epidemiology and Prevention, Copenhagen, Denmark, [3]National Institute for Public Health and the Environment, Centre for Infectious Disease Control, Bilthoven, Netherlands, [4]Croatian Institute of Public Health, Infectious Disease Epidemiology Service, Zagreb, Croatia, [5]University Clinic of Pulmonary Diseases and Allergy Golnik, Department of Tuberculosis, Golnik, Slovenia, [6]University of Porto, Institute of Biomedical Sciences Abel Salazar, Multidisciplinary Unit for Biomedical Research, Porto, Portugal, [7]Portuguese Northern Regional Health Administration, Public Health Department, Porto, Portugal, [8]National Institute for Health and Welfare, Department of Health Security, Helsinki, Finland, [9]Public Health England, Statistics Modelling and Economics Department, London, United Kingdom, [10]European Centre for Disease Prevention and Control, Unit of Surveillance and Response Support, Stockholm, Sweden, [11]Regional Public Health Service Groningen and Fryslân, Department of Tuberculosis Control, Groningen, Netherlands, [12]University Medical Centre Groningen, Department of Pulmonary Diseases and Tuberculosis, Groningen, Netherlands. e-mail: m.bakker@kit.nl

Background: Tuberculosis (TB) incidence is a key indicator of progress towards the World Health Organization End TB Strategy goals. In selected settings where TB surveillance is understood to be highly sensitive, TB incidence is derived from TB notification. In recognition that under-reporting of TB cases may still occur in settings with well-functioning surveillance, this study aimed to estimate TB notification completeness in Croatia, Denmark, Finland, the Netherlands, Portugal, and Slovenia.
Methods: We performed retrospective TB inventory studies to assess the observed TB notification completeness - the proportion of TB patients notified among the total number of TB patients observed after record linkage - in at least three national TB-related registers. Record linkage was through either a unique identifier or a combination of proxy identifiers. Capture-recapture analyses (CRC) by multiple-source log-linear models estimated the number of unobserved TB patients. We used this number to estimate the notification completeness.
Results: Observed completeness of national TB notification is 73.9% in Croatia, 98.7% in Denmark, 83.6% in Finland, 81.6% in the Netherlands, 85.8% in Portugal, and 100% in Slovenia. Using the estimate derived from CRC analyses provided TB notification completeness of 98.4% for Denmark (95% confidence interval [CI] 97.9% - 98.5%), 76.5% for Finland (95% CI 63.7% -

81.3%) and 77% in Portugal (95% CI 74.3% - 79.1%). CRC analysis yielded implausible results or was methodologically invalid in the other three countries.
Conclusions: The results suggest TB notification completeness to vary from 73.9% to 100%. The major problem was verification of TB records in hospital, primary care or public health registers. This influences the observed and estimated completeness. Studies, which aim to measure completeness of notification will benefit from prior scrutiny of hospital episode and primary care registers, to ensure that only true positive TB cases are included.

PS-25-773-01 An assessment of availability of policies and guidelines for childhood TB management in Zimbabwe, 2018

S Mashizha,[1] C Sandy,[1] A Mahomva,[2] TH Nyamundaya,[2] E Tachiwenyika,[2] T Mapuranga,[1] [1]Minisrty of Health and Child Care, National TB Control Program, Harare, Zimbabwe, [2]Elizabeth Glaser Pediatric AIDS Foundation, Technical, Harare, Zimbabwe. e-mail: smashizha@pedaids.org

Background: Zimbabwe has high TB morbidity and mortality rates and yet falls below the World Health Organization (WHO) benchmark of reporting 10-15% pediatric cases of all TB cases to the national program. A desk review of childhood TB national policies was conducted to identify gaps.
Methods: We conducted a desk review on current TB policy documents and guidelines in 2018 using a childhood TB policy and practice benchmarking tool, developed by EGPAF in collaboration with the WHO. The documents reviewed represented all relevant official documentation available as of May 30, 2018. The assessment aimed at evaluating country preparedness for childhood TB programming, focusing on political and financial framework to support health systems in pediatric TB case finding, diagnosis, treatment, monitoring and evaluation (M&E), preventive treatment, integration and collaboration.
Results: The TB national strategic plan (NSP) 2017-2020 has a childhood TB section which includes childhood TB contact investigation, treatment and preventive treatment. The NSP does not include adverse effects to medicine, Bacille Calmette-Guerin coverage, M&E, and operational research. Childhood TB budgets are included in NSP and Global Fund funding requests (2017-2019).
The national guidelines address use of non-sputum specimens, including stool for Xpert MTB/Rif testing in children, but do not include periodic systematic pediatric TB screening in high-prevalence areas. Nor do they include integration of childhood TB into other childhood programs (shown by absence of childhood TB screening algorithms in the Integrated Management of Childhood Illnesses guidelines). There is no national pediatric TB technical working group (TWG) and human resource capacity-building remains limited.
Conclusions: Zimbabwe has many required childhood TB policies and guidelines, but gaps remain. Updating the NSP, treatment guidelines and including funding allocations in Global Fund concept notes, to ensure all WHO recommendations are adopted from models of care implemented to integration of TB with existing maternal and child health services, is recommended

PS-25-774-01 Putting political literacy for the regional's legislative councils in Indonesia to face End TB 2035 Program

R Machmud,[1] M Muchtar,[2] H Delyuzar,[3] [1]Andalas University, Public Health and Community Medicine, Padang, Indonesia, [2]Andalas University, Nutrition, Padang, Indonesia, [3]Jaringan Kesehatan Masyarakat, NGO, Medan, Indonesia. e-mail: rizandamachmud@med.unand.ac.id

Background and challenges to implementation: Most of regional's legislative councils in Indonesia are not aware of facing the End TB 2035 Program. It impacts to low budget allocation, lack of facilities and infrastructure, and absence of policies that are beneficial to End TB 2035 program.
Intervention or response: The study has been implemented in 6 regions in West Sumatera Province Indonesia for 5 years, under the Community empowerment people against Tuberculosis (CEPAT) project led by Jaringan Kesehatan Masyarakat (JKM). We set engagement of the Provincial and District Level Health Leaders through 14 advocacy workshops/meetings. The program began with the workshop of TB CEPAT program, which attended by the Governor or representative, Head of the Provincial Health Office, representatives of parliament, the Major of each region, leaders of community organization, NGO leaders, and journalists. Regular advocacy meeting was set with Provincial/District to increase the awareness of TB problems or TB Literacy and establish the commitment to support the TB program.
Results and lessons learnt: CEPAT JKM success to advocate the district leaders to increase the budget allocation in TB program with average 136% in 6 districts. The leaders provide good access and facility for TB patients' treatment continuity and integrated action for Local Policy/Regulation of TB control environment. This program increases local government's awareness about cadre's utilization for TB control in the community. The leaders support all active cadres through universal health access by covering their insurance payment through APBD (local budget revenue and expenditure). The impact is increasing the CDR from 58.2% to 69.52% and Success rate from 60.98% became 93.03% in West Sumatera from 2013 to 2016.
Conclusions and key recommendations: Local councils' provinces and cities/regencies are as decision-makers who can provide political and financial support for End-

TB 2035 policy. Appropriate strategies such as political commitment, policy support, social acceptance and system support are needed to reach decision-makers, to communicate and enlist their support.

PS-25-775-01 Determinants of quality of care in tuberculosis care services in Chennai - a patient's perspective

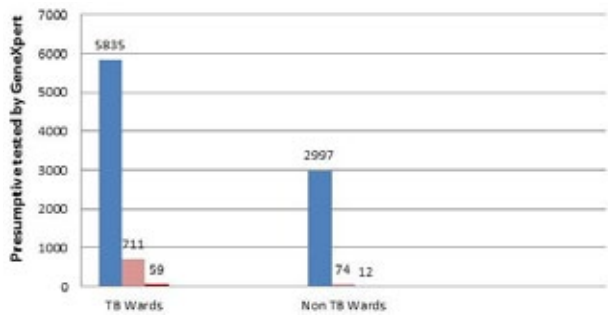
M Periyasamy,[1] S Ovung,[1] D Arumugam,[1] B Watson,[2] SR Dhanapal,[1] AM George,[1] VB Sukumar,[1] K Dharuman,[1] B Thomas,[1] S Kumar,[1] [1]National Institute of Research in Tuberculosis, Social and Behavioural Research, Chennai, India, [2]National Institute of Research in Tuberculosis, Statistics, Chennai, India. e-mail: murugesan.p@nirt.res.in

Background: In order to achieve favourable TB treatment outcome it is vital to provide patient-centric good quality TB care services. Thereby, it is important to understand what determines patients' perception on quality of care for better TB treatment adherence, which is crucial in TB control. This paper presents a conceptual framework which was used in developing a tool to measure patients' perception on quality of TB care services.
Methods: In order to understand patients' perception, 72 qualitative interviews were conducted in the public and public-private mix TB care settings. The patient interviews were transcribed and translated; open coded and constructs were developed based on grounded theory approach. A conceptual framework was developed to include all the aspects of patients' perception.
Results: Patient's perception on quality of care was grounded on four determinants such as support from the health providers, availability of services, support services from the system and basic infrastructure facilities. The first determinant is good support from the doctors and health visitors in terms of diagnosis confirmation, explanation on treatment course, education on possible adverse effects of drugs and addressing co-morbidities. Secondly, availability of services such as drugs, diagnostic tests including tests for EPTB and drug resistance, one point care. Thirdly, support services such as providing the patient with sufficient information on diseases, nutritional support and creating awareness. The fourth determinant is basic infrastructure facilities. Furthermore, the thought process influencing these factors were Patients past experiences, expectation, provider reputation, knowledge on what services to expect and functional status after illness.
Conclusions: Understanding the determinants would help us in prioritizing the resource allocation to achieve patient-centric good quality of care. Providing patient centric care would improve TB treatment outcome.

PS-25-776-01 The FAST approach for fast detection of Rif Sensitive or Resistant cases in a tertiary care hospital in Bangladesh

MH Khan,[1] S Rahman,[1] M Ul Alam,[1] N Saki,[2] T Roy,[3] H Hussain,[4] [1]Challenge TB Bangladesh, DR TB, Dhaka, Bangladesh, [2]National Tuberculosis Control Program, DR TB, Dhaka, Bangladesh, [3]Interactive Research and Development, DR TB, Dhaka, Bangladesh, [4]Interactive Research and Development, Management, Singapore, Singapore. e-mail: mkhan@msh.org

Background and challenges to implementation: FAST (**F**inding TB or MDR-TB patients **A**ctively, **S**eparating **S**afely and **T**reating **E**ffectively) is a TB infection control strategy for rapid diagnosis and effective treatment. GeneXpert was used for diagnosis. Through FAST, after diagnosis, rifampicin-sensitive TB (RS-TB) cases are transferred from non-TB wards to TB wards and rifampicin resistant TB (RR-TB) cases (from both TB and non-TB wards) are transferred to MDR-TB wards.
Intervention or response: Since 2017, the FAST approach has been used on all patients admitted in the medicine, non-TB, and TB wards (including patients diagnosed with smear microscopy) at National Institute of Diseases of the Chest & Hospital. In non-TB wards, GeneXpert was used to diagnose RS-TB and in TB wards.
Data was extracted between January and December 2018 from the medical records of the National Tuberculosis Reference Laboratory (NTRL). Upon verification of records, all diagnosed TB patients (both RS and RR patients) were treated accordingly.
Results and lessons learnt: During this period, 8,832 presumptive cases were identified through the FAST approach. Among these, 5,835 (66%) and 2,997 (34%) were from TB and non-TB wards respectively. In TB wards 711(12.19%) cases were detected as RS-TB and 59 (1.01%) as RR-TB. In non-TB wards, these numbers were 74 (2.4%) and 12 (0.04%) respectively. In total, 785 (8.89%) of RS-TB cases and 71 (0.80%) of RR-TB cases were detected.
Presumptive and case detection rates were higher between July and September segment of 2018 due to high turnover of patients in wards, cause may be the seasonal variation.



[Comparison between TB and Non TB Wards in 2018]

Conclusions and key recommendations: Data indicates that FAST is an effective strategy to detect MTB/RR-TB patients rapidly in a tertiary level specialized hospital like NIDCH which facilitates a process of early diagnosis, safe separation, and effective treatment to control TB infection in a hospital setting.

PS-25-777-01 Non-adherence as a predictor of clinical outcomes among MDR-TB patients in the Philippines

CL Valdez,[1] R Crowder,[2] DM Geocaniga-Gaviola,[1] E Lopez,[1] C Berger,[2] R Destura,[3] M Kato-Maeda,[2] A Cattamanchi,[2] AMC Garfin,[1] [1]Department of Health, Disease Prevention and Control Bureau, Manila, Philippines, [2]University of California, Division of Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [3]University of the Philippines National Institutes of Health, Institute of Molecular Biology and Biotechnology, Manila, Philippines.
e-mail: cldcvaldez.ntp@gmail.com

Background: Non-adherence was found to be the strongest predictor of unfavorable outcomes among patients with drug-susceptible tuberculosis (TB). We analyzed data from the Philippines National Tuberculosis Control Program (NTP) to examine adherence and other predictors of treatment outcome among patients with multidrug-resistant (MDR) TB.
Methods: A random sample of patients treated for MDR TB from 2013-2016 were included. Multivariable proportional hazards regression was used to predict unfavorable outcome (treatment failure or death) using baseline and on-treatment indicators. Adherence was calculated as the number of days doses were taken divided by the days of treatment until the date of outcome. Patients lost to follow-up (LTFU) were excluded from the primary analysis, and included as either all having favorable or unfavorable outcomes in sensitivity analyses.
Results: Of 352 patients included, median age was 43 (IQR 33-52), 33% (95% CI 28-38) were female, 30% (95% CI 25-35) lived in the National Capital Region (NCR), 51% (95% CI 45-56) had BMI <18.5 at baseline, 97% (95% CI 94-98) had a previous history of TB treatment, 30% (95% CI 25-35) had a cavitary chest X-ray at baseline, and 24% (95% CI 19-30) had a sputum smear grade of 3+ at baseline. Median adherence was 77% (IQR 57-95), and 78% (95% CI 74-83) achieved culture conversion within six months of treatment.
220 patients (63%) had a favorable outcome (cured or treatment completed), 27 (8%) failed treatment or died, and 105 (30%) were lost to follow-up. Lack of culture conversion within 6 months was the strongest predictor of unfavorable outcomes, followed by non-adherence (>10% missed doses), smear grade of 3+ relative to ≤1+, and older age (Table 1).
Conclusions: Medication adherence was a strong predictor of treatment outcome among patients with MDR TB. Strategies to improve treatment adherence are critical to improving MDR TB treatment outcomes.

	LTFU Excluded Unadjusted HR (95% CI)	LTFU Excluded Adjusted HR (95% CI)	LTFU = favorable Unadjusted HR (95% CI)	LTFU = favorable Adjusted HR (95% CI)	LTFU = unfavorable Unadjusted HR (95% CI)	LTFU = unfavorable Adjusted HR (95% CI)
Age (continuous)	1.02 (0.99-1.05)	1.04 (1.01-1.07)	1.02 (0.99-1.05)	1.03 (1.00-1.06)	1.00 (0.99-1.01)	1.01 (0.99-1.02)
Female	0.97 (0.44-2.16)	0.86 (0.36-2.07)	1.02 (0.46-2.29)	1.13 (0.49-2.63)	0.93 (0.64-1.35)	1.02 (0.70-1.48)
Cavitary CXR at baseline	0.57 (0.23-1.42)	0.69 (0.25-1.89)	0.59 (0.24-1.47)	1.05 (0.39-2.87)	0.62 (0.41-0.93)	0.71 (0.46-1.09)
BMI<18.5	2.61 (1.09-6.2)	2.49 (0.93-6.64)	2.80 (1.17-6.67)	2.10 (0.85-5.18)	1.07 (0.75-1.51)	0.87 (0.61-1.25)
National Capital Region	2.12 (0.99-4.54)	2.07 (0.82-5.22)	2.02 (0.94-4.31)	1.45 (0.59-3.57)	1.47 (1.03-2.10)	1.56 (0.78-1.70)
Smear grade (2+)	0.81 (0.27-2.45)	0.48 (0.13-1.77)	0.80 (0.26-2.42)	0.80 (0.24-2.68)	0.94 (0.60-1.48)	1.05 (0.65-1.69)
Smear grade (3+)	1.54 (0.67-3.56)	4.87 (1.59-14.95)	1.61 (0.70-3.72)	2.18 (0.81-5.86)	1.06 (0.70-1.62)	1.52 (0.95-2.42)
Lack of culture conversion within 6 months	21.01 (9.19-48.43)	35.34 (11.95-104.53)	17.06 (7.35-39.57)	15.75 (6.12-40.54)	6.87 (4.83-9.77)	6.71 (4.54-9.90)
Adherence (>10% missed doses)	5.54 (1.90-16.14)	5.81 (1.88-17.97)	3.64 (1.25-10.62)	2.61 (0.85-8.00)	4.70 (2.77-7.96)	4.07 (2.39-6.95)

[PS-25-777-01 Table 1. Predictors of unfavorable treatment outcome among 352 MDR TB patients in the Philippines]

PS-26-D6 Addressing TB in vulnerable populations (2)

PS-26-778-01 Sputum collection and transportation services for identification of TB cases in hard-to-reach difficult terrain in Nepal

SK Shrestha,[1] R Bhattrai,[2] A Thapa,[3] T Chhetry,[2] BS Tinkari,[3] [1]Save the Children, Global Fund, Technical, Kathmandu, Nepal, [2]Save the Children, Global Fund, Kathmandu, Nepal, [3]National Tuberculosis Center, NTP, Kathmandu, Nepal. e-mail: suvesh.shrestha@gmail.com

Background and challenges to implementation: Nepal has envisioned to identify additional 20,000 new TB cases by 2021 by finding and diagnosing "missing cases" through improving access to care in remote places by introducing sputum collection and transport system (SCT). To achieve envisioned goal, NTP have initiated SCT in 38 high burden districts from non-microscopic center to microscopic center and from non-GeneXpert center to GeneXpert center.
Intervention or response: This article was to access the reach of SCT and calculate the yield during one year of implementation from March 2018 till March 2019. SCT was introduced in hard to reach health facility where there is difficult to access of health serviced. Hard to reach health facility is defined as those non-microscopic centers which are at-least 15km far from nearest heath facility or where there is no regular access to transportation and takes at-least one-hour by walking to nearest MC. Sputum was also transported of presumptive DR cases from non-GeneXpert to GeneXpert center.
Results and lessons learnt: In total 1,315 non-microscopic center were linked in SCT. In total 24,629 presumptive TB cases were identified, and their sputum was transported to Microscopic center. Out of those sputum transported 1,062 (4.3%) TB cases were diagnosed. Higher proportion of 99.5% diagnosed TB cases were enrolled in treatment. Similarly, 499 non-GeneXpert sites were linked in transportation and 1,877 sputum were transported for Xpert testing and 49 RRTB cases were diagnosed and 48 of them were enrolled in treatment.
Conclusions and key recommendations: The results of this study highlight the feasibility of establishment of SCT services in hard-to-reach areas of Nepal where geographical terrain poses challenge to access health services. In the absence of SCT services, TB cases would not have been notified to the system contributing to the missing cases. SCT would benefit TB programmes but need to prioritize in quality services to increase yield and needs to expand elsewhere.

PS-26-779-01 The effect of incarceration on tuberculosis treatment outcomes in Brazil, 2009-2017

J O'Marr,[1] KS Walter,[1] CCM Gonçalves,[2] D Arakaki-Sanchez,[3] J Croda,[2,4] JR Andrews,[1] [1]Stanford University School of Medicine, Department of Infectious Disease and Geographic Medicine, Stanford, CA, United States of America, [2]Federal University of Mato Grosso do Sul, School of Medicine, Campo Grande, MS, Brazil, [3]Ministry of Health of Brazil, Tuberculosis National Control Programme, Brasilia, DF, Brazil, [4]Oswaldo Cruz Foundation, Public Health, Campo Grande, MS, Brazil. e-mail: jamiesonomarr@gmail.com

Background: Prisoners bear a disproportionate and increasing burden of tuberculosis in Brazil. However, little is known about treatment outcomes and care gaps in this population.
Methods: We obtained data on sociodemographic and clinical characteristics and TB treatment outcomes using Brazil's national disease registry from 2009 to 2017. We conducted multivariable logistic regression to quantify the effect of incarceration on the probability of treatment success among new adult TB cases. We controlled for sex, age, self-reported race, education status, diagnosis year, HIV status, and reported use of alcohol and tobacco.
Results: TB treatment outcomes were reported for 97.3 % of non-incarcerated and 94.4 % of prisoners. Among these, the treatment success was 70.4 % among non-incarcerated individuals and 76.7 % among prisoners. In multivariable regression, prisoners were more likely to have treatment success (adjusted odds ratio [AOR] 1.57 95 % CI 1.12-1.39). Directly observed therapy (DOT) was associated with improved treatment outcomes (AOR 1.93, 95 % CI 1.84-2.01). Access to DOT was significantly higher among prisoners (77.0 %) compared to those outside prison (56.1 %) ($p < .0001$), and this explained the superior outcomes among prisoners. Among prisoners, women (AOR 0.69, 95% CI: 0.56-0.86), self-reported black (AOR 0.73, 95% CI 0.63-0.84) or mixed-race individuals (AOR 0.80, 95% CI 0.73-0.89), HIV-coinfected (AOR 0.36, 95% CI 0.31-0.42), and those reporting alcohol use (AOR 0.63, 95% CI 0.55-0.72) were less likely to have treatment success.
Conclusions: Prisoners have a greater odds of treatment success than those outside prisons, an effect entirely mediated by increased exposure to DOT. Treatment success among both incarcerated and non-incarcerated populations is below international targets. Expanding access to DOT and other interventions to improve outcomes is needed, particularly in populations with poorer outcomes such as women, black or mixed-race inmates, HIV co-infected individuals and those reporting alcohol use.

PS-26-780-01 Effectiveness of bedaquiline-containing MDR-TB regimens in patients treated in a Peruvian prison

S Perea,[1] D Guerra,[1] E Osso,[2] RI Calderon,[1] L Lecca,[1] KJ Seung,[2,3] ML Rich,[3] MF Franke,[2] [1]Socios En Salud Sucursal Peru, TB Program, Lima, Peru, [2]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [3]Brigham and Women's Hospital, Division of Global Health Equity, Boston, MA, United States of America.
e-mail: sperea_ses@pih.org

Background: Suboptimal conditions in prisons, such as overcrowding, inadequate diet, and limited access to medical care, may promote tuberculosis (TB) transmission and jeopardize TB treatment outcomes. We describe outcomes of patients treated with a bedaquiline (Bdq)-containing multidrug-resistant (MDR) TB treatment under programmatic conditions in a Peruvian prison.
Methods: Through the endTB initiative, the Peruvian National Tuberculosis Program introduced Bdq as part of MDR-TB treatment. We report six-month sputum culture-conversion and end-of-treatment outcomes among patients who initiated a Bdq-containing MDR-TB regimen between February 2016 and December 2017 at the Lurigancho Penitentiary Establishment (LPE). A nurse from the nongovernmental organization, Socios En Salud, visited patients regularly to monitor adverse events and treatment response. Due to a lack of laboratory capacity to perform hematology and biochemistry tests, a lab technician visited the LPE to collect samples and take them to an external laboratory. We supported access to tomography scans.
Results: Twenty-eight patients initiated a Bdq-containing regimen, all of whom were male. One (3.6%) had diabetes, none had HIV infection, 15 (54%) had XDR-TB, 7 (25%) had pre-XDR-FQ and 6 (21.4%) had pre-XDR-Inj. Median age was 28.5 (interquartile range: 26 to 35.5). All 13 patients with culture positive sputum at baseline experienced sputum culture conversion by six-months. Eleven patients (39.3%) were cured (10 while in prison, 1 after release), and nine (32.2%) remained on treatment at the time of writing (six incarcerated patients and three released, Table 1).

Outcome	Prisoner patients	Released patients
Cured	10 (35.7%)	1 (3.6%)
LTFU	0 (0%)	3 (10.7%)
Not evaluated	0 (0%)	2 (7.1%)
Died	2 (7.1%)	0 (0%)
Failed	1 (3.6%)	0 (0%)
In treatment	6 (21.5%)	3 (10.7%)

[Table 1. Comparison of end-of-treatment outcome between prisoner patients and released patients treated with a Bdq-containing MDR-TB treatment]

Two died while in prison, and treatment failed in one incarcerated patient. Three were lost-to-follow-up (10.7%), all after release, and end-of-treatment outcome could not be evaluated in two released patients.
Conclusions: We were able to provide effectively treat and monitor incarcerated patients treated with a Bdq-containing regimen. This cohort experienced a high rate of culture conversion and favorable end-of-treatment outcomes; however, post-release treatment support may be necessary to prevent loss-to-follow-up.

PS-26-781-01 Increases in tuberculosis cases in prisons offset control gains in the general population in Brazil

KS Walter,[1] CCM Gonçalves,[2] AI Ko,[3] RD Oliveira,[4] ADS Santos,[5] L Martinez,[1] D Arakaki-Sanchez,[6] JR Andrews,[1] J Croda,[2,7] [1]Stanford University, Department of Medicine, Stanford, CA, United States of America, [2]Federal University of Mato Grosso do Sul, School of Medicine, Campo Grande, MS, Brazil, [3]Yale School of Public Health, Department of Epidemiology of Microbial Diseases, New Haven, CT, United States of America, [4]Federal University of Mato Grosso do Sul, Postgraduate Program in Infectious and Parasitic Diseases, Campo Grande, MS, Brazil, [5]Federal University of Grande Dourados, Postgraduate Program in Health Sciences, Dourados, MS, Brazil, [6]Ministry of Health, National Tuberculosis Control Program, Brasília, DF, Brazil, [7]Oswaldo Cruz Foundation, Public Health, Campo Grande, MS, Brazil. e-mail: kwalter@stanford.edu

Background: Despite a strong national tuberculosis (TB) program, the incidence rate of TB in Brazil has remained essentially stable in recent years, declining modestly from 45/100,000 in 2009 to 44/100,000 in 2017, while estimated new cases increased from 88,000 to 91,000. However, the leveling off of country-wide TB incidence conceals an increasing burden of disease in vulnerable populations.
Methods: We examined trends in incidence of new and relapsed cases of TB in Brazil from 2009-2017, using Brazil's national disease registry, SINAN, by incarceration status, age, and sex. We estimated incidence with census data from IGBE and incarceration data, available through 2016, from the Brazilian Ministry of Justice.
Results: From 2009 to 2017, the proportion of reported TB cases among prisoners increased from 6.4 to 11.8%, among the 97.4% of cases with documented incarceration status. Over this time period, Brazil's incarcerated population grew 53 % (from 473,626 to 726,712 people). Due to the growth in the incarcerated population, the number of incident TB cases in prisons rose from 5,456 (2009) to 10,494 (2017), more than offsetting the 1,631 reduction (79,901, 2009 to 78,270, 2017) in incident TB cases in the general population. In 2016, the burden of TB attributable to prisons varied between states and correlated with state incarceration rate (Pearson ρ 0.72, $p < 0.001$). Nationally, the incidence rate of TB

among prisoners was stable, 1152/100,000 in 2009 and 1156/100,000 in 2016, while incidence outside prisons decreased from 41.8/100,000 to 36.2/100,000. The rate ratio for TB among incarcerated compared to non-incarcerated populations increased from 27.6 to 31.9.
Conclusions: In Brazil, prisoners bear a disproportionate and increasing burden of TB. The rapid rise in the incarceration rate and exceedingly high risk of TB in prisons are undermining progress in reducing TB in the general population, achieving the Sustainable Development Goals, and meeting End TB targets.

PS-26-782-01 Drivers of quality in TB control in South African correctional facilities

R Chimatira,[1] F Chimatira,[1] [1]Public Health ACTION TEAM, phAT, Cape Town, South Africa.
e-mail: raymondchimatira@gmail.com

Background: Prisoners are at high risk of developing tuberculosis (TB), causing morbidity and mortality. This study describes an exploratory operational research project using a qualitative system dynamics approach to identify the factors that interact to drive quality in TB control in South African correctional facilities.
Methods: A rapid review utilising streamlined systematic review methods and was conducted according to a pre-defined protocol. The search was run in PuMed, as well as Google and Google Scholar. Thematic content analysis was used to minimally organise and describe the data set in rich detail, and to interpret various aspects of the research topic.
Results: Results from the analysis identified key behavioural, structural, communication and relationship issues that together determine the quality of TB-related services delivered in correctional facilities. The clusters produced 21 variables, examples of which are: "offenders' perception of services"; "effectiveness of quality leadership"; "effectiveness of interventions"; "knowledge of what works"; "ability to measure quality"; "fit with Department of Correctional Services/partner goals"; "conflict over objectives"; "responsiveness of correctional system"; and "provider exposure to consequences of poor TB control". A causal loop diagram was developed as an analytical tool to attempt to understand how the issues interact through a series of positive and negative feedback loops to drive quality at a systems level.
Conclusions: Using this framework as a guide, we can develop an understanding of the key issues, opportunities and obstacles that drive quality in TB control interventions in South African correctional facilities. This pilot project demonstrates the utility of the system dynamics method, rather than rigorous policy analysis based on empirical evidence. The conceptual framework will help inspire new approaches to extend and enhance the quality of traditional TB control efforts in correctional facilities.

[Causal Loop Diagram TB Control in Correctional Facilities]

PS-26-783-01 Cross-district transmission of multidrug-resistant tuberculosis in Shenzhen, a newly developed metropolis of China with massive numbers of young migrant workers

Q Jiang,[1,2] Q Liu,[1,2] L Ji,[2] J Li,[2] C Yang,[3] H Takiff,[4,5] W Tan,[2] W Yu,[2] Q Gao,[1,2] [1]Fudan University, School of Basic Medical Sciences, Shanghai, China, [2]Shenzhen Center for Chronic Disease Control, TB Control, Shenzhen, China, [3]Yale University, School of Public Health, New Haven, CT, United States of America, [4]Institut Pasteur, Integrated Mycobacterial Pathogenomics Unit, Paris, France, [5]Nanshan District Center for Chronic Disease Control, TB Control, Shenzhen, China. e-mail: jiangqi10tb@163.com

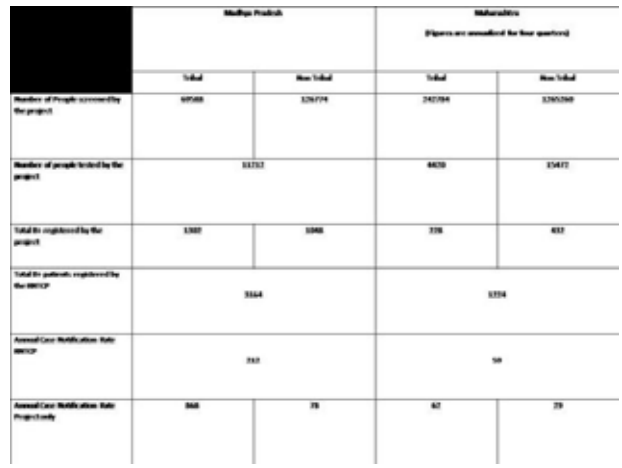
Background: Population movement could extend the multidrug-resistant tuberculosis (MDR-TB) transmission further than a city limit and complicate the global prevalence. We sought to identify the high risk populations and transmission sites of MDR-TB in Shenzhen, the most common destination for internal migrants in China.
Methods: We collected and whole-genome sequenced MDR-TB clinical strains isolated in Shenzhen from 2013 to 2017, and defined genomic-clustered strains as having ≤12-SNP differences. Risk factors for MDR-TB transmission were identified by comparing bacteriological backgrounds, demographic and clinical characteristics of patients infected with either clustered or unique strains. To explore the epidemiological links and geographic sites of transmission, we invited the genomic-clustered patients to an in-depth social network investigation on their close contacts and frequently visited sites.
Results: The study included 417 cases with sequencing data; 65% (271/417) of the MDR-TB patients had no previous history of anti-TB treatment, and 25.2% (105/417) were genome-clustered based on a 12-SNP cutoff, suggesting recent transmission of MDR-TB. Adjusted by the Beijing genotype and resistance to fluoroquinolones, the relative risk of students having a clustered strain was 4.05 (95% confidential intervals [CI], 1.06-17.0) times greater than other patients. Probable links through residences within two kilometers of each

other were identified in only 22.9% (22/96) of the pairs of clustered cases, while the spatial distance between residences of cases in each genomic-cluster averaged 8.76 kilometers. Other than household members, confirmed epidemiological links were also identified among classmates and workplace colleagues.
Conclusions: These findings demonstrate that MDR-TB transmission is a serious problem in Shenzhen city. While most transmission seems to occur between people without obvious epidemiologic links, there is also evidence that transmission may occur in schools or workplaces, which should therefore be included as targeted sites for case detection.

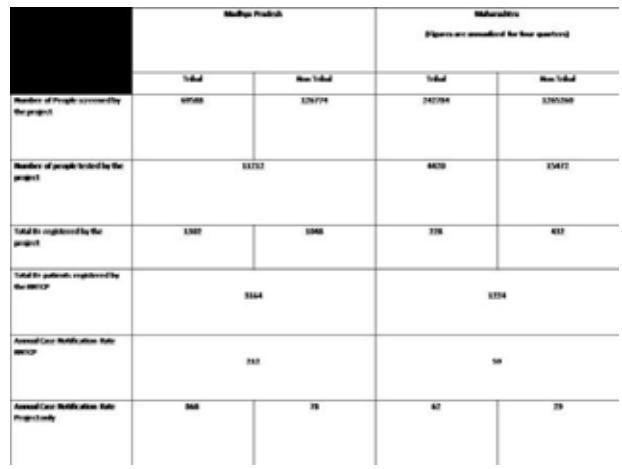
PS-26-784-01 Comparative study of TB among two different tribal groups in central India through community-based active case finding intervention

A Vyas,[1] BS Ghosh,[2] J Creswell,[3] A Khan,[4,5] RH Stevens,[6] S Gupta,[7] [1]Ashakalp Healthcare Association, TB REACH Project, Jaipur, India, [2]Ashakalp Healthcare Association, TB REACH Project, Nagpur, India, [3]Stop TB Partnership, Grants and Innovation, Geneva, Switzerland, [4]Stop TB Partnership, Innovations & Grants Team, Geneva, India, [5]TB REACH, Innovations & Grants Team, Geneva, India, [6]UNOPS, Monitoring and Evaluation, Manchester, United Kingdom, [7]Ashakalp Healthcare Association, Program Management, Nagpur, India.
e-mail: ashvini.vyas@kalphealth.org

Background and challenges to implementation: Sahariyas in Madhya Pradesh and the Gondi and other tribes in Maharashtra face severe access barriers to health care because of their remote locations, poor education, infrastructure, vulnerable social conditions, and extreme poverty. TB prevalence among Sahariyas has been documented above 3,000/100,000 but minimal data exist for TB among the Gondi and others. TB services are generally passive: the person feeling ill must seek care and these groups may suffer due to lack of outreach of health services.
Intervention or response: A TB REACH community-based active case finding intervention was conducted which engaged local youth who were trained to identify presumptive cases and collect and transport sputum specimens to microscopy centres. These community health workers had a fixed catchment area where they carried out ACF for one year. They were paid a fixed honorarium, petrol allowance, communication allowance and incentives to identify and initiate a patient on treatment. Incentives were paid upon notification of patients in national TB notification systems. All identified patients by the project were notified to the RNTCP.
Results and lessons learnt: The table shows the number of people screened and diagnosed with TB across the different populations. Large differences in TB rates were found between the two states and tribal groups as well as between tribal and non-tribal populations. The ratio of annual notification rates, tribal vs non tribal is 11.1 and 2.1 in Madhya Pradesh and Maharashtra respectively.
Conclusions and key recommendations: Tribal groups likely face various access barriers for TB care. Active case finding strategies which link people in need to TB services lead to significant gains in case notification. ACF can be adopted to reach key populations who face access barriers to health care.



[Comparative study of TB among two different tribal groups in central India]

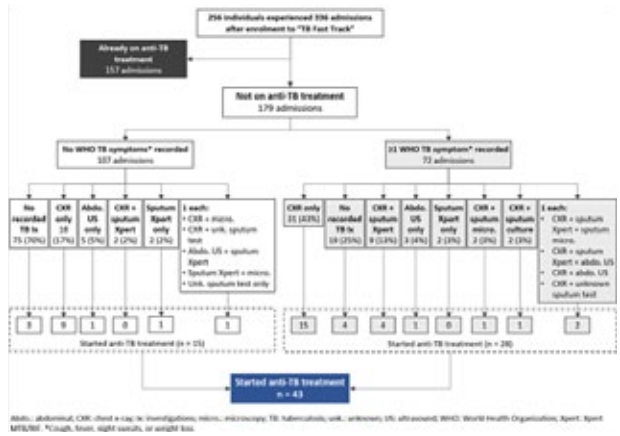


[Comparative study of TB among two different tribal groups in central India]

PS-26-785-01 Investigation of TB in HIV-positive adult inpatients in South African hospitals: data from TB Fast Track

PG Beckwith,[1] M Tlali,[2] S Charalambous,[2,3] GJ Churchyard,[1,2,4] KL Fielding,[4,5] CJ Hoffmann,[6] S Johnson,[7] N Wood,[8] AD Grant,[1,3,9] AS Karat,[1] [1]London School of Hygiene & Tropical Medicine, Department of Clinical Research, London, United Kingdom, [2]The Aurum Institute, Research, Johannesburg, South Africa, [3]University of Witwatersrand, School of Public Health, Johannesburg, South Africa, [4]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [5]London School of Hygiene & Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom, [6]John Hopkins University, School of Medicine, Baltimore, MD, United States of America, [7]Foundation for Professional Development, Innovations, Pretoria, South Africa, [8]North Bristol NHS Trust, Anaesthetics, Bristol, United Kingdom, [9]Africa Health Research Institute, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa. e-mail: alison.grant@lshtm.ac.uk

Background: Tuberculosis (TB) remains an important cause of morbidity in HIV-positive people, yet many remain undiagnosed despite hospitalisation. We aimed to identify gaps in the diagnostic pathway among adults with advanced HIV admitted after enrolment to the TB Fast Track trial (included in which were HIV-positive adults [≥18 years]; CD4 ≤150 cells/μL; attending primary health clinics; not taking antiretroviral therapy [ART] or anti-TB treatment).
Methods: Data were abstracted from hospital files for all admissions identified from 2013-2015. Causes of admission were classified by a physician (PB), with criteria pre-specified for likelihood of diagnosis ('definite' [culture- or polymerase chain reaction-positive], 'probable' [smear-positive or radiological features], 'possible' [clinicopathological features]). Investigations for TB were assessed in individuals not on TB treatment (Figure).
Results: 265 adults (141 [53%] female; median age 38.7 [interquartile range {IQR} 33-46] years; median CD4 46 [IQR 22-83] cells/μl; 155 [58.5%] on ART) experienced 336 admissions. 110/336 (32.7%) admissions were TB-related: 60 (17.9%) new TB diagnoses (eight 'definite', 25 'probable', 27 'possible') and 50 (14.8%) with worsening TB symptoms on anti-TB treatment.
Individuals were not on anti-TB treatment in 179/336 (53.3%) admissions: cough was recorded in 52 (29.1%), fever in 25 (14.0%), night sweats in 22 (12.3%), and weight loss in 40 (22.4%). In 72 admissions with symptoms recorded, sputum was collected 19 (26.4%) times and a chest x-ray done 48 (66.7%) times (Figure). 43 people were initiated on anti-TB treatment: 28 (65%) reported ≥1 World Health Organization TB symptom and 10 (23%) had a sputum-based investigation (5/43 [11.7%] were treated based on a positive sputum result).
Conclusions: A third of admissions were related to TB. Sputum-based investigations were used infrequently in those with TB symptoms and most people started on anti-TB treatment did not have microbiological evidence of TB. Better diagnostics and training around guidelines are needed.



[In-patient investigations for TB among HIV-positive adults admitted after enrolment to TB Fast Track]

PS-26-786-01 High prevalence of undiagnosed tuberculosis among key populations at risk for HIV in Papua New Guinea

B Willie,[1] S Badman,[2] R Narokobi,[1] J Gabuzzi,[1] S Pekon,[1] M Kupul,[1] P Hou,[1] A Amos-Kuma,[1] A Vallely,[2] A Kelly-Hanku,[1,2] [1]Papua New Guinea Institute of Medical Research, Sexual and Reproductive Health Unit, Goroka, Papua New Guinea, [2]UNSW Sydney, Kirby Institute for Infection and Immunity, Sydney, NSW, Australia. e-mail: a.kelly@unsw.edu.au

Background: Papua New Guinea (PNG) has a triple burden of tuberculosis (TB), multi drug-resistant TB, and TB/HIV co-infection. PNG has a case notification rate of 333 per 100,000 in 2016. PNG's HIV epidemic is concentrated among, female sex workers (FSW), men who have sex with men (MSM), and transgender women (TGW), but little is known about the burden of TB among them. Here, we screened and tested 2960 and 1714 individuals respectively for TB in a recent Bio-behavioral Survey (BBS).
Methods: Respondent driven sampling (RDS) methodology was used to recruit participants in three PNG cities (Port Moresby, Lae, and Mt. Hagen) from June 2016 to December 2017. Inclusion criteria for FSW were born a female, aged ≥12 years, spoke English or Tok Pisin, sold or exchanged sex in the past 6 months and had a valid study coupon. For MSM/TGW the criteria were born a male, aged ≥12 years, spoke English or Tok Pisin, had engaged in oral/anal sex with a male in the past 6 months and had a valid study coupon. We screened for TB using the WHO four symptom TB algorithm: cough, night sweats, and fever for more than two weeks and weight loss. Eligible participants provided sputum and were tested for pulmonary TB using the portable GeneXpert™ platform.

Results: Based on GeneXpert™ results, the estimated rate of TB prevalence among FSW was 1200, 700 and 200 per 100,000 in Port Moresby, Lae and Mt. Hagen, respectively. The prevalence rate among MSM/TGW was 1000, 1200 and 1400 per 100,000.
Conclusions: This study showed a much higher TB prevalence rate of undiagnosed pulmonary TB among FSW and MSM/TGW compared to the general population. This estimate is likely to be conservative given we did not screen or test for extra-pulmonary TB. Key populations should be prioritized in PNG's response to TB.

PS-26-787-01 Tuberculosis in nomadic schools and communities in Adamawa State, Nigeria

S John,[1] S Abdulkarim,[1,2] F Atiku Abubakar,[3] E Ubochioma,[4] [1]Adamawa State Agency for Control of AIDS, Health, Yola, Nigeria, [2]Janna Health Foundation, Health, Yola, Nigeria, [3]Ministry of Health, Health, Yola, Nigeria, [4]National TB Control Program, Health, Abuja, Nigeria. e-mail: wizemannstv2@gmail.com

Background and challenges to implementation: Nigeria ranks 6th among High TB Burden countries globally, however, the country detects only 24% of its estimated TB cases. There are an estimated 9.3 million Nomads in Nigeria out of which 450,000 are in Adamawa, 1 of its 36 States. Poor access to TB services, overcrowding and poor ventilation, prevalent consumption of unpasteurized milk and poor knowledge and awareness on TB among others are factors influencing TB transmission among Nomads. With support from Stop TB Partnership through its Challenge Facility for Civil Society Round 8 grants, TB Control Services was launched in Nomadic Primary Schools and Communities. This paper aims to demonstrate results of 9 months Active TB Case Finding (ACF) in Nomadic Schools and communities of Adamawa State.
Intervention or response: ACF was implemented in 74 Nomadic Schools and 52 Nomadic Communities from 1st June 2018 to 28th February, 2019. The process involved mapping, advocacy, identification of Volunteers, training of General Health Workers (GHWs) and Volunteers on sputum collection, transportation and documentation. Sputa were tested by GeneXpert. Community screening days were organized with Nomadic School teachers and Community Leaders; Volunteers provided treatment support.
Results and lessons learnt: 150 Volunteers, 25 GHWs were trained on TB screening, diagnosis and treatment. 36,321 Nomads were verbally screened out of which 3,077 (8.5%) presumptive TB cases were identified; 1,232 (40%) were females. 175 all forms of TB cases were notified including 149 Bac+ and 23 children; 53 (36%) of the Bac+ cases were females. No Rifampicin resistant TB case was detected. Lack of appropriate guidelines for Nomadic Community engagement, location of communities in Hard-to-Reach areas and language barrier were some key challenges encountered during implementation.
Conclusions and key recommendations: Nomadic Pastoralists have high TB rates. Large-scale ACF interventions among Nomads and other vulnerable populations can improve TB case detection.

PS-27-C10 Optimising the use of GeneXpert

PS-27-789-01 Integrating a portable, battery-powered GeneXpert device into contact investigations: implications for early case finding and time-to-treatment initiation - Buffalo City Metro Health District, South Africa

A Medina-Marino,[1] D Bresenham,[1] R Mawarire,[1] C Bezuidenhout,[1] P Ngwepe,[1] SS Shin,[2] N Ngcelwane,[3] M Van der Walt,[4] [1]Foundation for Professional Development, Research Unit, East London, South Africa, [2]University of California, School of Nursing, Irvine, CA, United States of America, [3]Buffalo City Metro Health District, TB Program, East London, South Africa, [4]South African Medical Research Council, TB Platform, Pretoria, South Africa. e-mail: andrewm@foundation.co.za

Background: Low uptake of community-to-clinic referrals for TB testing by those that screen positive during home-based household contact investigations is a barrier to diagnosis and treatment initiation of secondary cases. We investigated the acceptability and feasibility of home-based TB testing of household contacts using a portable, battery-powered GeneXpert point-of-care device.
Methods: Households of TB patients receiving treatment at six public-sector clinics in Buffalo City Metro Health District, Eastern Cape Province, were screened for TB per South African national guidelines (July 2018 and April 2019). Homes in which at least one individual screened positive for TB were randomized (1:1) to receive either a referral for clinic-based TB testing (control), or a home-based TB test with referral for treatment initiation (intervention). Home-based testing was performed using a portable GeneXpert GX1 device powered by an external battery. Referral uptake, time-to-clinic presentation and time-to-treatment initiation was recorded for all participants.
Results: A total of 97/495 (19.6%) household contacts screened positive for TB, of which 95 (97.9%) consented to study participation; 46 were referred for clinic-based TB testing (control) and 49 were offered home-based TB testing (intervention). Sputum was collected from 45% of symptomatic contacts for home-based testing, of which 13.6% tested positive for TB. Of these, 66% presented for treatment initiation.
In comparison, 15.7% of individuals referred for testing (control) presented to a clinic. Time-to-clinic presentation was 1 vs 3.7 days for intervention and control arm

participants, respectively. Time-to-treatment initiation was 1 vs 17.3 days for intervention and control arm participants, respectively.

Conclusions: Home-based TB testing using a portable GeneXpert device is highly acceptable. Feasibility was moderated by the ability to produce a sputum for testing. Improved referral uptake and decreased time-to-treatment initiation among intervention arm participants suggests that integrating point-of-care diagnostic testing into household contact investigations may represent a new strategy for active TB case finding.

PS-27-790-01 Initial X-ray followed by GeneXpert tests: new hope to save the lives of millions of Bangladeshi people

S Islam,[1] G Raihan,[1] F Khatun,[1] MA Islam,[1] S Reza,[1]
[1]BRAC, Communicable Diseases Programme, Dhaka, Bangladesh. e-mail: akramul.mi@brac.net

Background and challenges to implementation: TB is associated with a lot of morbidity and mortality worldwide. Same scenario is in high burden countries like Bangladesh with high prevalence of drug resistant TB cases (estimated). Identify more TB cases early is a major constraint in the country as National TB Program (NTP) is still widely dependent on microscopy. According to Bangladesh TB prevalence survey in 2015 to 2016, smear microscopy could identify only 37% of the TB cases where 92% by Gene X-pert. Moreover, 90% of the bacteriologically confirmed cases were identified by chest X-ray screening.

Intervention or response: Considering the high reliability and rapid diagnostic ability, BRAC a development organization in partnership with NTP established 23 TB diagnostic centers with Gene X-pert machines in combination of X-ray and made those functional from January 2018. All TB presumptive were screened by X-ray and those who had abnormal X-ray findings were confirmed by X-pert test.

Results and lessons learnt: From January to December 2018, in 23 TB diagnostic centers, a total of 245,745 TB presumptives were screened by x-ray and 49,625 (20.19%) were found abnormal. Among abnormal X-ray findings, 7,765 were clinically diagnosed, 38,960 were tested by gene x-pert of which 6, 209 (16%) drug sensitive and 186 (0.48%) rifampicin resistant TB cases were diagnosed. During this period 14,585 DR TB presumptive were tested by x-pert and 157 (1.08%) RR TB detected.

Conclusions and key recommendations: Bangladesh government should focus more on scaling up X-ray and X-pert machines for initial screening of TB presumptive followed by early identification and prompt start of treatment to improve TB out come in this high TB burden setting. Moreover, double benefit should be considered as X-pert was found as an effective tool for rapid identification of both drug sensitive and drug resistant TB cases.

PS-27-791-01 Diagnostic accuracy of Xpert MTB/RIF assay for detection of extra-pulmonary tuberculosis

J Shastri,[1,2] R Set,[1] D Shah,[3] [1]T N Medical College & Nair Hospital, Microbiology, Mumbai, India, [2]Kasturba Hospital for Infectious Diseases, Molecular Biology, Mumbai, India, [3]Municipal Corporation of Greater Mumbai, TB, Mumbai, India. e-mail: dtomhbc@rntcp.org

Background: WHO endorsed Xpert MTB/RIF assay, has been evaluated for pulmonary TB in a number of studies but very few investigations have been reported for extrapulmonary specimens. The present study evaluates the performance of Xpert MTB/RIF assay in diagnosis of extrapulmonary TB (EPTB).

Methods: To determine overall and sample wise sensitivity and specificity of Xpert MTB/RIF assay for diagnosis of EPTB in comparison to culture on Lowenstein Jensen (LJ) medium.

The present study was laboratory based at a tertiary care centre in Mumbai between March 2017 to June 2018. Seven hundred and thirty eight specimens including pus, body fluids, lymph node aspirates, tissues and biopsies from clinically suspected cases of EPTB were subjected to Ziehl Neelsen staining, Xpert MTB/RIF assay and culture on LJ medium. Of these 9 were contaminated on culture and 7 showed error on Xpert MTB/RIF. Therefore 722 specimens were analysed. Statistical analysis was done using medcalc statistical software.

Results: The sensitivity, specificity of Xpert MTB /RIF assay for diagnosis of EPTB were 78.57% (95% CI 59.05 to 91.7 %) and 94.79 % (95% CI 92.89 to 96.3 %). Amongst culture positive cases, sensitivity of Xpert MTB/RIF assay was 87.5% in smear positive and 75 % in smear negative cases.

Xpert MTB/RIF showed maximum sensitivity of *M.tuberculosis* detection from lymph node specimens 100% (95% CI 39.7 to 100.00%) and body fluids other than pleural fluids 100% (95% CI 15.81% to 100.00%) followed by pus aspirates 90% (95% CI 55.5 to 99.75%).

Conclusions: Our results establishes that rapidity and simplicity of Xpert MTB /RIF assay with a good sensitivity and specificity for lymph node specimens, body fluids other than pleural fluids and pus aspirates makes it a promising tool in the diagnosis of EPTB. However, pleural biopsy was found to be a preferable to pleural fluid specimen.

PS-27-792-01 Assessment of the Xpert MTB/RIF Ultra Assay on Mycobacterium tuberculosis complex in extra-pulmonary samples

S Smaoui,[1,2] E Mhiri,[2,3] S Hachicha,[1,2] A Ghariani,[2,3] S Kammoun,[1,2] C Marouane,[1,2] A Ghorbel,[1,2] D Gamara,[4] L Slim,[2,3] F Messadi Akrout,[1,2] [1]Regional Laboratory of Hygiene Tertiary Health Care Hedi Chaker, Microbiology, Sfax, Tunisia, [2]Faculty of Pharmacy, University of Monastir, Microbiology, Monastir, Tunisia, [3]Laboratory of Microbiology Abderrahmen Mami, Microbiology, Ariana, Tunisia, [4]Direction Management of Basic Health Care, Management of Basic Health Care, Tunis, Tunisia. e-mail: ssalmahch@gmail.com

Background: New techniques assay such as Xpert MTB/RIF have been developed in order to facilitate rapid diagnosis of TB. But, their sensitivity remains poor particularly on paucibacillary extrapulmonary specimens. A next-generation assay Xpert MTB/RIF Ultra (GX-Ultra) has recently been designed to try to overcome this limitation.Herein, we evaluated retrospectively the performance of this GX-ultra on different types of extrapulmonary specimens from different anatomic sites.
Methods: Extra-pulmonary specimens were prospectively included, and analysed in the Mycobacteria Laboratory of Ariana, Tunisia and regional laboratory of Hygiene Sfax,Tunisia during the years 2017 and 2018. For each sample, smear examination, culture on solid and liquid media, and GX-ultra assays were performed.
Results: A total of 497 specimens were included in our study. Compared to the smear examination, sensitivity and specificity of GX Ultra were 97.7% (95%CI, 88.4-99.6%) and 75.2% (95% CI, 71-80) respectively.
Sensitivity and specificity of GX Ultra, in comparison with culture, were 84.2% (95%CI, 72.6-91.5%) and 75.45% (95% CI, 71.2-79.2) respectively. The highest sensitivity was obtained in samples of abscess aspirates (100%) and lymph nodes (89.3%), followed by tissue specimens (75%), and sterile fluids (50%). Among the 3 samples presented mutations related to rifampicin resistance, one was confirmed by phenotypic and genotypic methods. The two others samples have negative culture.
Conclusions: GX-Ultra showed good sensitivity in paubacillary specimens, making it a useful tool for rapid EPTB diagnosis.

PS-27-793-01 Stool for bacteriologic confirmation in childhood intra-thoracic TB: a private TB programme experience

S Siddiqui,[1] K Asif,[1] A Anwar,[1] H Ali,[1] M Hamid,[1] N Khursheed,[2] F Adnan,[2] F Amanullah,[1] [1]Indus Health Network (IHN), Global Health Directorate, Karachi, Pakistan, [2]Indus Health Network (IHN), Laboratory, Karachi, Pakistan. e-mail: sara.siddiqui@ghd.ihn.org.pk

Background: Bacteriologic confirmation in childhood TB is difficult due to paucibacillary disease and difficulty in obtaining sputum samples. Alternate samples include gastric aspirates and stool for Xpert MTB/RIF.
Methods: We retrospectively studied 67 children diagnosed with intrathoracic TB (pulmonary TB) at the Indus Hospital TB clinic from May 2017 to April 2019. In addition to a history, physical examination, chest Xray, TST these children had also been tested with a single stool sample for Xpert MTB/RIF.
Results: Children diagnosed with pulmonary TB (PTB) were 67, with a mean age of 6 years and an equal male, female representation. Of this cohort 17/67 (25%) were bacteriologically confirmed, 13/67 (19.4%) were stool Xpert positive, and 23/67 (34.3%) were probable PTB. Of the bacteriologically positive patients 4/17 (25%) were found to be Rifampicin resistant. Of the confirmed patients 11/17 (65%) had consolidation on chest Xray and 50% had recent history of exposure to TB.
Conclusions: Under programmatic conditions, stool for Xpert MTB/RIF is a good alternative to respiratory sampling in children for drug sensitive and drug resistant TB confirmation in a low resource high burden setting.

PS-27-794-01 Maintenance of Genexpert instruments in Nigeria: lessons learned from an authorised service provider

F Ajiboye,[1] J Scholten,[2] B Nsa,[3] I Huitema,[4] C Ehimanre,[1] A Adeyomoye,[1] T Panda,[5] N Nwokoye,[6] [1]KNCV Tuberculosis Foundation, Cepheid, Abuja, Nigeria, [2]KNCV Tuberculosis Foundation, Laboratory, The Hague, Netherlands, [3]KNCV Tuberculosis Foundation, Programs, Abuja, Nigeria, [4]KNCV Tuberculosis Foundation, Programs, The Hague, Netherlands, [5]KNCV Tuberculosis Foundation, Cepheid, Kano, Nigeria, [6]KNCV Tuberculosis Foundation, Laboratory, Abuja, Nigeria.
e-mail: prisca.ajiboye@kncvtbc.org

Background and challenges to implementation: In 2017, Genexpert was endorsed as the initial TB diagnostic in Nigeria. Maintenance of the Genexpert is essential to optimize functionality. A high incidence of machine breakdown was reported mostly related to the users and maintenance. As the authorized service providers (ASP), we are the first line of support for use of Genexpert. We document our experiences and lessons learned.
Intervention or response: As ASP, we received updated trainings frequently. The provision of a toll free line for all customers and a dedicated email address was used

to troubleshoot reported cases. We provided retraining for end users and mentored a team of super users to troubleshoot and replace parts. We provide feedback for stakeholders.

Results and lessons learnt: The majority of reported faults were from failed modules which were mainly heat-related. Alternative power backup plans did not support air conditioning for Genexpert. Other failures were the result of users not performing routine maintenance while high error rates were typically user-related. Long instrument downtime was typically from delays in reporting and providing supporting documents.

Customers should be informed on the terms and conditions of the Genexpert at procurement. Minimal installation requirements should be met for optimal functionality. Stakeholders should review maintenance processes with users and ensure SOPs are followed. Faults reports should be sent in promptly with accompanying documentation.

From the manufacturer side, we have had the opportunity for an open dialogue to expedite shipment of modules, spare modules, spare parts and, most recently, an in-country repair center to further expedite repairs.

Conclusions and key recommendations: The maintenance of Genexpert in Nigeria has been perceived to be the sole duty of the manufacturer. However, maintenance of the Xpert system is a shared function starting with the users. Understanding the terms and conditions of functionality should be made a priority for all users. Programs and end users should meet minimal requirements for installations.

PS-27-795-01 Unsuccessful Xpert MTB/RIF test results in Mozambique: causes and cost implications

A Teixeira Chongo,[1] D Jaintilal,[2] K Azam,[2] L De Morais,[2] HE Coelho Hamene,[3] I Pinto,[1] [1]Ministry of Health, Central Laboratory Department, Maputo, Mozambique, [2]American Society for Microbiology, International Affairs, Maputo, Mozambique, [3]Ministry of Health, National Tuberculosis Control Program, Maputo, Mozambique. e-mail: dinisjaintilal@hotmail.com

Background and challenges to implementation: Mozambique, one of the high burden countries of TB, TB/HIV coinfection and MDR-TB, have rolled out GeneXpert since 2011 to improve TB case detection. Unsuccessful Xpert MTB/RIF results could impact the performance of NTP, being crucial to understand its causes, implications for patient management and costs.

Intervention or response: For proper implementation, training of GeneXpert users and site supervision was conducted, provincial focal points were established for local support. Retrospective analysis of Xpert MTB/RIF results from January 2017 to December 2018 was conducted using data uploaded through GxAlert to determine the rate of unsuccessful results (error, invalid and no result), causes and cost implications.

Results and lessons learnt: A total of 111,825 Xpert MTB/Rif results were uploaded from 64 instruments in 2017 and 158,151 results from 72 instruments in 2018, an increase of 42%. TB detection rates were 14.8% in 2017 and 12.8% in 2018, whilst Rifampicin resistance rates were 9.3% and 9%, respectively. There were 12,040 (10.8%) unsuccessful tests in 2017 and 13,003 (8.2%) in 2018, contributing to losses of 120,400USD and 130,030USD in 2017 and 2018 (cost based on 10USD/cartridge). Error rate was 5.6% in 2017 and 5.2% in 2018. Invalid results rate was 3.4% in 2017 whereasin 2018 was 1.3%, representing a decrease of 47% suggesting an increased adherence to SOPs. No result rate remained at 1.8% throughout the 2 years. Technical errors were more frequent (64%), that may be caused by human factors, compromised probe integrity and module failure (error codes 5007, 5006 and 2008), followed by electrical connection issues with 15% (error codes 2126, 2127 and 2122).

Conclusions and key recommendations: Unsuccessful Xpert MTB/RIF results are high in Mozambique with cumulative losses reaching 250,430 USD in two years. Optimal placement of GeneXpert instruments (functional air conditioning and uninterrupted power supply) and continuous training and supervision can render better performance and reduce costs associated to unsuccessful results.

PS-27-796-01 Testing for TB, HIV and hepatitis using GeneXpert platform in Africa: challenges, lessons learnt and the way forward in the era of sustainable development goals

J Iragena,[1] F Mavhunga,[2] W Nkhoma,[3] M Gasana,[2] H Lago,[1] [1]World Health Organization, African Region (Afro), HIV, TB and Hepatitis, Brazzavile, Congo, [2]World Health Organization, African Region (Afro), TUB, Brazzavile, Congo, [3]World Health Organization, African Region (Afro), TUB, Harare, Zimbabwe. e-mail: iragenaj@who.int

Background and challenges to implementation: Xpert MTB/RIF® is the recommended initial diagnostic test in all persons with signs and symptoms of TB. Utilization of GeneXpert platforms for TB in Africa is suboptimal, leaving space for their use for other diseases such as HIV -Early Infant Diagnostics (EID) and viral load (VL), and Hepatitis C, and following 2017 WHO information note on use of multi-disease testing devices.

Intervention or response: We collected data on the number of GeneXpert instruments and cartridges per country in 23 high HIV/TB burden countries in Africa during 2017 and 2018. We evaluated the annual number of TB tests per instrument per site for 10 high volume sites in each country. Based on number of tests and needs analy-

sis, we computed the spare capacity to potentially integrate EID and VL testing onto these platforms. EID and VL testing volume and needs were calculated based on the number of people on ART and HIV-exposed infants.
Results and lessons learnt: Utilization of GeneXpert for TB varied between 20% and 60% across countries and sites. Testing volume for TB increased and decreased in some sites between 2017 and 2018, but there was still excess capacity for EID and VL testing. Countries integrating EID and targeted VL testing using GeneXpert for TB showed increased device utilization between 50-80 % for some sites, while others had less than 50%.
Conclusions and key recommendations: Integration of EID and VL testing on GeneXpert is feasible and can increase device utilization without negatively impacting TB services; joint HIV and TB programming can enhance efficiencies. Harmonization of policy and alignment of such components as training, supply management, financing, and service delivery, is crucial. Pre-requisite to consider include site selection, assessment, pilot and analysis to informed decision-making to avoid TB service disruption. The low numbers of TB specimens should first be investigated before deciding to use the "excess" GeneXpert capacity for HIV testing.

PS-27-797-01 Experience using rapid molecular testing for TB diagnosis in Namibia

AM Thomas,[1] I Katjao,[1] N Ruswa,[2] [1]Ministry of Health and Social Services, Directorate Special Programs, Windhoek, Namibia, [2]KNCV Challenge TB, National TB Leprosy Program, Windhoek, Namibia.
e-mail: talbertina@yahoo.com

Background and challenges to implementation: Namibia introduced recording tools for drug-resistant tuberculosis in 2007 and started systematic reporting in 2009. Diagnosis and treatment are availed at no cost to the affected Namibians. However, missed cases of DR-TB have always been a concern since the first nationwide drug resistance survey, which estimated that 7% of bacteriologically confirmed cases had rifampicin resistance.
Intervention or response: Namibia introduced the molecular testing with Xpert MTB/RIF in 2013, scaling up in 2014 in time for the 2nd DRS, where universal access to Xpert testing was ensured. A new diagnostic algorithm was introduced by way of a circular, in 2017, in which all presumptive cases undergo rapid molecular testing for TB with Xpert MTB/RIF. Additionally, expertise advice was provided to start treatment without delay. Data for DR-TB diagnosis was captured with a web-based reporting system(E-TB manager).
Results and lessons learnt: The overall diagnosis of confirmed DR-TB has increased since 2010, from 285 (69% of expected cases) to 417 (99% of expected cases) in 2017. Of the cases notified, 97% were started on treatment in 2017. The proportion of all TB cases that are bacteriologically confirmed has increased from 47% to 66%.
Conclusions and key recommendations: Rapid molecular testing, as recommended by World Health Organization, could accelerate finding of missing DR-TB cases and initiation of treatment. This diagnostic method should be maintained in all districts and regions.

PS-27-798-01 Sample panels to support the development of nucleic acid-based diagnostic assays for Mycobacterium tuberculosis

J Cantera,[1] L Lillis,[1] H White,[1] D Boyle,[1] [1]PATH, Diagnostics Program, Seattle, WA, United States of America. e-mail: jcantera@path.org

Background: Low cost and accurate point-of-care nucleic acid diagnostic tests for tuberculosis (TB) are needed for disease-management in high burden countries. Challenges to diagnostic test development includes a lack of access to independently prepared, uniform, quantified and biosafe samples that can validate early prototyping of novel tools.
Methods: PATH created three TB sample panels; two panels comprised of inactivated TB (iTB) cells and a third with active TB or non-TB mycobacteria (NTM). The first panel used serial dilutions of iTB-cells spiked into synthetic sputum (SS). The second panel used a similar spiking strategy but with human sputum (HS) and a rifampin resistant iTB strain. Raw sputa were initially screened by culture before pooling and spiking with iTB. Thirteen sputum samples tested culture-positive for either TB or NTM were used to create a third clinical sputum (CS) panel. Representative samples from each panel were screened by smear microscopy, quantitative PCR and Xpert MTB/RIF.
Results: The qPCR analyses of SS and HS panels confirmed all samples contained iTB in a range from 10^5 to 10^1 cells/mL. TB-positive sputum samples were inadvertently identified in screening and used to create CS panel. Xpert data for each panel verified the presence or absence of TB DNA from these samples. Pearson correlation of qPCR and Xpert assay data was high ($R=0.998$). Higher bacterial loads were corroborated by smear microscopy.
Conclusions: PATH have created three qualified panels of TB samples that are available to technology developers including one contrived panel (SS) that is biosafe because it is not derived from clinical sources. These will support technology developers to verify the analytical performance of their prototype technologies before accessing qualified clinical samples which are expensive and often difficult to acquire, especially in low prevalence countries where appropriate clinical samples are typically infrequent.

ABSTRACT PRESENTATIONS SATURDAY 2 NOVEMBER 2019

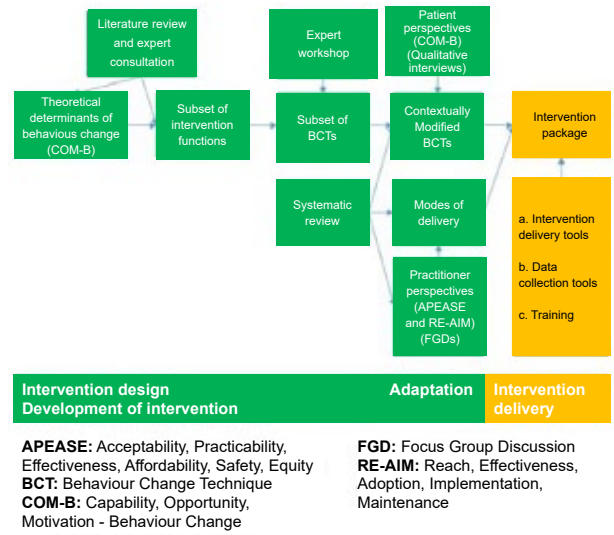
ORAL ABSTRACT SESSION (OA)

OA-25-C13 Smoking cessation: from research to implementation

OA-25-466-02 Developing a smoking cessation intervention in a rural healthcare setting in South India using the Behaviour Change Wheel

A Srinivasaiyer,[1,2] K Bissell,[3] S Mysore,[2] C Prasad,[2] C Bullen,[1] [1]The University of Auckland, National Institute for Health Innovation, Auckland, New Zealand, [2]Swami Vivekananda Youth Movement, Medical Specialties, Saragur, India, [3]The University of Auckland, School of Population Health, Auckland, New Zealand.
e-mail: ananthkumarsriyer@gmail.com

Background: Cognisant of the multidimensional drivers of smoking behaviour, we used Michie's Behaviour Change Wheel (BCW) framework to design a smoking cessation intervention in a rural healthcare setting in India, one that would not only address the local context and interplay of factors at various levels, and inform evaluation, but also provide for scale-up across different settings.
Methods: The smoking cessation intervention was developed in two phases using the BCW framework. Phase one: Identifying key target behaviours and their determinants, and mapping behavioural change techniques (BCT) through iterative consultations and a workshop with experts: Phase two: Contextual adaptation of the selected BCTs and implementation strategies through qualitative interviews and focus group discussions with smokers and the healthcare team implementing the intervention: Data were analysed thematically with reference to the COM-B (Capability-Opportunity-Motivation-Behaviour Change) model and RE-AIM framework. The intervention was adapted to the local context.
Results: The target behaviour was 'smokers quit smoking at all places and at all times'. Key barriers to quitting were: lack of knowledge about the consequences of smoking; peer pressure; easy availability of bidi/cigarettes; and absence of public stigma for smoking. The key enabler was perceived concern about negative consequences of smoking on the family. We selected 26 BCTs and developed a behavioural support resource for lay counsellors. The BCW-based smoking cessation intervention was highly acceptable to users and healthcare team. The key modes of delivery identified were physician-led hospital-based identification and brief advice, lay counsellor-led cessation support and health worker-led home-based follow-up.
Conclusions: Contextual adaptation of the BCW framework provides an acceptable and practical approach to developing a smoking cessation intervention in a rural Indian context.



[Development of the Smoking Cessation Intervention]

OA-25-467-02 Tobacco cessation training for counsellors through "hybrid learning through technology": a pilot project in collaboration with NIMHANS, Bangalore

Prabhakara,[1,2] P Chand,[2] M Selvarjan,[3] S Deshpandey,[3] [1]State Tobacco Control Cell, Department of Health and Family Welfare, Government of Karnataka, Bengaluru, India, [2]NIMHANS, Psychiatry, Bengaluru, India, [3]State Tobacco Control Cell, Department of Health and Family Welfare, Bengaluru, India.
e-mail: biprabhakar.kar@gmail.com

Background and challenges to implementation: One of the key areas of the NTCP is to establish tobacco cessation clinics and train health personnel to identify tobacco users and help them to quit. At the district level implementation has been subsumed under the overarching umbrella of the National Health Mission to bring in synergy at different levels of health care delivery. The lack of trained and skilled health care professionals in tobacco cessation has been a significant problem in its effective implementation. With this background, State Tobacco Control Cell in collaboration with NIMHANS, Bengaluru conducted online training program for TCC counsellors under NTCP.

Intervention or response: Participants were also offered a digitally enabled course on tobacco cessation which to be delivered remotely through contemporary technology. Although it was optional, all the counsellors consented and the mobile application were installed on their smart phones through google play store. Two of them who did not have a smart phone were advised to connect through the toll-free phone number.
Results and lessons learnt: All the counsellors were able to virtually join the Tobacco Cessation Centre, NIMHANS Hub for at least one clinic. More than half participated in five of the six tele-clinics. 62.96% (n=17) of the counsellors presented 25 patient case summaries and consulted with the NIMHANS Tobacco Cessation Centre experts. 21 counsellors (77.78%) completed three e-learning assignments on their smartphones. Majority of participants (80%) used smartphone with 4G connections to join the tele ECHO clinics.
Conclusions and key recommendations: It has been feasible to connect an academic hub i.e. TCC NIMHANS to the counsellors of 16 remote districts of Karnataka and conduct multipoint videoconference based tele ECHO clinics. The learners are comfortable in adapting new technology based learning as evidenced by higher rate of e-learning completion. These findings suggest this new innovative learning model using technology can be an important way for effective training.

OA-25-468-02 Smoking cessation interventions in low- and middle-income countries: a systematic review

A Srinivasaiyer,[1,2] K Bissell,[3] S Mysore,[2] C Prasad,[2] C Bullen,[1] [1]The University of Auckland, National Institute for Health Innovation, Auckland, New Zealand, [2]Swami Vivekananda Youth Movement, Medical Specialties, Saragur, India, [3]The University of Auckland, School of Population Health, Auckland, New Zealand.
e-mail: ananthkumarsriyer@gmail.com

Background: Eighty percent of the world's 1.1 billion smokers live in low- and middle-income countries (LMICs). Smoking cessation is vital to reducing tobacco related morbidity and mortality. However, most smoking cessation research occurs in high-income countries and its applicability to LMICs is unclear. This systematic review aimed to synthesise evidence on delivery strategies and outcomes of smoking cessation interventions undertaken in LMICs.
Methods: We included studies in healthcare or community settings with or without a control group and quit rate outcomes reported at least six months from the start of the intervention. Search terms were tobacco, smoking, cessation, intervention and trial. We searched studies between 2000-2018 in the Cochrane CENTRAL database, Medline Ovid, EMBASE, and PsychINFO, in the reference list of included studies and consulted experts in tobacco addiction research.
Results: Of the 6,379 identified studies, only 34 met our criteria: 26 (76%) studies involved smoking cessation intervention in a hospital setting; 3 in a community setting and 5 involved cessation as part of a multi-component lifestyle management intervention. Nine studies (26.5%) included pharmacotherapy and behavioural support; 25 (73.5%) involved behavioural support alone. Smokers were recruited through out-patient screening, local organisations, mass media and community-based screening.
Major intervention strategies included: cessation support by physicians and health workers; community-based group support; cessation support in TB or diabetes clinics; and cessation support as part of a lifestyle intervention. Quit rates ranged from 2.6%- 77.5% and were highest in studies in specialised clinics and lowest among multicomponent lifestyle interventions.
Conclusions: Integrating smoking cessation into existing specialised clinics yields best cessation outcomes but reaches few people. Integration of cessation support into healthcare systems in LMICs appears feasible but outcomes vary depending on the strategy used. The paucity of studies in LMICs and inconclusive evidence regarding the addition of pharmacotherapy warrants further research.

OA-25-470-02 The challenge of e-cigarettes in Latin America and the Caribbean

N Parra,[1] A Bacelar Gomes,[1] R Sandoval,[1] [1]PAHO, NMH, Washington, United States of America.
e-mail: parranat@paho.org

Background: Cigarette smoking is decreasing worldwide; a public health gain that could be jeopardized by an increasing consumption of electronic cigarettes. Different approaches for the regulation of e-cig have been documented globally. This study aims to present the current situation of e-cig use among youth in Latin America and the Caribbean (LAC) in the context of existing regulations.
Methods: This is a descriptive study of the use of e-cig using data from latest Global Youth Tobacco Survey and a survey of the regulatory approaches used for their control.
Results: The cigarette smoking prevalence among countries within the Region varies from 1.4% in Antigua and Barbuda to 19.6% in Argentina. Although cigarettes are the most consumed tobacco product, six out of 18 countries that have e-cig data for youth, presented higher prevalence rates of e-cig use than cigarettes smoking.
In Trinidad and Tobago, the prevalence of e-cig use is 2.5 times higher than cigarette smoking. As of 2018, 16 of the 33 LAC countries regulate e-cigarette use, including 7 countries with comprehensive bans on their commercialization. In the remaining 17 countries no regulations were identified.

Conclusions: Although there is no available data on e-cig consumption for a trend analysis, it is clear that in several countries these products are being consumed by young people to the same extent as cigarettes. This, in a regional context where the national regulatory approaches vary greatly.
Strengthening the monitoring of the use of these products and implementing effective regulations for their control poses a challenge for tobacco control in the region, that compounds the need to address the pending gaps regarding traditional tobacco product regulation and counteracting the interference of the tobacco industry.

OA-25-471-02 Effectiveness of behavioural counselling in smokeless tobacco cessation among adult users reporting to a dental hospital: a randomised controlled trial

A Kumbhalwar,[1] S Hegde-Shetiya,[2] P Kakodkar,[2] H Gupte,[3] [1]Dr. D. Y Patil Dental College and Hospitial, D Y Patil Vidyapeeth, Department of Public Health Dentistry, Pune, India, [2]Dr. D.Y. Patil Dental College and Hospital, Dr. DY Patil Vidyapeeth, Department of Public Health Dentistry, Pune, India, [3]Narotam Sekhsaria Foundation, Health Vertical, Mumbai, India. e-mail: sahana.hegde@dpu.edu.in

Background: Smokeless tobacco (SLT), by definition, is a tobacco that is consumed in un burnt form, either orally or nasally, and is commonly known as chewing tobacco, oral tobacco, spit or spitting tobacco, dip, chew or snuff**.** To assess the effectiveness of behavioral counseling for smokeless tobacco cessation among adult users in Dental Hospital setting.
Methods: Patients visiting Dental College and Hospital in Maharashtra for oral health check-up and who were exclusively using SLT were enrolled for the study. Randomized controlled trial with concurrent parallel study design which consisted of two arms was conducted.
A total 200 participants were randomly allocated. Fagerstrom Test for Nicotine Dependence level and transtheoretical stage of change was assessed at the baseline. The behavioral cessation counseling and motivational interviewing was provided in study arm and brief advice to those in control arm.
The counseling was provided at baseline, and followed up through telephone to assess the change in the frequency of use of smokeless tobacco products and abstinence of the participants from SLT use. Bio-chemical validation with urine cotinine test was done to confirm abstinence. Non- parametric tests were applied to test the hypothesis.
Results: 200 self-employed males in the age group of 28-37 years most were in pre-contemplation stage and were on low dependency level. At six months from enrolment, frequency of consumption within and between the two groups significantly showed a difference as there was reduction in consumption.24.4% participants in the study group and 10% in the control group abstained from the habit at the 6th month with the loss to follow up of 10% in each of the groups.
Conclusions: The behavioral intervention with motivational interviewing considered as effective method in promoting smokeless tobacco cessation among adults.

OA-25-472-02 Regulatory approaches to protect bystanders from passive exposure to aerosol of E-cigarettes in European countries

B Amalia,[1,2,3] M Fu,[1,2,3] E Fernández,[1,2,3] [1]Institut d'Investigació Biomèdica de Bellvitge-IDIBELL, Tobacco Control Unit, Barcelona, Spain, [2]Institut Català d'Oncologia (ICO) - WHO Collaborating Centre for Tobacco Control, Tobacco Control Unit, Barcelona, Spain, [3]University of Barcelona, School of Medicine and Health Sciences, Barcelona, Spain. e-mail: bamalia@idibell.cat

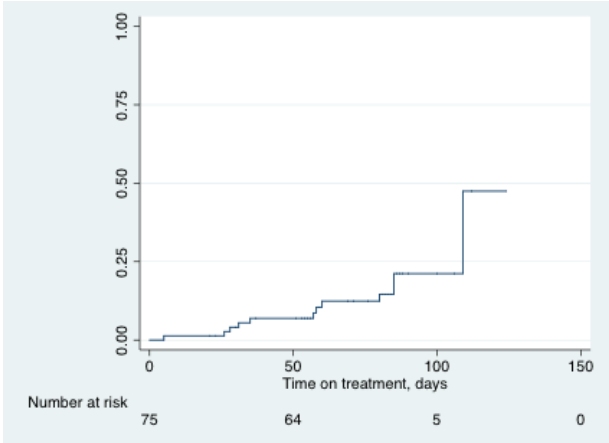
Background: Little is known about exposure to secondhand aerosols from electronic cigarettes (e-cigarettes). This study describes policies regulating the use of e-cigarettes in public and private places among countries within World Health Organisation (WHO) European Region, to identify barriers and promoters for adopting the regulation, and to evaluate their compliance with the WHO Framework Convention on Tobacco Control.
Methods: An online survey was conducted among in-country experts from 53 countries of WHO European Region during May-July 2018. The survey collected data on national and sub-national policies regulating e-cigarette use in 27 public and private sites, level of difficulties in adopting the regulation, as well as support and compliance with the regulations. Proportion (%) of each measure across groups of countries was estimated. Factors associated with the regulation adoption were identified with Poisson and linear regression analyses.
Results: Responses from 48 out of 53 countries were collected. Among them, 58.3% had legislation on e-cigarette use at national level, and 10.4% at sub-national level. Twenty-one out of 27 sites were regulated. Only 1/3 of countries adhered to the WHO FCTC recommendation. Regulations were more frequent among European Union (EU) countries. Education facilities were the most regulated sites (58.3% countries), while private areas (homes, cars) were the least regulated ones (39.6%). Difficulties and support in adopting the national legislations, as well as compliance with regulation, were all in moderate levels. Country's smoking prevalence, and income level were all plausibly linked with the number of sites regulated by country´s policy.
Conclusions: Although most WHO European Region countries had introduced national regulation for e-cigarette use in public places, many countries still lack rules to protect bystanders in indoor settings. Efforts should be made to overcome barriers in passing nation-wide e-cigarette use legislation.

OA-26-C3 Safety of DR-TB treatment: part 1

OA-26-473-02 Risk factors for hypothyroidism including ethionamide exposure in patients on treatment for multidrug-resistant tuberculosis

R Court,[1] MT Chirehwa,[1] L Wiesner,[1] N de Vries,[2] J Harding,[3] T Gumbo,[4] G Maartens,[1] H McIlleron,[1]
[1]University of Cape Town, Division of Clinical Pharmacology, Cape Town, South Africa, [2]Brooklyn Chest Hospital, Department of Medicine, Cape Town, South Africa, [3]DP Marais Hospital, Department of Medicine, Cape Town, South Africa, [4]Baylor Research Institute, Center for Infectious Diseases Research and Experimental Therapeutics, Dallas, TX, United States of America.
e-mail: richard.court@uct.ac.za

Background: Hypothyroidism is reported to occur in up to 69% of patients treated for multidrug-resistant tuberculosis (MDR-TB). However, there are limited prospective data in sufficiently powered cohorts describing the incidence of and risk factors for hypothyroidism in patients on MDR-TB treatment.
Methods: We recruited participants on therapy for MDR-TB between July 2015 and September 2017 from two TB hospitals in Cape Town. At the time of the study, the standard treatment regimen included pyrazinamide, moxifloxacin, kanamycin, terizidone, ethambutol, and ethionamide/isoniazid. Para-aminosalicylic acid (PAS) was used infrequently as a substitute drug. Thyroid stimulating hormone (TSH) was measured at baseline and at 4,8 and 12 weeks after treatment initiation. Subclinical hypothyroidism was defined as a TSH above the upper limit of normal (>5.33 mIU/L), and overt hypothyroidism as a TSH>10 mIU/L.
We measured ethionamide plasma concentrations predose and at 2,4,6,8 and 10 hours post-dose using liquid chromatography mass spectrometry. Using Cox proportional hazard modelling, we explored whether the following variables were associated with subclinical hypothyroidism: sex, HIV status, age, prior MDR-TB treatment and ethionamide area under the concentration-time curve ($AUC_{0\text{-}10}$).
Results: We recruited 148 participants, 130 of whom had data available for analysis. Median age was 34.9 years, 81 (62.3%) were HIV-positive, 78 were men and 24 (18.5%) had been treated for MDR-TB previously.
The ethionamide median peak concentration (C_{max}) and $AUC_{0\text{-}10}$ was 3.7 (range: 1.3 to 7.5) μg/mL and 17.4 (range: 6.2 to 49.7,) μg*h/mL respectively.
Seventeen (13.1%) participants developed subclinical hypothyroidism, and two (1.5%) developed overt hypothyroidism. On univariate and multivariate regression, none of the factors we explored were associated with the development of subclinical hypothyroidism.
Conclusions: We describe a lower prevalence of hypothyroidism in patients treated for MDR-TB than previously reported, possibly due to most treatment regimens including ethionamide without PAS. Ethionamide exposure was not associated with the development of hypothyroidism.



[Time to subclinical hypothyroidism in patients on treatment for multidrug-resistant tuberculosis]

OA-26-474-02 Using innovative technology for monitoring drug adverse events: a case of smartphone-based apps for hearing assessments among MDR-TB patients

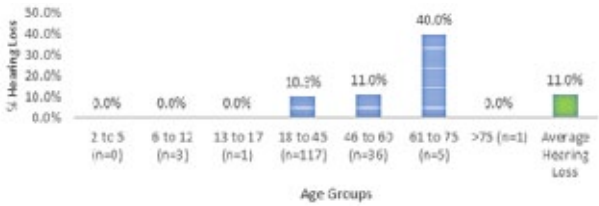
JP Otuba,[1] S Zawedde-Muyanja,[2] K Mutesasira,[1] N Kirirabwa,[1] S Turyahabwe,[3] S Adakun,[4] J Likichoru,[4] A Nkolo,[1] [1]University Research Co., LLC, Technical, Kampala, Uganda, [2]Infectious Diseases Institute - College of Health Sciences, Makerere University, OR, Kampala, Uganda, [3]Ministry of Health, NTLP, Kampala, Uganda, [4]Mulago National Referral Hospital, Internal Medicine, Kampala, Uganda. e-mail: jotuba@urc-chs.com

Background and challenges to implementation: Multidrug resistant tuberculosis (MDR-TB) is an emerging public health concern in Uganda. Due to limited options, treatment of MDR-TB involves use of injectable drugs (Kanamycin) associated with hearing impairment. Monitoring for hearing loss using conventional audiometers requires sound proof rooms and specialized training, limiting its applicability in low-resource settings.
The USAID Defeat TB project, a five-year technical assistance mechanism to the Uganda National TB and Leprosy Program (NTLP) procured and piloted smartphone-based app (Shoebox®) for monitoring hearing loss.
Intervention or response: We piloted the smartphone-based (Shoebox®) technology at the National Referral Hospital and conducted outreaches using the app at Regional Referral Hospitals. Pure tone audiometry (PTA) was conducted from 30th April 2018 to 30th March 2019, using Shoebox®, a clinically validated, automated

audiometer optimized for use without a sound booth. During MDR TB review clinics, trained staff conducted baseline and monthly hearing assessments for patients on injectable drugs.

Shoebox® data was uploaded onto a cloud-based portal to centralize access, management and analysis. Hearing loss was classified using Brocks classification and the Common Terminology Criteria for Adverse Events (CTCAE) with a bilateral PTA > 25 Db HL. All patients that developed hearing loss had Kanamycin dose reduction or substitution with Amikacin, Capreomycin or Bedaquiline.

Results and lessons learnt: Of 164 patients that had a hearing assessment using Shoebox®, 73 (44.5%) were female, 18 (11%) patients developed hearing loss *(figure 1)* over the 11-months period. Ability to conduct assessments without a sound booth enabled bedside evaluations and access among patients in remote areas during outreaches. Remote data access by hearing specialists enabled audiogram review and virtual support for patient management decision.



[Figure 1: Burden of hearing loss among patients tested with Shoebox®]

Conclusions and key recommendations: Smartphone-based apps can be effectively used for screening for drug-induced hearing loss in Uganda. This technology is scalable to peripherally located MDR-TB centers to optimize early detection and prevention of disabling hearing loss.

OA-26-475-02 Compassionate use of delamanid-based regimens in adults and children (≥ 6 years) for drug-resistant TB: a five-year update

S Ghosh,[1] J Hafkin,[2] N Hittel,[3] A Martin,[4] M Destito,[5] M Kawasaki,[6] [1]Otsuka Novel Products GmbH, Clinical, Munich, Germany, [2]Otsuka Pharmaceutical Development & Commercialization, Global Clinical Development, Princeton, NJ, United States of America, [3]Otsuka Novel Products GmbH, TB Global, Munich, Germany, [4]Otsuka Novel Products GmbH, International Medical and Clinical Operations, Munich, Germany, [5]Otsuka Novel Products GmbH, Public Affairs and Global Alliance Management, Munich, Germany, [6]Otsuka Pharmaceutical Co., Ltd., Anti-Tuberculosis Project, Tokyo, Japan.
e-mail: sghosh@otsuka-onpg.com

Background: The Otsuka-led Compassionate Use (CU) program was initiated in 2014 to provide delamanid access to MDR-TB patients with limited treatment options. The safety and preliminary efficacy results of patients enrolled since 01 Feb 2014 until 28 Feb 2019 are presented here.

Methods: MDR-TB patients aged ≥6 years with weight >20 kg were enrolled. Delamanid was administered 100 mg BID for patients with weight ≥35 kg or 50 mg BID for patients weighing between 20-35 kg, as part of an appropriate combination regimen for 24 weeks.

Results: 199 patients were enrolled and started on a delamanid-based regimen. The average age at treatment initiation was 35 years and 38% (76/199) of patients were female. 31/199 (16%) were children and 9/31 (29%) of them received delamanid 50 mg BID. 122/199 (61%) of patients had XDR-TB, 66/199 (33%) were HIV co-infected with an average CD4 count of 289, and 105/199 (53%) received delamanid in combination with bedaquiline. As of 28 Feb 2019, 155/199 (78%) of patients completed a 24-week treatment course of delamanid.

78% (121/155) of patients were culture positive prior to delamanid initiation; of these 96/121 (79%) achieved culture negativity by the end of delamanid treatment. 89% (16/18) of paediatric patients; 77% (60/78) of patients with XDR-TB; and 91% (39/43) of patients with HIV co-infection achieved a negative 24-week culture status.

The most commonly reported AEs were nausea, vomiting, and QTcF interval prolongation. 156 serious adverse events (SAEs) were reported in 55/199 patients, including 18 deaths. 34% of SAEs were reported as related to delamanid. Among paediatric age group, 8 SAEs were reported in 3 patients, of which 5 SAEs in one patient were attributed to delamanid. No children died during delamanid treatment.

Conclusions: Overall, delamanid-based regimens were efficacious and well tolerated in adults and children enrolled in the CU program.

OA-26-476-02 Drug-induced hypothyroidism: magnitude and patient characteristics among MDR-TB cohorts in Uganda

JP Otuba,[1] S Zawedde-Muyanja,[2] K Mutesasira,[1] N Kirirabwa,[1] S Turyahabwe,[3] A Nkolo,[1] [1]University Research Co., LLC, Technical, Kampala, Uganda, [2]Infectious Diseases Institute, College of Health Sciences, Makerere University, OR, Kampala, Uganda, [3]Ministry of Health, NTLP, Kampala, Uganda. e-mail: jotuba@urc-chs.com

Background: Drug-induced hypothyroidism is a rare adverse event caused by Multi-drug resistant tuberculosis (MDR-TB) treatment using ethionamide. Evaluation of thyroid function at public health facilities in Uganda is not conducted due to health system limitations. The burden of hypothyroidism among MDR-TB patients is unknown. The objective of the study was to determine the prevalence of hypothyroidism among MDR-TB patients at seven hospitals.

Methods: Retrospective review of 165 patient records on treatment with an ethionamide based regimen. 154 patients were exposed to thyroid stimulating hormone (TSH) test between 1st March and 31st October 2018. TSH immunoassays were conducted at a private laboratory. Limits of detection of the test were: 0.005 to 1,000 μIU/Ml with normal range being 0.27 to 4.2 μIU/mL. Clinical hypothyroidism was defined as at least one TSH result of > 10μIU/mL Thyroxin therapy and withdrawal or dose reduction of ethionamide was instituted for patients with hypothyroidism. Chi square test was used to determine factors associated with hypothyroidism.

Results: Of 154 patients, 54 (35.1%) were female, median age was 35 (IQR 2-76) years. The median TSH level was 3.2 (0.5 - 255) μIU/mL 63 (41%) patients had elevated TSH levels (> 4.1 μIU/mL) and 27 (17.5%) confirmed with clinical hypothyroidism.

Of 27 patients with clinical hypothyroidism, 4 (14.4%) were female, median age 41 (IQR 7-64) years, median TSH level 17 (10.25-255) μIU/mL. 10 (37%) patients were from one hospital (Fort portal). 13 (48%) patients were MDR-TB/HIV co-infected, all on ART. 12 (92.3%) patients were on a TDF/3TC/EFV based regimen. Males had a greater likelihood to develop hypothyroidism (OR 3.7, 95% CI, p=0.03) as shown in table 1 below.

Variable	Odds Ratio	Confidence Interval	P-value
HIV+	1.22	0.5-2.7	1.81
Male	3.7	1.2-11.4	0.03
Age (≥ 35 years)	1.84	0.7-4.4	0.24

[Table 1: Other factors associated with Hypothyroidism]

Conclusions: Nearly one-fifth of MDR-TB patients receiving ethionamide in Uganda have hypothyroidism. TSH screening is critical for timely detection of hypothyroidism, thyroxin replacement and ethionamide withdrawal or substitution.

OA-26-477-02 Bedaquiline use and QT interval prolongation: an analysis from drug-resistant tuberculosis cohorts in Chechnya and Uzbekistan

J Achar,[1] P du Cros,[2] M Tillyashaykhov,[3] N Parpieva,[4] Z Khaidarkhanova,[5] A Sinha,[6] J Singh,[7] K Wing,[8] [1]MSF UK, Manson Unit, London, United Kingdom, [2]Burnet Institute, TB Elimination and Implementation Science, Melbourne, VIC, Australia, [3]Ministry of Health, Ministry of Health, Tashkent, Uzbekistan, [4]Ministry of Health, Tuberculosis Institute, Tashkent, Uzbekistan, [5]Ministry of Health, Republican TB Dispensary, Grozny, Russian Federation, [6]Médecins Sans Frontières, Operational Centre Amsterdam, Minsk, Belarus, [7]Médecins Sans Frontières, Operational Centre Amsterdam, Tashkent, Uzbekistan, [8]London School of Hygiene and Tropical Medicine, Faculty of Epidemiology and Population Health, London, United Kingdom. e-mail: jay.achar@london.msf.org

Background: Clinical studies have suggested an association between bedaquiline (Bdq) and QT interval prolongation. QT prolongation greater than 500ms or 60ms above baseline are risk factors for life-threatening cardiac arrhythmias. This study combines programmatic and research datasets from Uzbekistan and the Russian Federation to investigate the association between Bdq use in the treatment of drug-resistant tuberculosis (DR-TB) and change in QT interval.

Methods: We conducted a historical cohort study using descriptive, classical and regressions methods to compare the change in Fridericia-adjusted QT interval (QTcF) after 30 (+/- 3) days of treatment between patients receiving and those not receiving bedaquiline as part of their DR-TB regimen. Adults receiving treatment requiring routine ECG monitoring were included. Those without available ECG data at baseline and after 30 days were excluded.

Results: Of 619 eligible patients, 255 (45%) had sufficient ECG data to be included. Mean QTcF change amongst those exposed to bedaquiline was 14.7ms (95% CI 8.4 - 30.0, $p < 0.001$) and 20.1ms (95% CI 14.6 - 25.7, $p < 0.001$) amongst those unexposed. After adjusting for age, gender and baseline QTcF, no association between bedaquiline exposure and QTcF change was detected (-1.0ms, 95% CI -7.7 - 5.5, $p = 0.76$). No patients ceased treatment due to QTcF prolongation or developed Grade 4 QTcF changes. Grade 3 QTcF changes were seen in 10% of patients, 12% amongst those receiving bedaquiline and 8% amongst those unexposed. Restriction to patients receiving moxifloxacin and clofazimine detected no association between bedaquiline exposure and QTcF change (1.0ms, 95% CI -6.3 - 8.2, $p = 0.79$).

Conclusions: Our results do not support the hypothesis that addition of bedaquiline to treatment regimens for DR-TB is associated with increases in QTcF change after 30 days of treatment.

OA-26-478-02 QT prolongation in patients treated for MDR-TB with bedaquiline in Lima, Peru

I Carpio,[1] L Lecca,[2] E Osso,[3] C Flanagan,[4] M Franke,[3] S Atwood,[3] C Mitnick,[3] [1]Socios En Salud Sucursal Peru, TBC, Lima, Peru, [2]Socios En Salud Sucursal Peru, Managing Director, Lima, Peru, [3]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [4]Partners in Health, Partners In Health, Boston, MA, United States of America.
e-mail: icarpio_ses@pih.org

Background: Since 2015, Partners In Health and the Peru Ministry of Health have been implementing the endTB Observational Study throughout Lima, Peru. endTB treats multidrug-resistant tuberculosis (MDR-TB) patients with bedaquiline-containing regimensunder programmatic conditions. The endTB study is generating important data on adverse events related to these treatment regimens, including on QT interval prolongation, an adverse event of particular clinical interest. The endTB Clinical Guide suggests patients receiving QT-prolonging drugs undergo monthly ECG monitoring. This study will review the frequency of QTcF prolongation adverse events in this endTB cohort in Peru.
Methods: We describe all cases of clinically relevant QTcF prolongation, defined as QTcF > 500ms, in patients receiving bedaquiline as part of their MDR-TB regimen through the endTB Observational Study.
Results: 112 MDR-TB patients initiated bdq-containing regimens between February 2016 and June 2017 and have been followed to date. 67% of cases were male. Median age was 34.3 years (IQR 25-40.2). 50.8% had an XDR resistance profile at baseline, 40.1% had pre-XDR. 93.7% had been previously treated with second-line drugs. At baseline, 15.1% had low BMI and 11.6% had diabetes. Not a single adverse event of QT prolongation was reportedin this population during the study period.
Conclusions: The study of this 112-patient cohort suggests no evidence of QT prolongation in patients receiving bedaquiline as part of their MDR-TB treatment regimen.

OA-26-479-02 Proof of concept: integrated tablet-based hearing and ECG testing for Mozambican patients with drug-resistant TB

I Manhiça,[1] C Mutaquiha,[1] P Zindoga,[1] MJ Pires Machai,[2] N Cumbi,[3] M Arago Galindo,[3] J Creswell,[4] ZZ Qin,[4] R Chiau,[5] J Cowan,[5,6] [1]Mozambique Ministry of Health, National TB Program, Maputo, Mozambique, [2]FHI 360, Challenge TB, Maputo, Mozambique, [3]MSF, TB, Maputo, Mozambique, [4]Stop TB Partnership, TB REACH, Geneva, Switzerland, [5]Health Alliance International, TB, Maputo, Mozambique, [6]University of Washington, Department of Global Health, Seattle, WA, United States of America. e-mail: ivanmca2004@yahoo.com.br

Background and challenges to implementation: Mozambique has one of the highest rates of both TB (551 cases per 100,000) and MDR-TB (8,800 cases annually) in 2017 per WHO estimates. The implementation and scale-up of short-treatment regimens, bedaquiline (BDQ) and delamanid (DLM) as therapies for DR-TB in low and middle-income countries is limited by the lack of affordable, simple, internet-enabled drug toxicity monitoring platforms such as ECG and audiology testing. As a result, patients with DR-TB experience preventable serious adverse drug events.
Intervention or response: With support from TB REACH, HAI, MSF and FHI360/Challenge TB the Mozambican National TB Program (NTP) procured and began piloting 53 SHOEBOX enabled tablets (audiometers for hearing screening) and 24 SmartHeart Pro ECGs. These were distributed to health facilities across all provinces in Mozambique starting in July 2018.
Results and lessons learnt: In the first 9 months more than 802 SHOEBOX audiology tests and 148 SmartHeart Pro ECG tests have been performed. However, twenty-four SHOEBOX systems have performed less than 5 tests during this time, whereas others have run more than 90 tests showing the variable uptake by facility. During this time abnormal audiology results were noted in over 59 patients resulting in discontinuation of an injectable aminoglycoside and replacement usually with BDQ or in some cases DLM. Only one patient was noted to have a QTcF longer than 450 msec with a SmartHeart Pro ECG. Challenges included securing reliable 3G data SIM cards, ensuring that devices got to final destinations, and uptake of testing at some facilities.
Conclusions and key recommendations: This project demonstrated that tablet-based audiology and ECG testing is possible for MDR-TB patients in Mozambique, and that SHOEBOX audiology testing in particular identified patients that can benefit from individualized regimens. With recent WHO recommendations to deprioritize injectable aminoglycosides audiology testing for MDR-TB patients may become less relevant. A more formal validation study and impact evaluation is ongoing.

OA-26-480-02 Effect of bedaquiline and concurrent lopinavir-ritonavir or clofazimine on QTcF prolongation

J Brust,[1] S Wasserman,[2] N Gandhi,[3] G Maartens,[4] C Viljoen,[5] A Campbell,[6] P Harrington,[6] C Zhang,[7] G Meintjes,[8] The PROBeX Study Team [1]Albert Einstein College of Medicine, Divisions of General Internal Medicine & Infectious Diseases, Bronx, NY, United States of America, [2]University of Cape Town, Wellcome Centre for Infectious Diseases Research in Africa, Cape Town, South Africa, [3]Rollins School of Public Health, Emory University, Departments of Epidemiology, Global Health & Infectious Diseases, Atlanta, GA, United States of America, [4]University of Cape Town, Division of Clinical Pharmacology, Cape Town, South Africa, [5]University of Cape Town, Division of Cardiology, Cape Town, South Africa, [6]Rollins School of Public Health, Emory University, Department of Epidemiology, Atlanta, GA, United States of America, [7]Albert Einstein College of Medicine, Division of General Internal Medicine, Bronx, NY, United States of America, [8]University of Cape Town, Institute of Infectious Disease and Molecular Medicine, Cape Town, South Africa. e-mail: sean.wasserman@gmail.com

Background: Drug-induced prolongation of the QT-interval increases the risk of ventricular arrhythmia and sudden cardiac death. Bedaquiline and clofazimine both prolong the QT-interval, but the effect of concurrent lopinavir-ritonavir, which increases plasma bedaquiline concentrations twofold, has not been examined.
Methods: We enrolled participants with MDR- or XDR-TB with or without HIV who were receiving a bedaquiline-containing regimen into a prospective, observational cohort study in South Africa. Standardized TB and antiretroviral treatment regimens were chosen by clinic providers. ECGs were performed in triplicate, 5 minutes apart, prior to initiation of bedaquiline and again at Months 1, 2, and 6. QT-intervals were measured by a single cardiologist and corrected using Fridericia's formula (QTcF). Mean QTcF intervals were calculated at each study visit. Differences were compared using t-tests.
Results: Of the 196 participants included in this analysis, 112 (57%) participants were female and the median age was 33 (IQR 27-49) years. 124 (63%) participants were HIV-infected. 182 (93%) participants received concurrent clofazimine and 15 (12% of HIV-infected participants) received lopinavir-ritonavir. The mean QTcF at baseline was 404.8ms. Mean QTcF at M1, M2, and M6 were 419.0, 420.8 and 426.6ms, respectively. Mean maximum QTcF for all participants was 432.1ms and the median time to maximum QTcF was 58.5 days (IQR 28-168). Among participants receiving clofazimine, the mean maximum QTcF was 432.4ms, compared with 427.9ms in those not receiving clofazimine (p=0.55). Among participants receiving concurrent lopinavir-ritonavir, the mean maximum QTcF was 436.1ms, compared with 431.8ms in those not receiving lopinavir-ritonavir (p=0.52). Mean increase in QTcF from baseline to Month 6 was 23.1ms and did not differ based on receipt of concurrent clofazimine or lopinavir-ritonavir. Four (2%) participants experienced a QTcF >500ms at any time point. All four received concurrent clofazimine and one received lopinavir-ritonavir.
Conclusions: When given with concurrent clofazimine and/or lopinavir-ritonavir, bedaquiline rarely prolongs the QTcF interval >500ms.

	Baseline QTcF, mean (SD)	Month 1, mean (SD)	Month 2, mean (SD)	Month 6, mean (SD)	Maximum QTcF, mean (SD)
All participants	404.8 (21.8)	419.0 (25.1)	420.8 (24.9)	426.6 (22.3)	432.1 (25.0)
Received clofazimine	404.8 (21.9)	418.7 (25.5)	420.6 (25.2)	426.7 (22.4)	432.4 (25.5)
Did not receive clofazimine	404.5 (19.7)	424.3 (16.6)	427.9 (9.8)	427.0 (16.9)	427.9 (15.9)
Received lopinavir-ritonavir	407.7 (16.7)	420.5 (31.7)	409.8 (14.8)	433.0 (18.1)	436.1 (25.0)
Did not receive lopinavir-ritonavir	404.5 (22.1)	418.9 (24.7)	421.6 (25.3)	426.0 (22.6)	431.8 (25.1)

[Mean QTcF interval at each study visit (milliseconds)]

OA-27-C2 Engaging the private sector in TB care

OA-27-481-02 What happens to TB patients notified from private sector in rural and urban settings? study from Maharashtra, India

S Suryawanshi,[1] H Shewade,[2] R Ramchandran,[1] S Mase,[1] S Kamble,[3] V Khatgaonkar,[4] K Rade,[1] P Malik,[1] P Jogewar,[3] [1]WHO Country Office, TB, Delhi, India, [2]Centre for Operational Research, International Union Against Tuberculosis and Lung Disease (The Union), TB, Delhi, India, [3]Directorate of Health Services, Maharashtra, TB, Pune, India, [4]Directorate of Health Services, Maharashtra, TB, Aurangabad, India. e-mail: suryawanshis@rntcp.org

Background: India accounts for more than 27 % of the global TB burden and 'missing' cases who remain undiagnosed or inadequately diagnosed in the private sector pose a big problem. The Government of India issued a Gazette requiring TB notification (2012) and since that time private sector notifications have increased. Home visits including screening of households and reporting interim/final treatment outcomes occur for patients notified from the public sector, however, little is known about patients notified from private sector.
Methods: This is a descriptive study conducted in seven districts of Maharashtra, India. TB patients notified by private facilities from Jan-March 2018 were interviewed three months after notification by trained staff using a

standard questionnaire and end of treatment outcomes were tracked. Data analysis was performed using Microsoft Excel.
Results: Of 395 TB patients notified by the private sector, 268 (68%) were males and 353 (89%) had pulmonary TB. Chest radiograph was used in 340 (86%) patients, 45 (11%) underwent smear microscopy, 4 (1%) histopathology, 3 (1 %) USG and 3 (1%) Xpert MTB/RIF assay. Levofloxacin, Ethionamide, Ofloxacin were commonly prescribed with first line anti-TB drugs. Only 79 (20%) people had a home visit by programme staff. At end of treatment, 228 (58%) completed treatment, 7 (2%) cured, 6 (2%) died, 1 (0.25%) failed, 51 (13%) lost to follow up, 12 (3 %) transferred out, 2 (1 %) misdiagnosed (cancer/no TB), 19 (5%) changed to public, 39 (10 %) still on private treatment, 30 (8 %) data was not available.
Conclusions: Unfavorable treatment outcomes were high. Quality diagnosis with microbiological confirmation, appropriate treatment and ongoing monitoring is lacking in the private sector. Better linkages between the public and private sector are required to ensure relapse free treatment for private sector.

OA-27-482-02 Comprehensive public-private patient management system for tuberculosis in India; enhancing the surveillance tool Nikshay 2.0

J Jaju,[1] M Mathews,[1] B Vadera,[1] S Achanta,[1] A Cross,[2] N Gupta,[2] R Rao,[3] KS Sachdeva,[3] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]Everwell Health Solutions Pvt. Ltd, Nikshay ICT Cell Bangalore, Bengaluru, India, [3]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India.
e-mail: jajuj@rntcp.org

Background: Notification of Tuberculosis by all health care providers, both public and private was made mandatory, through the Gazette of India, published on 19th of March 2018. 'Nikshay', the web-based case-based surveillance tool of 2012 was designed to facilitate the National TB Control Programme (RNTCP) to notify and manage patients diagnosed by public healthcare providers (PuHP) only. To address the need of case management by private healthcare providers as well, a comprehensive surveillance tool was devised in Nikshay 2.0.
Methods: The Nikshay 2.0 user interface, patient flow and data structures were aligned with the requirements of both PuHP and PrHP. In addition to the web portal, a user-friendly mobile App facilitates easier access to patient records via mobiles/tablets. In the new version, PrHP can now register themselves online and access Nikshay (with their own secure login credentials) and manage their patient records. Patients can be transferred to another healthcare provider from either public/private sector across the country, making patient management seamless. RNTCP partners from Non-Governmental sectors, who work as Public-Private sector interface, can also access Nikshay to manage notified TB cases. All RNTCP staff and PrHP were trained to use the new features. Output reports from Nikshay 2.0 helped programme monitoring. Real time data entry is being encouraged by RNTCP to make patient tracking simpler and faster.
Results: Registration of PrHP in the country has increased from 142 thousand in 2017 to 203 thousand in 2018. Private TB case notifications correspondingly increased from 0.37 million in 2017 to 0.54 million in 2018, a 45% increase in one-year.
Conclusions: Nikshay is evolving as an all-inclusive solution for use by the PrHP in India. The focus must be on sustaining resource allocation to strengthen such solutions, preparing them for newer emerging challenges as country moves towards TB Elimination.

OA-27-483-02 Pattern of referrals and diagnosis amongst different types of private practitioners in Chennai

R Ranganathan,[1] R Ananthakrishnan,[1] N Krishnan,[1] R Rangaswamy,[1] S Auguesteen,[1] R Thiagesan,[1] M Griffiths,[1] A Khan,[2] J Creswell,[3] [1]REACH - Resource Group for Education and Advocacy for Community Health, Programme Management Unit, Chennai, India, [2]Stop TB Partnership/TB REACH, Technical, Geneva, Switzerland, [3]Stop TB Partnership/TB REACH, Innovations and Grants, Geneva, Switzerland. e-mail: drraghini.reach@gmail.com

Background and challenges to implementation: India's private sector plays a huge role in diagnosing and treating TB. Private sector engagement is vital to reaching TB elimination goals. However, private sector is not a monolith and little is known about type of practitioners who diagnose TB, number of cases treated and yield by engaging different practitioners. It is important to know these patterns to target engagement strategies that maximize impact.
Intervention or response: Private practitioners (PPs) were mapped and engaged through one-to-one outreach. They were given vouchers for free X-rays and Xpert tests at private facilities to be issued to clients. This was backed by a network of Nakshatra centres which provided comprehensive services including sample collection, transport, treatment initiation, treatment adherence support, counselling, nutritional support and contact screening.
Results and lessons learnt: 2574 PPs were engaged during 2017-2018 including 108 Chest Physicians(CPs), 1,448 General practitioners (GPs) and 955 specialty practitioners (SPs). A total of 13,220 referrals were received from 1,107 PPs including 103(9%) CPs, 754(68%) GPs and 250(23%) SPs. PPs referred an average of 12 cases(Range 1 - 783). On average CPs referred 26 cases each, GPs referred 12 cases each and SPs referred 6 cases each. Referrals were in proportion to provider type (GPs 69%, SP 11%, CPs 20%). However, CPs contrib-

uted 30% (1341) of diagnosed TB cases. On average a CP diagnosed 13 cases(IQR 2 - 20) a GP 4 cases(IQR 1 - 4) and SPs diagnosed 2 cases(IQR 1- 2). 50% of referrals came from 46 practitioners of whom 75% were GPs and 80% of referrals came from 186 practitioners of whom 64% were GPs. CPs were more likely to diagnose MDR- TB.

Conclusions and key recommendations: These findings highlight the need to engage all types of practitioners for a successful private sector engagement strategy. Since 50% of referrals are from 95% practitioners, wider outreach to practitioners is important to identify ′missing cases′.

OA-27-484-02 A 360-degree comprehensive private sector engagement providing end-to-end support for people with TB in Chennai, India

R Ananthakrishnan,[1] R Thiagesan,[1] R Ranganathan,[1] N Krishnan,[1] R Rangasamy,[1] S Augusteen,[1] JJJ Anthonisamy,[1] A Khan,[2] J Creswell,[3] [1]REACH (Resource Group for Education and Advocacy for Community Health), Program Management Unit, Chennai, India, [2]Stop TB Partnership, Technical, Geneva, Switzerland, [3]Stop TB Partnership, Innovations & Grants, Geneva, Switzerland. e-mail: ramyardr.reach@gmail.com

Background and challenges to implementation: In India, there are an estimated 2 million "missing people with TB" with many of them believed to be treated in the private sector. Nearly 80% of patients in urban settings with TB-related symptoms seek care from private sector.

Intervention or response: An innovative TB REACH supported public-private-partnership initiative was implemented in Chennai, the fourth largest metropolitan in India (7.2 million). A network of Private healthcare providers was built for TB care services between the doctors, chemists, hospitals, laboratories and patients in the private sector at the sub-district level to ensure the cascade of care to TB presumptives/patients. Through Nakshatra Centers(*NC*) in private hospitals, quality assured diagnostics, treatment and support services were provided to TB patients. Trained Community Health Workers facilitated case notification and linkages with the TB program. They supported private practitioners with sputum collection, transportation, contact tracing and provided holistic care to patients.

Results and lessons learnt: Between 2017 to 2018, 2,574 PPs were sensitized and overall 16,751 referrals were received at 44 Nakshatra (PPM) centers. 6,549 referrals received free x-rays and 10,520 received free Xpert testing. Of 5,105 people with TB notified,55% had microbiological confirmation and treatment was initiated for 5041 (98.7%). Extra pulmonary TB accounted for 32% (n=1634). About 3,950 patients received treatment and adherence/nutrition support, risk assessment and counselling through the initiative.The treatment success was 84%. When compared with the year prior to the intervention, referrals increased by 260% from 4,605 to 12,146. Private sector notifications in Chennai increased by 1000% in 2018 compared to 2015.

Conclusions and key recommendations: The findings demonstrate the importance of involving different players in private health sector through collaboration for private sector engagement in TB program. The need and mechanism for providing holistic continuum of care to TB patients in the private sector has also been highlighted.

OA-27-485-02 Management of TB by private practitioners in Indonesia; a mixed-method study

B Alisjahbana,[1,2] BW Lestari,[3,4] PF Hadisoemarto,[3,4] N Afifah,[4] S McAlister,[5] R van Crevel,[6] P Hill,[5] [1]Hasan Sadikin Hospital, Internal Medicine, Bandung, Indonesia, [2]Universitas Padjadjaran, Infectious Disease Research Center, Bandung, Indonesia, [3]Universitas Padjadjaran, Faculty of Medicine, Department of Public Health & Epidemiology, Bandung, Indonesia, [4]Universitas Padjadjaran, Faculty of Medicine, Infectious Disease Research Center, Bandung, Indonesia, [5]University of Otago, Dunedin School of Medicine, Department of Preventive and Social Medicine, Dunedin, New Zealand, [6]University Medical Center St. Radboud, Department of Internal Medicine, Nijmegen, Netherlands. e-mail: b.alisjahbana@gmail.com

Background: Poor adherence of private practitioners (PPs) to the National Tuberculosis Program (NTP) may compromise the quality of TB care in Indonesia, as well as TB notification to the NTP. This study examines TB diagnosis and treatment by Indonesian PPs in an outpatient setting.

Methods: The study consisted of two parts. First, we sent 12 standardized 'mystery' patients to PPs, representing 4 scenario's of suggestive TB symptoms:
(1) history only;
(2) with negative microscopy;
(3) with positive microscopy results;
(4) with recent history of TB treatment default.
Second, in-depth interviews were performed with selected PPs and TB patients, transcribed, and inductive content analysis was performed.

Results: From 320 visits of standardized patients to 225 PPs three main conclusions appeared:
(1) 53% of PPs ordered chest X-ray irrespective of sputum microscopy results;
(2) 19% of PPs prescribed fluoroquinolones as first line TB treatment; and
(3) 80% failed to notify their TB patient to the NTP.
With regard to use of x-ray over smear microscopy, in-depth interviews revealed perceived diagnostic limitations of sputum examination, patient's preference, and clinical benefit by exclude other lung abnormalities as underlying reasons. With regard to fluoroquinolone use, patient's expectation, absence of TB-specific symptoms,

risk of losing patients, and disease severity were mentioned. Low notification rates among PPs were attributed to lack of resources, simplified mechanisms, standard reporting protocols and knowledge regarding mandatory TB notification.

Conclusions: These findings confirm that Indonesian PPs do not adhere to NTP guidelines. The use of chest x-ray as a first diagnostic test may be rational and helpful in diagnosis of TB and other diseases, but wide prescription of fluoroquinolones can increase drug resistance. Further efforts are needed to strengthen the role of PPs in TB control in Indonesia.

OA-27-486-02 Improving universal access to drug-resistant TB care in the private sector through effective treatment linkage model to the public sector and patient support system

N Dominic,[1] S Vijayan,[2] A Hegde,[1] R Chopra,[2]
[1]PATH, Health, Mumbai, India, [2]PATH, Health, Delhi, India. e-mail: ndominic@path.org

Background and challenges to implementation: The cost of treatment for drug-resistant tuberculosis (DR-TB) in India's private sector is prohibitive to much of the population. Additionally, the private sector lacks a quality-assured system for standardized treatment and long-term patient follow-up. PATH, in collaboration with the national TB control program in Mumbai, supported by the Centers for Disease Control and Prevention through Global Health Security Agenda funds, developed a model to link the private-sector DRTB patients to early, affordable, quality-assured programmatic management of DR-TB (PMDT) treatment in the public sector.

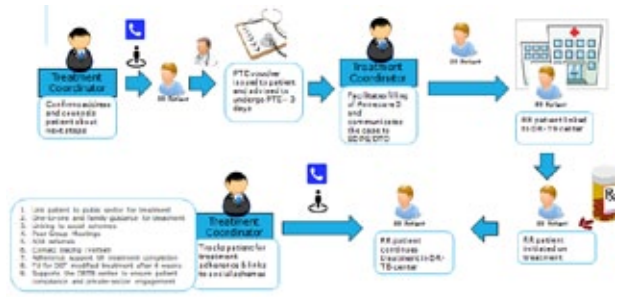
Intervention or response: TB presumptives identified by private providers were tested in the public sector free of charge using GeneXpert; upon diagnosis, they were followed up by treatment coordinators—field staff tasked with providing guidance to private-sector patients to accept public-sector treatment.

Treatment coordinators supported DR-TB patients in pretreatment evaluation in the private sector and fast-tracked appointments at public drug-resistant TB (PMDT) treatment centers.

Results and lessons learnt: In the last two years (March 2017-2019), 1,226 private-sector patients were diagnosed with DR-TB; 87 percent (1,066) were initiated into public-sector treatment and 5 percent (59) into the private sector. The remaining 8 percent have been assigned outcomes of migrated, died, and lost to follow-up before treatment initiation. Among the 1,066 initiated on treatment in the public sector, 65 percent are currently on treatment, 19 percent migrated, and 6.6 percent died.

The remaining were either lost to follow-up or a small number shifted back to the private sector for treatment continuation. More than 80 percent of private-sector patients who started treatment in the public sector were initiated within 14 days of diagnosis. These patients are then followed up through the end of treatment.

Conclusions and key recommendations: Effective private-public linkages help build trust among patients from the private sector and providers, ensuring early, affordable, and standardized DR-TB care for all while reducing out-of-pocket expenditure.



[The DR-TB private public linkages model. RR: Rifampicin Resistant; PTE: Pretreatment Evaluation; SDP]

OA-27-487-02 Anti-tuberculosis treatment stewardship in a private tertiary care hospital in India improves standards of TB diagnosis and treatment

A Kunoor,[1] B P Prabhu,[2] M Varsha Joseph,[3] S Sudheer,[3] PS Rakesh,[4] J Mary Philip,[3] J James,[3] V P Menon,[5] S K Singh,[3] [1]Amrita Institute of Medical Sciences & Research Centre, Pulmonary Medicine, Kochi, India, [2]Amrita Institute of Medical Sciences and Research Centre, General Medicine, Kochi, India, [3]Amrita Institute of Medical Science, Medical Administration, Kochi, India, [4]Amrita Institute of Medical Science, Community Medicine, Kochi, India, [5]Amrita Institute of Medical Science, General Medicine, Kochi, India. e-mail: akhileshkunoor@gmail.com

Background and challenges to implementation: The private sector accounts for more than half of the tuberculosis (TB) care delivered in India. The indiscriminate use of anti-tuberculosis drugs outside the Revised National TB Control Programme (RNTCP) is alleged to be an important factor fuelling the emergence of drug-resistant TB.

Intervention or response: A private tertiary care centre in India started an Anti-Tuberculosis Treatment Stewardship (ATTS) program in 2017. The hospital's ATTS is built on the already existing antimicrobial stewardship programme, which has been conducting daily audits of antibiotic prescriptions and monitoring appropriate prescription. The hospital's ATTS multidisciplinary team includes an administrator, a pulmonologist, an infectious disease specialist and clinical pharmacists. The team meets twice weekly to review patient records of all notified TB patients. The team assesses the appropriateness of anti-tuberculosis treatment for each case

following the '5Rs': Right indication, Right drug, Right dose, Right frequency and Right duration. The prescription is considered inappropriate if any of the 5Rs is incorrect. If any instance of "inappropriate" prescription were recognised, the stewardship team would file recommendations to the treating clinician. The compliance to these recommendations was also audited.

Results and lessons learnt: A total 231 TB patients records were evaluated till date. 57% of the cases were definitive TB as per RNTCP guidelines. Anti-tubercular therapy was appropriate for 64% of the total patient prescriptions. This improved from 56% in the first year to 72% in the second year. 95 instances of "inappropriate" prescriptions were evaluated and intervened by the team. Dosing of ATT (79%) was the most common reason for inappropriate therapy. Overall compliance with ATT stewardship recommendations was 45%. Standards of TB diagnosis and treatment can be improved by establishing antimicrobial policies and programmes in hospitals.

Conclusions and key recommendations: Anti TB stewardship mechanisms in private hospitals are feasible. Such mechanisms could improve the standards of TB diagnosis and treatment, thereby preventing emergence of drug resistance.

OA-27-488-02 Influencing provider behaviour through marketing management for use of fixed dose combinations in the private sector

RK Gandhi,[1] S Talekar,[2] U Waghmare,[2] [1]PATH India, TB Portfolio, Mumbai, India, [2]MCGM, RNTCP, Mumbai, India.
e-mail: rgandhi@path.org

Background and challenges to implementation: WHO recommends use of fixed drug combinations (FDC) for simplified patient compliance, increased adherence and uniformity of TB-care. However, the use of FDC has been as low as 10-12% for treatment of drug sensitive TB in private-sector in Mumbai.

Intervention or response: In a bid to optimally engage private providers in TB-care, a Private Provider Interphase Agency (PPIA) was introduced in Mumbai in 2014. Under this initiative, field officers conducted surveys of 511 private doctors and 230 pharmacists to understand their readiness and inclination to transition from individual formulations to FDCs. The logistics and supply chain requirements were ascertained. Based on survey results, 211 providers and 114 pharmacists were trained on standard prescription and dispensing processes to improve FDC usage in TB management. A communication toolkit was developed as a marketing tool to influence consumer behaviour. The field team prioritised providers to conduct multiple visits and use marketing relationships to successfully convert their prescription habits from individual drugs to FDCs. Categorisation of providers was based on TB patient load, visit frequency and resistance to switching to FDCs.

Results and lessons learnt: Between June 2017 to Mar 2018, of the 211 trained providers, 187 (88%) prescribed FDCs to their 2,945 patients. The FDC uptake has increased from 10% to 63% of the total patients notified by the end of March 2018. Pharmacists data helped devise the marketing strategy to establish the supply chain and logistics requirement for regular availability of FDC supplies in private pharmacies.

Conclusions and key recommendations: Effective use of marketing and relationship management coupled with correct communication and strategy implementation resulted in a successful scale up of the FDCs in the private sector through the PPIA network. For sustainable outcomes, this model is being up-scaled to National level for FDC management in the private sector, through Joint Effort to End-TB initiative of NTP

OA-28-C3 We're vulnerable to TB: don't forget us

OA-28-489-02 Imipenem through port-a-cath for extensively drug-resistant TB: experience from an NGO-run clinic, Mumbai, India

V Chavan,[1] A Dalal,[2] S Ravi,[1] SB Nagaraja,[3] P Thekkur,[4,5] AC Meneguim,[1] M Das,[1] S Kalon,[1] G Ferlazzo,[6] P Isaakidis,[6] [1]Médecins Sans Frontières (MSF) / Doctors without Borders, Medical, Mumbai, India, [2]Jupiter Hospital, Medical, Thane, India, [3]ESIC Medical College and PGIMSR, PSM, Bengaluru, India, [4]International Union Against Tuberculosis and Lung Disease, Center for Operational Research, Paris, France, [5]The Union South East Asia Office (USEA), Center for Operational Research, Delhi, India, [6]Médecins Sans Frontières (MSF) Southern Africa Medical Unit, Medical, Cape Town, South Africa.
e-mail: dralpadalal@gmail.com

Background: Imipenem is considered to be safe and effective for treatment of extensively drug-resistant TB. Injectable imipenem is recommended for extensively drug resistant (XDR) or pre-XDR TB patients with either resistance to or contraindication to second line drugs. Médecins Sans Frontières (MSF) independent clinic at Mumbai, clinic delivered Imipenem via port-a-cath through trained outreach workers in community in order to reduce repeated injection and hospitalization. We aim to describe our early experience on feasibility, culture conversion and treatment outcomes among patients initiated on Imipenem containing regimen in Mumbai, India.

Methods: We included a cohort of XDR-TB and pre XDR-TB patients initiated on Imipenem containing regimen during January 2015 to June 2018. Services at MSF clinic were delivered through its muti-disciplinary team of clinicians, nurses, psychologists, counselors and

consultant psychiatrists. The patient wise information on demographic details, drug susceptibility pattern, regimen composition, follow-up culture results and treatment outcomes was extracted from electronic database maintained at the clinic.

Results: A total of 73 patients received Imipenem containing regimen. The median age was 25 years(IQR:21-30) with Male:Female ratio of nearly 1:1. Forty-six(63%) had XDR-TB while 27(37%) had pre-XDR-TB. Of 58 patients who had completed six-months of treatment, 45(77%) had culture-conversion(median time: 2.5 months). Among 57 in whom treatment-outcomes were ascertained, 25(44%), 6(11%), 5(8%) and 21(37%) were cured, treatment-completed, failed and died respectively. 17 reported severe-adverse-events, SAE: 7 had blood-stream/port-site infection while 10 developed other SAEs(ulceration, suture break, port-a-cath block), however none of them led to grave consequences.

Conclusions: In XDR and pre-XDR TB patients, the delivery of Imipenem via port-a-cath through trained community outreach workers was feasible and there was low number of reported adverse-events. The culture-conversion rate and treatment-outcomes were promising. There remains a potential scope for National TB programmes to adapt similar less-invasive 'patient-friendly techniques' in management of complicated DR-TB patients.

OA-28-490-02 Incidence of anaemia among cohorts of DR-TB patients started on linezolid-containing regimen in Lesotho

M Asfaw,[1] L Oyewusi,[1] A Leta,[2] L Maama,[3] C Mitnick,[4] KJ Seung,[5] S McAnaw,[5] P Nkundanyirazo,[6] J Makaka,[2] D Holtzman,[7] [1]Partners in Health, Lesotho, Maseru, Lesotho, [2]Partners in Health, MDR TB Program, Maseru, Lesotho, [3]Ministry of Health, National TB Program, Maseru, Lesotho, [4]Harvard Medical School, Global Health and Social Medicine, Boston, MA, United States of America, [5]Partners in Health, End TB, Boston, MA, United States of America, [6]Partners in Health, DR TB Program, Maseru, Lesotho, [7]Partners In Health, MDR TB Program, Maseru, Lesotho.
e-mail: tb.hivteam@gmail.com

Background: Linezolid is an oxazolidinone, used in the treatment of serious gram-positive infections. It has recently been added to the group of "core" drugs recommended by the World Health Organization for treatment of drug-resistant tuberculosis (DR-TB). Accordingly, it will be used in drug combinations not previously evaluated for safety or efficacy for longer durations. Here, we compare the incidence of anemia, among patients exposed to linezolid, with others taking regimen without Linezolid other potential factors being shared among both groups.

Methods: An observational study patients enrolled on bedaquiline- and/or delamanid, between October 2015 to June 2017 in Lesotho, we divided them in to two groups' one group taking the new drugs with Linezolid (Lzd) and the other without. All adults with baseline hemoglobin > 10.5gm/dl are included and anemia is defined as hemoglobin < 10.5gm/dl after at least one week of exposure. Other factors and management are also discussed briefly.

Results: A total of 98 adult patients were enrolled in this period. 36 (36.73%), 48 (48.97%), 14 (14.28%), 22 (22.44%)received regimens containing bedaquiline, delamanid, both and Lzd respectively. 78 (79.56%) were HIV-coinfected. 19 (19.38%) cases had a drop in hemoglobin from baseline, of this 9 cases were among patients on Linezolid and it occurred after a median of 18 [IQR:16,61] days of linezolid exposure with mean drop in hemoglobin of 1.61. In unadjusted analyses, anemia was less common (95% CI: 0.52, 2.70) among linezolid exposed.

Other factors like HIV and Low Body Mass Index (BMI) were also associated with anemia. Most cases were managed with dose or frequency reduction, hence, permanent discontinuation was made in only 3 cases.

Conclusions: Anemia is common among DR TB patients with other comorbid conditions, particularly, HIV and low BMI and few cases are attributed to Linezolid. Those few cases can be managed with dose or frequency reduction and permanent discontinuation in rare cases.

OA-28-491-02 Linezolid for the treatment of extensively drug-resistant tuberculosis: a systematic review and meta-analysis

L Zhang,[1,2,3] S Bian,[2] F Sun,[4] S Zhan,[4] X Liu,[1,2,3]
[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Infectious Diseases, Beijing, China, [2]Chinese Academy of Medical Sciences and Peking Union Medical College, Centre for Tuberculosis Research, Beijing, China, [3]International Epidemiology Network, Chinese Academy of Medical Sciences and Peking Union Medical College, Clinical Epidemiology Unit, Beijing, China, [4]School of Public Health, Peking University, Department of Epidemiology and Biostatistics, Beijing, China.
e-mail: lifanzhang1982@126.com

Background: Studies have shown that linezolid (LZD) can be used to treat XDR-TB. We aimed to conduct a systematic review and meta-analysis to assess existing evidence concerning the efficacy and safety of LZD for XDR-TB treatment.

Methods: MEDLINE@OVID, PubMed, EMBASE, The Cochrane Library, Clinical Trials, Sinomed, CMCI, CNKI, VIP and the Wanfang database were systematically searched for randomized controlled trails, cohort studies, case series or case reports from January 2000 to December 2016. Summary estimates of the rates of sputum culture conversion and treatment success and the rates of adverse effects were calculated, and data that could not be combined were summarized and described qualitatively. The combined results were examined for heterogeneity, sensitivity and publishing bias.

Results: Twenty-two original studies with 302 patients with XDR-TB fulfilled the inclusion criteria. The pooled estimates for the proportions of sputum culture conversion and treatment success were 93.2% and 67.4% in XDR-TB patients with LZD treatment, respectively. The pooled estimates for the proportions of myelosuppression, peripheral neuropathy, optic neuritis and adverse reactions of the gastrointestinal tract were 42.5%, 26.0%, 19.0%, and 35.0%, respectively. Heterogeneity originated mainly from the initial dose of LZD (≤600 mg/d or> 600 mg/d), as patients with a high initial dose of LZD were more likely to have myelosuppression (48.4% vs. 24.8%) and adverse events of the gastrointestinal tract (41.3% vs.15.4%).
Conclusions: LZD appears to be effective for XDR-TB, but adverse events are common. An LZD dose ≤600 mg/d was suggested as the initial dose for treating XDR-TB patients in clinical practice.

OA-28-492-02 Easier said than done: the reality of treatment monitoring for patients with multidrug-resistant tuberculosis

H Huerga,[1] M Bastard,[2] B Kholikulov,[3] M Kikvidze,[4] YY Naing,[5] S Aiylchiev,[6] A Serobyan,[7] S Wanjala,[8] N Melikyan,[1] C Hewison,[9] [1]Epicentre, Epidemiology Department, Paris, France, [2]Epicentre, Epidemiology Department, Geneva, Switzerland, [3]Medecins Sans Frontieres, Medical Department, Minsk, Belarus, [4]Medecins Sans Frontieres, Medical Department, Tbilisi, Georgia, [5]Medecins Sans Frontieres, Medical Department, Yangon, Myanmar, [6]Medecins Sans Frontieres, Medical Department, Osh, Kyrgyz Republic, [7]Medecins Sans Frontieres, Medical Department, Yerevan, Armenia, [8]Medecins Sans Frontieres, Medical Department, Nairobi, Kenya, [9]Medecins Sans Frontieres, Medical Department, Paris, France.
e-mail: helena.huerga@epicentre.msf.org

Background: The WHO recommended monitoring schedule for multi-drug resistant tuberculosis (MDR-TB) treatment is essential for the early identification and management of potential adverse events. Médecins Sans Frontières (MSF) has supported the introduction of new and repurposed TB drugs in several countries in the context of the endTB project.
We report the frequency and incidence of key monitoring measures in the first 6 months of treatment in patients who received bedaquiline or delamanid containing regimens.
Methods: Patients started on bedaquiline or delamanid in Armenia, Belarus, Georgia, Kenya, Kyrgyzstan and Myanmar between April 2015 and June 2018 were included. Key monitoring measures were: clinical review visits and ECG recordings (for all patients), haemoglobin measurements and peripheral neuropathy clinical screen (for patients starting a regimen with linezolid), and audiometry (for patients starting a regimen with an injectable).
Results: Of the 575 patients who started treatment with bedaquiline or delamanid, 505 (87.8%) received linezolid and 286 (49.7%) an injectable. Overall, 88.2% of all patients and 96.7% of those on linezolid had respectively an ECG and haemoglobin done at treatment initiation while 57.0% of those on linezolid had a peripheral neuropathy clinical screening done and 51.8% of those on injectable had an audiometry (Table). While for each monitoring we expected 6 measures per patient in 6 months of follow-up, in reality for audiometry and peripheral neuropathy clinical screen, the numbers were much lower: 1.5 and 3.2 respectively.
Conclusions: ECG and haematology were done with good frequency. Peripheral neuropathy clinical screen was done only for some patients. Performing audiometry posed considerable challenges despite the support provided through MSF and the endTB project. Clinical monitoring of patients receiving linezolid should be reinforced. Injectable drugs should be avoided when possible and more resources are needed to ensure correct monitoring with audiometry when injectable drugs are necessary.

Monitoring measure	Patients with measure at treatment initiation, n/N (%)	Patients with at least one measure during follow-up, n/ (%)	Median number of follow-up measures among all [IQR]	Median number of follow-up measures among patients with at least one [IQR]	Median monitoring interval in days [IQR]	Incidence of monitoring measures per 6 patient-months, (95%CI)
Clinical visit	575/575 (100)	458/575 (79.7)	5 [1-6]	6 [4-6]	30 [28-35]	4.2 (4.0-4.4)
ECG	507/575 (88.2)	557/575 (96.9)	5 [4-6]	5 [4-6]	36 [30-56]	4.0 (3.9-4.2)
Peripheral neuropathy screen	288/505 (57.0%)	375/505 (74.3)	3 [0-5]	4 [3-5]	32 [29-42]	3.2 (2.9-3.4)
Haemoglobin	489/505 (96.8%)	494/505 (97.8)	5 [4-5]	5 [4-5]	33 [30-50]	4.6 (4.5-4.8)
Audiometry	148/286 (51.8%)	130/286 (45.5)	0 [0-3]	3 [1-4]	39 [30-57]	1.5 (1.3-1.7)

[Frequency and incidence of key monitoring measures in the first 6 months of treatment]

OA-28-493-02 Adverse events common due to linezolid in MDR-TB treatment: a nationwide cohort study

L Davies Forsman,[1,2] J-W Alffenaar,[3] T Schön,[4,5] C Giske,[6] J Jonsson,[7] J Bruchfeld,[1,2] [1]Karolinska Institutet, Division of Infectious Diseases Solna, Stockholm, Sweden, [2]Karolinska University Hospital, Department of Infectious Diseases, Stockholm, Sweden, [3]University of Sydney and Westmead Hospital, School of Pharmacy, Faculty of Medicine and Health, Sydney, NSW, Australia, [4]Linköping University Hospital, Department of Medical Microbiology, Linköping, Sweden, [5]Kalmar County Hospital, Sweden, Department of Clinical Microbiology and Infectious Diseases, Kalmar, Sweden, [6]Karolinska Institutet, Department of Laboratory Medicine, Stockholm, Sweden, [7]Public Health Agency of Sweden, Unit for Epidemiological Monitoring, Department of Public Health Analysis and Data Management, Stockholm, Sweden.
e-mail: lina.davies.forsman@ki.se

Background: Linezolid (LZD) is now recommended as one of the first choices in the treatment of multidrug-resistant tuberculosis (MDR-TB), despite the risk of serious adverse events (AE). The extent of AEs might be underestimated in high-burden countries with insufficient patient monitoring.
Therefore, we studied the frequency and risk factors of AEs due to LZD in consecutive MDR-TB patients in a low-endemic setting with vigilant monitoring.
Methods: In this nationwide cohort study, all MDR-TB patients in Sweden treated with LZD between 1999-2018 were included (n=93). Medical records were reviewed for serious AEs (polyneuropathy, aenemia and opticus neuritis). Risk factors for AEs were analysed with logistic regression.
Results: Between 1999-2014, 67 MDR-TB patients were treated with LZD of which 38 (55.9%) were male. Most patients originated from Sub-Saharan Africa and only one patient from Sweden. The median age at time of diagnosis was 29.5 years, with no difference between patients with or without AEs. A majority of patients received 600 mg of LZD (n=55, 80.9%, range 300-1200 mg) with a median dose of 10.3 mg/kg (IQR 9.0-11.5) and median treatment duration of 4.5 months (IQR 2.1-10.9).
Serious AEs during treatment of LZD were frequently seen (38 out of 67 patients, 56.7%), with treatment discontinuation in the majority of cases. The most common severe AE was polyneuropathy (n=21, 31.3%), anaemia (n=15, 22.4%) and opticus neuritis (n=5, 7.5%). Treatment success was 85.1% (n=57).
The average dose/kg of LZD was significantly associated with the occurrence of polyneuropathy (p=0.028 95% CI 1.02-1.50), especially for dosages exceeding 15 mg/kg (p=0.03, OR 12.4, 95% CI 1.24-124.2.) No association between the duration of LZD treatment and polyneuropathy was seen.
Conclusions: Serious AEs related to LZD treatment are common. The risk of polyneuropathy is dose-dependent. Regular monitoring regarding symptoms, examination of vision, peripheral touch and blood count is recommended.

OA-28-494-02 Treatment of multi- and extensively drug-resistant tuberculosis with bedaquiline containing regimens at the programmatic level. Belarus prospective cohort study

A Skrahina,[1] S Setkina,[2] H Hurevich,[1] V Grankov,[3] D Klimuk,[4] V Solodovnikova,[1] D Viatushka,[1] M Dara,[5] [1]The Republican Scientific and Practical Center for Pulmonology and TB, Clinical Department, Minsk, Belarus, [2]The Center of Examinations and Tests in Health Service, Pharmacovigilance, Minsk, Belarus, [3]World Health Organisation, Country Office, Minsk, Belarus, [4]The Republican Scientific and Practical Center for Pulmonology and TB, Department of Monitoring and Evaluation, Minsk, Belarus, [5]World Health Organisation, Regional Office for Europe, Copenhagen, Denmark.
e-mail: alena.skrahina@gmail.com

Background: Bedaquiline (Bdq) is a new drug effective against M/XDR-TB, which was granted accelerated approval by the United States Food and Drug Administration in 2012. To improve treatment outcomes in patients with multi- and extensively drug-resistant tuberculosis (M/XDR-TB) bedaquiline (Bdq) was programmatically introduced in Belarus in July 2015.
Methods: In line with the World Health Organization recommendations. Belarus national TB program developed measures to monitor safety and effectiveness Bdq containing regimens prospectively in the countrywide cohort study.
Results: By April 1, 2019, cumulative number of M/XDR-TB patients treated with Bdq was 1297; of them 392 had final treatment outcomes: median age - 36 years, 72% males; 46% new and 54% previously treated; 16% MDR+FQ and 14% MDR+second line injectables resistant, 65% XDR-TB. All patients experienced adverse events (AEs). The most common AE were: hyperuricemia, liver function impairment, hypokalemia, hypomagnesemia, cardiac abnormalities (incl. QT prolongation), nausea, vomiting, myelosupression, renal function impairment. Most of the AEs were mild and moderate and did not cause the treatment regimen to stop. The following final treatment outcomes were recorded: treatment success - 324 (83%); treatment failure 14 (4%); lost to follow up - 25 (6%); death - 29 (7%).
Conclusions: The results of Belarus countrywide prospective cohort study of Bdq containing regimens showed satisfactory safety profile and good final treatment outcomes even in the cohort with a significant proportion of XDR-TB.

OA-28-495-02 Early safety evaluation of bedaquiline for treatment of MDR-TB patients in China

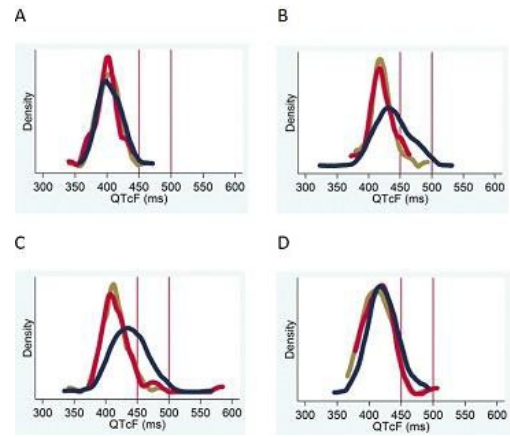
M Gao,[1] J Gao,[2] Y Liu,[3] S Xu,[4] L Li,[4] F Mi,[5] J Du,[4]
[1]Beijing Chest Hospital, Capital Medical University, TB Department, Beijing, China, [2]Beijing Chest Hospital, Capital Medical University, Clinical Center, Beijing, China, [3]Beijing Chest Hospital, Capital Medical University, National Clinical Center on Tuberculosis, Beijing, China, [4]Beijing Chest Hospital, Capital Medical University, Administration Office, Beijing, China, [5]Beijing Chest Hospital, Capital Medical University, Research Administration Office, Beijing, China.
e-mail: liuyuhong0516@126.com

Background: Bedaquiline was conditional approval in China since 2016 for treatment of multidrug-resistant tuberculosis (MDR-TB) and was piloted to be used as key component with optimized background regimen under strictly active pharmacovigilance via a national program named New anti-TB Drugs Introduction and Protection Program (NDIP) since early 2018. We evaluated 1 year safety profile of Bedaquiline containing regimen in patients with MDR-TB in China.
Methods: Eligible patients' enrollment started in February 2018.Participents had scheduled bi-weekly visits during the first 4 weeks and thereafter were clinically evaluated at 4-week intervals till the end of treatment. Regular electrocardiographic, renal and hepatic function, auditory and visual, blood and urine routine examinations were monitored. Any abnormal with clinical implication was requested to report via NDIP electronic system.
Results: 355 eligible MDR-TB patients were enrolled in 1 year. 65 (18.3%) had at least one treatment-emergent adverse event (TEAE). 9 (2.5%) had at least one serious TEAE. There were 141 cumulative adverse events reported in 1 year of which 36% were hepatoxicity at the top followed by Q-Tc interval prolongation at 15.6%. Both of them occurred at median 56-60days after Bedaquiline initiation. Electrolyte disturbance disorders, hemoptysis, renal impairment, hematological damage, gastrointestinal reaction and ototoxicity accounted for similar proportion. Death occurred in 1.1% (4/355) of participants. The reported deaths were related to acute respiratory failure, sudden ventricular fibrillation and acute renal failure. 2 of the 4 fatal events were considered to be possibly related to Bedaquiline.
Conclusions: Bedaquiline was well tolerated with comparatively high safety profile. As adverse effect profiles may change, strict pharmacovigilance should be performed and further evaluation is needed to determine its long-term safety performance.

OA-28-496-02 QT prolongation and its evolution over time in the STREAM 1 trial

G Hughes,[1] S Ahmed,[1] C Cook,[1] R Goodall,[1] P Phillips,[2] A Nunn,[1] S Meredith,[1] STREAM Collaboration [1]UCL, MRC Clinical Trials Unit, London, United Kingdom, [2]University of California (UCSF), Medicine, San Francisco, CA, United States of America.
e-mail: gareth.hughes@ucl.ac.uk

Background: STREAM-1 was a randomised phase 3 trial in rifampicin-resistant TB comparing a 9-11 month "short regimen" to a "long regimen" following WHO 2011 guidelines. ECG monitoring was undertaken for the first year after randomisation. QT prolongation (QT or QTcF ≥500 ms) was more frequent on the short regimen (11% vs. 6.4%, p=0.14), likely due to moxifloxacin (high-dose) and clofazamine in the short regimen. The long regimen included standard-dose moxifloxacin or levofloxacin. We examined the evolution of QTcF in trial participants over time.
Methods: Participants were analysed according to allocated regimen; those on the long regimen were subdivided by fluoroquinolone used. Mean QTcF and mean QTcF change from randomisation were calculated for each visit. Univariate kernel density plots were fitted to ECG data at randomisation (pre-dose), Week 16 (end of intensive phase on short regimen), Weeks 40 and 52.
Results: Mean QTcF and mean QTcF changes were greater on the short than long regimen, maximum difference in means between regimens was 24ms for QTcF at week 28 and 19ms for QTcF change at week 32. Both mean QTcF had returned to within 10ms of baseline at week 52. QTcF distributions by regimen (Fig 1) illustrate no difference at baseline, but a broadening of the distribution and a shift to the right in the short regimen apparent at weeks 16 and 40 (images B and C).



[Figure 1. Univariate kernel density plots of QTcF interval at baseline (A), 16 (B), 40 (C) and 52 (D) weeks reflecting pre-treatment, end of intensive phase, end of continuation phase and 1 year post randomisation. The lines correspond to the short regimen (blue), the long remine with moxifloxacin (red) and the long regimen with levofloxacin (brown)]

On the long regimen changes in QTcF were greater in patients receiving moxifloxacin than those receiving levofloxacin.

Conclusions: QTcF patterns suggest the short regimen, including clofazimine and high-dose moxifloxacin, alters the population QTcF distribution which is resolved by week 52, when most patients had completed treatment. Patients on the long regimen continued treatment for at least 18 months; any effect of treatment on QTcF would still be present at week 52.

SHORT ORAL ABSTRACT SESSIONS (SOA)

SOA-15-C4 Closing the gap: addressing challenges of identification and management of childhood TB

SOA-15-1146-02 Paediatric autopsy review in Ukraine to identify potential missed cases of paediatric tuberculosis

N Rybak,[1] L Haile,[2] A Galligan,[3] H Jenkins,[4] S Chiang,[5] Y Sheremeta,[6] K Mishyna,[7] V Petrenko,[6] S Gychka,[7] CR Horsburgh,[8] [1]Warren Alpert Medical School of Brown University, Division of Infectious Disease, Providence, RI, United States of America, [2]Brown University, Undergraduate Studies, Providence, RI, United States of America, [3]Warren Alpert Medical School of Brown University, Medical School, Providence, RI, United States of America, [4]Boston University School of Public Health, Biostatistics, Boston, MA, United States of America, [5]Warren Alpert Medical School of Brown University, Pediatric Infectious Disease, Providence, RI, United States of America, [6]National Medical O.O. Bogomolets University, Phthisiology, Kyiv, Ukraine, [7]National Medical O.O. Bogomolets University, Pathology, Kyiv, Ukraine, [8]Boston University School of Public Health, Global Health, Boston, MA, United States of America.
e-mail: tasharybak@gmail.com

Background: Pediatric tuberculosis (TB) is under diagnosed and underreported worldwide. Ukraine has the exceptional policy that >95% of all pediatric deaths undergo full autopsy, allowing the possibility to identify TB cases that were missed antemortem. We searched autopsy records to identify possible missed pediatric TB cases.
Methods: Non-forensic pediatric autopsy records (January-December 2017) were retrospectively reviewed from 4 hospitals in Kyiv, Ukraine. During initial review, autopsies with confirmed trauma, cancer, fetal death or congenital anomaly were excluded from further data collection. Detailed data, including final clinical diagnosis, cause(s) of death, ICD-10 code and final histopathological diagnosis, were extracted from the remaining records (TB smears and cultures were not performed). These records were further reviewed for a possible TB death and were excluded if they had an obvious non-infectious cause of death or death from a microbiologically confirmed infection not TB-related. From the remaining records, inclusion criteria for a "possible TB" death were presence of any of the following: sepsis, pneumonia, meningitis, granulomatous disease, or infection-related multi-organ failure.
Results: 635 autopsy records underwent initial review and of those, 179 were selected for detailed data collection. Of these 179 records, 94 neonatal deaths (age < 28 days) were excluded due to high rates of birth related infections/complications and low likelihood of TB. Of the 85 patients remaining, one child had confirmed TB and 32 additional children met our definition for "possible TB" deaths.
Conclusions: Ukrainian autopsy policy offers a unique opportunity for case-finding for pediatric TB patients that were not diagnosed prior to death. This study demonstrates that there are a substantial number of possible active TB cases that may have been missed. Prospective sample collection on such autopsies may help to determine the magnitude of missed TB cases. Further epidemiological investigations into these missed TB deaths may provide critical information to prevent future deaths.

SOA-15-1147-02 Performance of tuberculosis symptom screening for children and adolescents living with HIV (CALHIV) in six high TB-HIV-burden countries in eastern and southern Africa

B Vonasek,[1,2,3] D Dhillon,[1,4] T Devezin,[1,4] S Dlamini,[1,5] H Haq,[1] J Sanders,[2,6] A Kay,[1,4,5] J Bacha,[1,2,7] K Simon,[2,3,8] A Mandalakas,[1,4] [1]Baylor College of Medicine, Department of Pediatrics, Houston, TX, United States of America, [2]Baylor College of Medicine, Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Houston, TX, United States of America, [3]Baylor College of Medicine, Children's Foundation, Lilongwe, Malawi, [4]Baylor College of Medicine, Global Tuberculosis Program, Houston, TX, United States of America, [5]Baylor College of Medicine, Baylor Swaziland TB Center of Excellence, Mbabane, Eswatini, [6]Baylor College of Medicine, Children's Foundation, Maseru, Lesotho, [7]Baylor College of Medicine, Children's Foundation, Mbeya, Tanzania, United Rep., [8]PEPFAR, Technical Support to Programs in the Southern Africa Region, Lilongwe, Malawi.
e-mail: vonasek@bcm.edu

Background: Despite limited evidence, the World Health Organization (WHO) recommends actively screening CALHIV for TB symptoms at every clinical encounter to improve TB case detection. As TB/HIV care is scaled up for CALHIV, the performance of this TB screening approach needs comprehensive assessment.
This study evaluates the performance of a four-question TB symptom screen in CALHIV at seven sites across six high TB/HIV burden countries in southern and eastern Africa.
Methods: We performed a retrospective longitudinal cohort study of seven HIV clinics in Uganda, Tanzania (Mbeya and Mwanza), Malawi, Lesotho, Eswatini, and Botswana from January 2014 to June 2017. Data was extracted from electronic medical records for patients under 20 years of age with documented HIV infection. Incident TB disease cases were defined as those initiating anti-TB treatment within 30 days of TB diagnosis and with no previous diagnosis of TB disease at that facility.

The most recent symptom screen result within the 30 days preceding a diagnosis of TB disease was analyzed. In accordance with WHO guidelines, any current fever, cough, poor weight gain, or recent TB contact defined a positive screen in children. Any current fever, cough, weight loss, or drenching night sweats defined a positive screen in adolescents.

Results: Our data set analyzed 20,706 patients collectively completing 316,740 clinic visits that included 240,161 documented TB symptom screens and 35,701 (14.9%) positive TB screens. 1592 patients had documented TB disease, of which 1212 (76%) fit inclusion criteria for incident TB disease. TB symptom screen performance measures are shown in the table.

Conclusions: While specificity and negative predictive value performed well, the sensitivity and positive predictive value of the TB symptom screen were low in out study population. In areas with a high burden of HIV-associated TB, more targeted and accurate screening approaches are needed to optimally identify TB disease in CALHIV.

Measure	Estimation	95% Confidence Interval
Sensitivity	61.2%	58.4-64.0%
Specificity	88.8%	88.7-88.9%
Positive Predictive Value	3.2%	3.0-3.4%
Negative Predictive Value	99.7%	99.7-99.7%
Positive Likelihood Ratio	5.5	5.2-5.7
Negative Likelihood Ratio	0.44	0.41-0.47

[Performance measures for four-question TB symptom screen.]

SOA-15-1148-02 Engagement of a paediatric specialty hospital for systematic screening of childhood TB in Ho Chi Minh City, Viet Nam

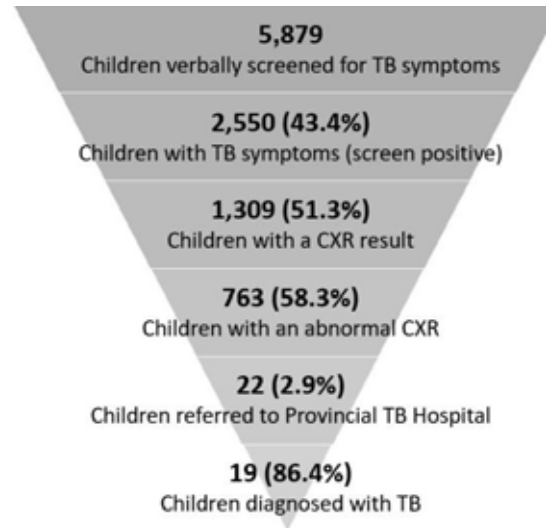
NTT Le,[1] RJ Forse,[1] AJ Codlin,[2] GC Do,[3] NTN Le,[4] CDB Nguyen,[4] HV Le,[5] GT Le,[6] TN Vu,[6] LNQ Vo,[7,8]
[1]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [3]Pham Ngoc Thach Lung Hospital, Quality Assurance Department, Ho Chi Minh City, Viet Nam, [4]Pediatric Hospital 1, Provincial Steering Department, Ho Chi Minh City, Viet Nam, [5]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [6]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam, [7]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [8]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam.
e-mail: rachel.forse@tbhelp.org

Background and challenges to implementation: Child TB should represent 8.3-10.3% of Viet Nam's total TB burden. However, only 3.5% of the country's TB notifications are among children <15 years. In Ho Chi Minh City, there are no systematic TB screening programs being implemented in the city's pediatric hospitals.

Intervention or response: As part of the TB REACH-funded Zero TB Viet Nam project, we piloted systematic screening for TB at the inpatient and outpatient departments of Children's Hospital 1 using medical students as screeners. The screening form had been successfully used to increase child TB notification in Pakistan and was adapted for the local context. If a child screened positive, pediatricians then conducted a clinical examination and indicated them for chest X-ray (CXR) screening and testing with the Xpert MTB/RIF assay. Pediatricians then referred children with confirmed and suspected TB to the Provincial TB Hospital for further diagnosis and treatment initiation.

Results and lessons learnt: 5,879 children were verbally screened, of which 2,550 screened positive (43.4%). Pediatricians indicated 1,309 of these children for CXR screening (51.3%), resulting in the detection of 763 abnormal CXRs (58.3%). Just 8 of children with abnormal CXRs (1.0%) were then tested on Xpert. 22 children with suspected TB (2.9%) were referred the Provincial TB Hospital; 19 of these referrals (86.4%) were diagnosed with TB and initiated on treatment. The TB detection rate in this pilot was 323/100,000, which is over 21x Viet Nam's estimated TB incidence rate for children (15/100,000).

Conclusions and key recommendations: Although this program diagnosed TB in high rates for the setting, there were several large drop offs in the TB care cascade resulting from pediatricians hesitating to follow the prescribed diagnostic algorithm. Future facility-based pediatric TB screening interventions in Viet Nam must build the capacity of general pediatricians to follow diagnostic algorithms and to improve testing rates through the collection of gastric aspirates and stool specimens.

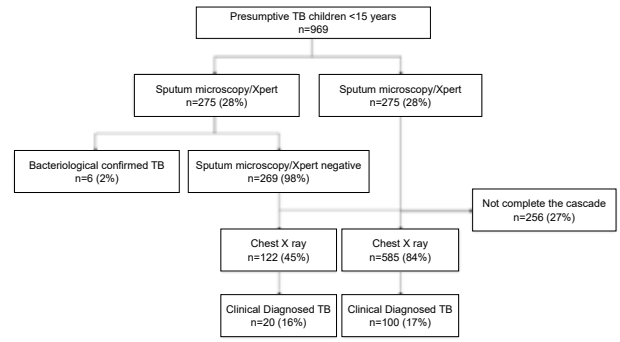


[Childhood TB care cascade]

SOA-15-1149-02 An assessment of the diagnosis process of childhood TB in Myanmar

KWY Kyaw,[1,2] S Satyanarayana,[2] AM Kumar,[2,3] NTT Kyaw,[1,2] S Aye,[4] NL Oo,[5] KK Htwe,[6] CC San,[6] ST Aung,[7] [1]International Union Against Tuberculosis and Lung Disease, Operational Research Department, Mandalay, Myanmar, [2]International Union Against Tuberculosis and Lung Disease, Center for Operational Research, Paris, France, [3]International Union Against Tuberculosis and Lung Disease, Center for Operational Research, Delhi, India, [4]International Union Against Tuberculosis and Lung Disease, Monitoring, Evaluation, Accountability and Learning Unit, Mandalay, Myanmar, [5]International Union Against Tuberculosis and Lung Disease, TB, Mandalay, Myanmar, [6]Ministry of Health and Sports, National Tuberculosis Programme, Nay Pyi Taw, Myanmar, [7]Ministry of Health and Sports, Department of Public Health, Nay Pyi Taw, Myanmar.
e-mail: dr.khinewutyeekyaw2015@gmail.com

Background: Diagnosis of TB disease in children is challenging and enhanced quality diagnosis using appropriate diagnosis algorithm is needed in high TB burden countries. In this study we assessed how TB disease was diagnosed in children with presumptive pulmonary TB in relation to the diagnostic algorithm specified by the National TB Programme in eleven townships of Myanmar, where International Union Against Tuberculosis and Lung Disease has been working.
Methods: This was a cohort study using routinely collected data of children with presumptive pulmonary TB during January-June 2018. We defined failure to complete the diagnosis algorithm if the chest radiography was not done in children with negative or not recorded sputum result among symptomatic children. Log binomial regression was used to assess the factors associated with failure to complete diagnostic algorithm.
Results: Of the 1,061 children enrolled in presumptive TB registers, 969 (91.3%) had one or more symptoms of TB (cough, fever, loss of weight, night sweat, enlarged lymph node), 78 (7.3%) were asymptomatic and 14(1.3%) had no record for presence or absence of symptoms. The mean (standard deviation) age was 7(3) years, 292 (28%) were under 5-year-old and 147 (14%) had history of contact with active TB. Of the 969 symptomatic children, 275 (28%) underwent sputum tests (either smear microscopy or Xpert MTB/Rif test) and of the remaining, 707 (73%) children underwent chest radiography. Among them, 6/275 (2%) were bacteriologically-positive and 120/707 (17%) were clinically diagnosed as TB. Of 969, 256 (26%) did not complete the diagnosis algorithm as shown in figure 1. Children aged 10-15 years [relative risk 1.7, 95% CI 1.4-2.1] and females [1.2, 1.1-1.3] were more likely to fail to complete the diagnostic algorithm.
Conclusions: Three-fourths of the children with presumptive TB completed the diagnostic algorithm. The underlying reasons for non-compliance to diagnostic algorithm needs future research.



[Diagnosis of childhood TB in eleven selected project townships between January-June 2018, Myanmar]

SOA-15-1150-02 Retrospective evaluation of TB diagnosis using GeneXpert MTB/Rif® in Mozambican children

C Mutemba,[1] I Munyangaju,[2] N Ramanlal,[3] I Manhiça,[1] WC Buck,[4] [1]Mozambique Ministry of Health, TB Control Program, Maputo, Mozambique, [2]Elizabeth Glaser Pediatric AIDS Foundation, TB, Maputo, Mozambique, [3]Fundacao Ariel Glaser Contra o SIDA Pediatrica, TB, Maputo, Mozambique, [4]University of California Los Angeles, Pediatrics, Maputo, Mozambique.
e-mail: wchrisbuck@gmail.com

Background: The Mozambique National TB Control Program (NTP) introduced GeneXpert MTB/Rif® (GX) in 2011 and has been steadily expanding capacity, with 89 machines currently in use and sample referral networks for sites without machines. National guidelines recommend GX as the preferred diagnostic test in children, but still emphasize clinical TB diagnosis given lack of access to diagnostics in many parts of the country.
The 12,522 children treated in 2018 was an increase of 86% from 2015, but this equates to a pediatric case detection rate of just 54.4%, and only 12.3% were bacteriologically confirmed. There is little data available through routine reporting detailing how children are diagnosed, and whether improvements can be attributed to GX scale-up.
Methods: The Pediatric Technical Working Group of the NTP is conducting a national retrospective analysis of laboratory registers at sites with GX. Children 0-14 years with diagnostic testing (GX or microscopy) between January 2017 and December 2018 are included. Testing for treatment control is excluded. Data is collected by PEPFAR-supported clinical partners with NTP personnel.
Results: Preliminary results for three provinces which have completed data collection are presented. Only 6.5% of treated cases (261/4039) were confirmed by GX. GX positivity ranged from 3.2-9.5%, with 0.6-14.1% Rifampicin resistance detected in TB positive samples. Over one quarter (26.3%) of children tested were 0-4 years, but only 9.4% of samples were gastric aspirates or induced sputums. Province-specific results are detailed in **Table 1**.

	Cabo Delgado	Gaza	Maputo Province	Total
# children treated (drug-sensitive TB)*	839	1919	1281	4039
# children treated (MDR TB)*	0	10	15	25
# sites with GX	3	6	11	20
• # children tested	856	1927	2262	5045
• 0-4 yrs (#/%)	221 (25.8%)	731 (37.9%)	377 (16.7%)	1329 (26.3%)
• Gastric asp. or induced sputum (#/%)	159 (18.6%)	176 (9.2%)	138 (6.1%)	473 (9.4%)
• GX performed (#/%)	838 (97.9%)	1677 (87.0%)	1978 (87.4%)	4493 (89.1%)
• GX positive (#/%)	37 (4.4%)	160 (9.5%)	64 (3.2%)	261 (5.8%)
• Rif positive (#/%)	1 (2.7%)	1 (0.6%)	9 (14.1%)	11 (4.2%)

*[Table 1: Testing and Treatment by Province, 2017-2018 Aggregate Data, (*data from NTP annual reports)]*

Conclusions: While GX may have had a small contribution to increased pediatric TB treatment in Mozambique, it is not yet at scale sufficient to reduce reliance on clinical diagnosis. Invasive methods for specimen collection for younger children are under-utilized and access to GX could be improved with introduction of testing on stool and nasopharyngeal aspirates. This will be particularly important for improved diagnosis of drug-resistant TB in children.

SOA-15-1151-02 Standardised childhood tuberculosis case notification in limited source setting: experience of Afghanistan

MN Samadi,[1] GQ Qader,[1] MK Rashidi,[1] MK Seddiq,[2] N Ahmadzadah,[2] M Melese,[3] PG Suarez,[3]
[1]Management Sciences for Health (MSH), Challenge TB, Kabul, Afghanistan, [2]National Tuberculosis Control Program, National Tuberculosis Control Program, Kabul, Afghanistan, [3]Management Sciences for Health (MSH), Health Program Group, Arlington, WA, United States of America. e-mail: nazimsamadi@yahoo.com

Background and challenges to implementation: In Afghanistan, children under the age of 18 make 43% of the total general population. According to the 2018 WHO report, Tuberculosis (TB) new/existing cases among children under the age of 15 year were estimated to be 7,500 ranging between (4,300-11,000) in 2017. However, in 2014, the NTP notified 4,451 (49%) of it. The aim of this assess was to explore the role of new approach to diagnose TB among children.
Intervention or response: The National TB Program (NTP) in partnership with local stakeholders developed standard operation procedures (SOP) to diagnosis childhood TB and trained healthcare providers on it. The NTP revised guidelines for testing and diagnosis and used combination of clinical signs & symptoms, Tuberculin Skin Test (TST) readings, and chest X-rays (CXRs) findings. The diagnostic criteria contains signs and symptoms of TB, skin reaction to TST above 10 mm and CXR suggestive of TB. The NTP made available X-rays, TST availability in health facilities and trained the staffs on SOP for children. Further, one pediatrician was hired to facilitate and report quality diagnosis among children.
Results and lessons learnt: The number of children diagnosed with TB increased from 4,451 in 2014 to 10,446 in 2018 (135% increase). The proportion of children out of all TB cases notified was 14% in 2014 and increased to 21.7% in 2018. The male to female ratio of children under 5 was almost 1:1 in every year [see Table 1]
Conclusions and key recommendations: According the WHO estimate of childhood TB for 2017, the country notified all childhood TB cases and there were no missing cases in the country. In 2018, the national target set was to notify 10,800, the goal was almost achieved with 10,446 (96.7%) cases notified.

Year	All form of TB cases (new & relapse)	TB cases among children under 15 (%)	Childhood TB (<15 years, Disaggregated by gender) Male	Childhood TB (<15 years, Disaggregated by gender) Female
2014	31,746	4,451 (14%)	2,168	2,283
2015	35,878	4,951 (13.7%)	2,537	2,414
2016	41,954	6,365 (15.1%)	3,248	3,117
2017	46,640	9,732 (20.8%)	4,806	4,926
2018	48,131	10,446 (21.7%)	5,214	5,232

[All from TB case notification among children in Afghanistan (2014-2018)]

SOA-15-1152-02 Effect of active follow-up via phone of child TB patients on tuberculosis treatment outcomes in Kabul city: document review

SM Sayedi,[1] A Hamim,[1] MK Rashidi,[1] G Qader,[1] L Manzoor,[2] MN Samadi,[1] P Suarez,[3] BA Maseed,[1] D Safi,[1] [1]Management Sciences for Health (MSH), Challenge TB (CTB) Project, Kabul, Afghanistan, [2]Ministry of Public Health (MoPH), National Tuberculosis Program (NTP), NTP, Kabul, Afghanistan, [3]MSH, MSH, Arlington, VA, United States of America.
e-mail: msayedi@msh.org

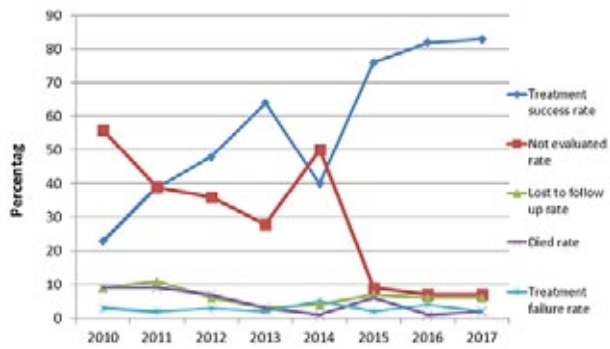
Background and challenges to implementation: In 2010, Kabul's population was 4,227,000, with 45% children under the age 15. The management of tuberculosis (TB) among children in Kabul was very poor due to only two specialized hospitals had the capacity to provide TB services for children. Concurrently, treatment follow-up was poor and disorganized, resulting in a treatment success rate (TSR) of only 23% for children. The aim of

this study was to investigate an active follow-up system using phones and its impact on the treatment success rate among child TB patients in Kabul city.

Intervention or response: In early 2015, the Challenge TB (CTB) project introduced a phone tracking system to monitor child TB patients who transferred out of specialized children's hospitals by health care staff to other facilities for treatment follow up. CTB provided health facility staff with mobile phones and pre-paid monthly cards to enable them to contact individual patients under treatment and their health facilities. The study team collected TSR data via phone from patients and health facilities, along with data from the National TB Program (NTP) TB reporting forms.

Results and lessons learnt: In 2010 at the baseline data collection, 206 child patients registered for TB treatment. Of the total children registered for treatment, 48 (23%) were successfully treated, 19 (9%) died, 19 (9%) were lost to follow-up, 6 (3%) had treatment failure, and 114 (55%) were not evaluated. In 2017, baseline data was collected which found 1,715 child TB cases were put into treatment. Of those 1,715 children, 1,428 (83%) were successfully treated, 32 (2%) died, 98(6%) were lost to follow-up, 39 (2%) had treatment failure, and 118 (7%) were not evaluated (See Figure 1).

Conclusions and key recommendations: The study revealed that using phone intervention to actively follow-up on TB child patients helped to significantly improve the TSR of children under the age 15 in Kabul.



[Table 1:Trend of treatment outcome among children in Kabul, 2010-20017]

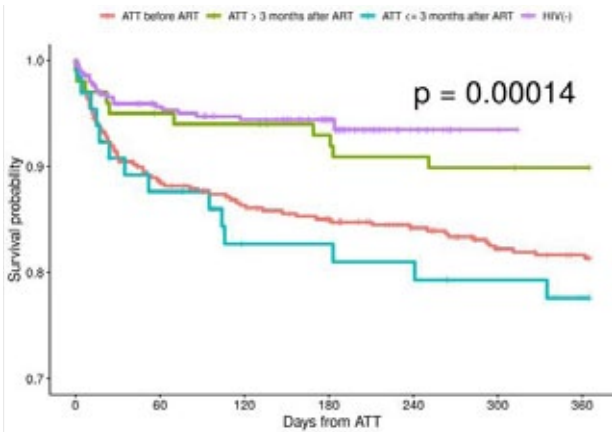
SOA-15-1153-02 Tuberculosis treatment outcomes among children in rural southern Mozambique: a 12-year retrospective study

E Nacarapa,[1,2] TD Moon,[3] D Osorio,[4] JM Ramos,[5] E Valverde,[6] [1]TINPSWALO Association - Fight AIDS and TB Vicentian Association, Research Unit, Chokwe, Mozambique, [2]Carmelo Hospital of Chokwe, Infectious Diseases, Chokwe, Mozambique, [3]Vanderbilt University Medical Center, Division of Pediatric Infectious Diseases, Nashville, TN, United States of America, [4]Macia Health Center, Pediatric Division, Macia, Mozambique, [5]University General Hospital of Alicante and Miguel Hernandez University of Elche, Department of Internal Medicine, Elche, Spain, [6]Aurum Institute, Operations Aurum International, Maputo, Mozambique. e-mail: edynacarapa@gmail.com

Background: Globally, tuberculosis (TB) remains a serious cause of morbidity and mortality for children. Mozambique is one of the 30 high TB and TB/HIV burden countries. This study aimed to assess treatment outcomes of childhood TB in Chókwè District, Mozambique.

Methods: A retrospective cohort study of children < 15 years of age treated for TB from 2006-2017 was conducted at Carmelo Hospital Chókwè (CHC). Descriptive statistics were used to summarize patient characteristics. Treatment outcomes stratified by HIV status were compared with chi-square. Multivariable logistic regression was used to estimate the odds of a favorable TB treatment outcome. Kaplan-Meier curves were used to estimate cumulative incidence of death.

Results: 933 cases of childhood TB were enrolled, 45.9% of which were female and 49.6% were < 5 years old. 762 (83.6%) cases had a favorable TB treatment outcome. Unfavorable outcomes were higher among children aged 0-4 years (65.8% vs. 34.2%; p< 0.001). Being aged 5-14 years was associated with lower risk of death (HR=0.435; 95% CI=0.299-0.632).



[Kaplan- Meier plot for TB Children enrolled at CHC (2006-2017) by ART status in relation to TB treat]

Those starting anti-TB treatment (ATT) ≤ 3 months after antiretroviral therapy (ART) initiation had a survival probability of approximately 75% at one year, com-

pared to 95% survival for those who were HIV-negative.
Conclusions: The majority of children in this cohort had favorable TB treatment outcomes. Worse outcomes were observed for younger children and if ATT started ≤3 months after initiation of ART. Rigorous screening for TB and isoniazid preventative therapy (IPT) may reduce the burden of TB in this population and lead to better outcomes.

SOA-15-1154-02 Injectable-free regimens containing bedaquiline and delamanid for adolescents with rifampicin-resistant tuberculosis in Khayelitsha, South Africa

E Mohr,[1] A Reuter,[1] J Furin,[2] A Garcia-Prats,[3] V De Azevedo,[4] V Mudaly,[5] Y Kock,[6] L Trivino-Duran,[7] J Hughes,[3] [1]Medecins Sans Frontieres, DR-TB, Khayelitsha, South Africa, [2]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [3]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatric and Child Health, Faculty of Medicine and Health Sciences, Cape Town, South Africa, [4]City of Cape Town Department of Health, Primary Health Care Health Department, Cape Town, South Africa, [5]Western Cape Provincial Department of Health, Health Programmes, Cape Town, South Africa, [6]National Department of Health, DR-TB Programme, Johannesburg, South Africa, [7]Medecins Sans Frontieres, Coordination Office, Cape Town, South Africa.
e-mail: msfocb-khayelitsha-drtb-epi@brussels.msf.org

Background: Limited data exist on the use of bedaquiline and delamanid in adolescents with rifampicin-resistant tuberculosis (RR-TB) as a result of limited access to these medications in this age group. We describe RR-TB treatment of adolescents (ages 10-19 years) with injectable-free regimens containing these drugs in Khayelitsha, South Africa.
Methods: This retrospective cohort study included adolescents initiating injectable-free RR-TB treatment regimens containing bedaquiline and/or delamanid from February 2015 to June 2018. We report sputum culture conversion (SCC), adverse events (AEs), and interim treatment outcomes.
Results: Twenty-two patients were included; 13 (59%) were males, median age at treatment initiation was 17 years (interquartile range [IQR] 15-18), and six (27%) were HIV-positive (median CD4 count 191 cells/mm^3 [IQR 157-204]). Eight (36%) patients had RR-TB with fluoroquinolone resistance; 10 (45%), eight (36%), and four (18%) patients received regimens containing bedaquiline, delamanid, or the combination of bedaquiline and delamanid, respectively. The median times on bedaquiline and delamanid were 5.6 (IQR 5.5-8.4) and 9.4 (IQR 5.9-14.4) months. Eleven (50%) patients received a regimen containing linezolid (600mg daily aside from one patient who received 300mg daily). Overall, there were 49 AEs of interest which occurred in 17 (77%) patients; AEs are described in Table 1.

	Median (IQR) time to onset (months)	Grade 1 Instances / patient	Grade 2 Instances / patient	Grade 3 Instances / patient	Grade 4 Instances / patient	Total Instances / patient
Alanine Aminotransferase Increased	2.2 (1.5-3.5)	8 N=4 (18%)	2 N=2 (9%)	0	0	10 N=4 (18%)
White Blood Cell Decreased	6.4 (1.80-19.0)	14 N=6 (27%)	0	0	0	14 N=6 (27%)
Anaemia	2.4 (1.8-4.6)	8 N=5 (23%)	8 N=6 (27%)	3 N=2 (9%)	1 N=1 (5%)	20 N=7 (32%)
Thrombocyto-paenia	1.3	0	0	0	1 N=1 (5%)	1 N=1 (5%)
QTcF prolongation	3.0 (2.0-4.5)	4 N=4 (18%)	0	0	0	4 N=4 (18%)
Total of each grade	3.0 (1.8-6.5)	34 N=16 (73%)	10 N=7 (32%)	3 N=2 (9%)	2 N=2 (9%)	4 N=4 (18%)

[Adverse events of interest among adolescents who received injectable-free RR-TB treatment regimens containing bedaquiline and/or delamanid]

Fourteen (64%) patients had pulmonary TB and were culture positive at bedaquiline and/or delamanid initiation; among these SCC at month 6 was 79%. Final outcomes for the 22 adolescent included in this study were as follows: 17 (77%) successfully treated, two (9%) lost to follow-up, two (9%) treatment failure, and one (5%) died.
Conclusions: Adolescents commonly fail to benefit from drugs that are being used safely in adults. This study found that injectable-free regimens containing bedaquiline and/or delamanid in a programmatic setting were efficacious, well tolerated and should be routinely used for treatment of RR-TB in this age group.

SOA-15-1155-02 Palatability and acceptability of routinely used formulations of levofloxacin, moxifloxacin and linezolid among South African children treated for multidrug-resistant tuberculosis

JL Winckler,[1] HR Draper,[1] HS Schaaf,[1] LE Van der Laan,[1] AC Hesseling,[1] AJ Garcia-Prats,[1] [1]Stellenbosch University, Paediatrics, DTTC, Cape Town, South Africa. e-mail: janawinckler@sun.ac.za

Background: Medication acceptability and palatability may influence adherence and treatment success. However, there are few suitable paediatric formulations of medications for multidrug-resistant tuberculosis (MDR-TB) treatment and limited data on the acceptability of existing formulations in children.
Methods: We studied the acceptability and palatability of the routinely available formulations of linezolid (600 mg tablets swallowed whole or 20 mg/mL suspension), levofloxacin (250 mg tablets swallowed whole or crushed with water) and moxifloxacin (400 mg tablets swallowed whole or as extemporaneous suspension) in

Drug and formulation type		Levofloxacin Liquid	Levofloxacin Solid	Moxyfloxacin Liquid	Moxyfloxacin Solid	Linezolid Liquid	Linezolid Solid
Self Reported assessment	Child disliked taste (%)	100.0	33.3	90.0	25	50	66.7
	Child disliked smell (%)	66.7	22.2	90	0	33.3	50
	Child felt amount/volume was too large or much too large (%)	66.7	44.4	70	50	33	0
Observed Assessment	Child disliked taste (%)	N/A	N/A	77.8	N/A	25	N/A

[SOA- 15 -1155-02 Table. Palatability results table by formulation type]

South African children 0-17 years of age routinely treated for MDR-TB. Acceptability was defined as the overall suitability of the formulation, including dose volume or size and palatability, the overall acceptance of taste, smell, volume or size, and texture of an oral medication. For young children unable to self-report, caregivers or study team observed children's intake and documented the amount swallowed, and the child's reaction. A visual analog scale (VAS) and facial hedonic scale was used by older children to rate taste, smell, look and texture.

Results: 11 observed assessments were done by study staff in young children (median age 3.7 years, range 1.8 to 4.3). 15 older children provide self-reported assessments (median age 12.0 years, range 7.8-12.9). See the table for summary of the results.

Conclusions: Crushed tablets of levofloxacin and moxifloxacin had poor acceptability and poor palatability, which is not ideal for use in children and could lead to poor adherence, vomiting and difficulty in administration. Although the linezolid suspension was acceptable to the majority of children, it is very expensive and not widely available. Although limited by a small sample size, this study illustrates the fundamental importance of paediatric formulations of antituberculosis drugs that are palatable and easily administered to children.

SOA-16-A3 TB diagnostic innovations

SOA-16-1157-02 Development and evaluation of novel bio-safe filter paper-based kits for sputum microscopy and transport to directly detect Mycobacterium tuberculosis and associated drug resistance

D Anthwal,[1,2] S Lavania,[3] RK Gupta,[1] A Verma,[4] VP Myneedu,[4] V Malhotra,[5] NK Gupta,[6] R Sarin,[4] S Haldar,[1,2] JS Tyagi,[2,3] [1]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Experimental Medicine and Biotechnology, Chandigarh, India, [2]Translational Health Science and Technology Institute, Center for Bio-Design and Diagnostics, Faridabad, India, [3]All India Institute of Medical Sciences (AIIMS), Department of Biotechnology, New Delhi, India, [4]National Institute of Tuberculosis and Respiratory Diseases, Department of Microbiology, New Delhi, India, [5]TB Hospital, Department of Microbiology, Ambala, India, [6]Advanced Microdevices Pvt Ltd, Mdi, Ambala, India.
e-mail: anthwal.divya14@gmail.com

Background: India has the highest burden of Tuberculosis (TB) and multidrug-resistant TB (MDR-TB) in the world. Finding the 'missing' millions is a major challenge in TB control. Innovative technology is the need of the hour to identify these cases that remain either undiagnosed or inadequately diagnosed due to the unavailability of appropriate tools at primary healthcare settings.

Methods: We developed and evaluated 3 kits, namely 'TBChek' (containing BioFM-Filter device), 'TBact Transport' (containing *Trans*-Filter device) and 'TB DNA' kits. These kits enable bio-safe equipment-free concentration of sputum on filters and improved fluorescence microscopy at primary healthcare centres, ambient temperature transport of dried inactivated sputum filters to central laboratories and molecular detection of drug resistance by PCR and DNA sequencing (Molecular-Drug Susceptibility Testing [Mol-DST]).

Results: In a 2-site evaluation (n=1190 sputum specimens) on presumptive TB patients, BioFM-Filter smear exhibited an increase in positivity of 7%and 4% over ZN smear and LED-FM smear, respectively and an increment in smear grade status (1+ or 2+ to 3+) of 16% over ZN smear and 20% over LED-FM smear.

The concordance between BioFM-Filter microscopy vs. ZN and LED-FM smear was 91-93% (κ value=0.73-0.8). The sensitivity of Mol-DST in presumptive MDR-TB and XDR-TB cases(n=148) was 90% for Rifampicin (95% confidence interval [CI], 78-96%), 84% for Isoniazid (95% CI, 72-92%), 83% for Fluoroquinolones (95% CI, 66-93%) and 75% for Aminoglycosides (95% CI, 35-97%), using phenotypic DST as the reference standard. Test specificity was 88-93% and concordance was ~89-92% (κ value=0.8-0.9).
Conclusions: The patient-friendly kits described here address several of the existing challenges and are designed to provide 'Universal Access' to rapid TB diagnosis, including drug-resistant disease. Their utility was demonstrated by application to sputum at 2 sites in India. Our findings pave the way for larger studies in different point-of-care settings, including high-density urban areas and remote geographical locations.

SOA-16-1158-02 CAPTURE-XTTM concentration and isolation of bacteria from sputum using a novel microfluidic-dielectrophoretic technology to enable rapid diagnosis of Mycobacterium tuberculosis (TB) in clinical samples

HE Murton,[1] C Adams,[1] K Gizynski,[1] J Dhillon,[2] CM Moore,[2] E Boada,[1] D McGurk,[1] L Schmid,[3] PD Butcher,[2] J O'Halloran,[4] [1]QuantuMDx, Group Ltd., Newcastle Upon Tyne, United Kingdom, [2]St Georges University, Institute for Infection and Immunity, London, United Kingdom, [3]QuantuMDx, Clinical Assay, Newcastle Upon Tyne, United Kingdom, [4]QuantuMDx, R&D, Newcastle Upon Tyne, United Kingdom.
e-mail: jonathan.ohalloran@quantumdx.com

Background: To achieve the global efforts to End TB, diagnostics with increased sensitivity and expanded drug susceptibility testing (DST) are required. Equally or arguably more importantly, TB diagnostics which are affordable, and suitable for true point-of-care (POC) implementation are required to reach the missing millions.
Methods: Many diagnostic tools fail to access all bacilli present in a patient sample due to the complexity of sputa, resulting in reduced sensitivity. QuantuMDx have developed CAPTURE-XT™ pathogen concentration to overcome this issue, enabling the extraction and concentration of TB bacilli from sputum providing an optimised input for molecular analysis. The lab-on-a-chip technology uses Dielectrophoresis to concentrate and purify *Mycobacterium* in a methodology suitable for adaptation to laboratory-free POC application. Comparison of CAPTURE-XT to Culture and Smear microscopy was undertaken in a 100-patient blinded sample trial using characterised and bio-banked sputum samples (provided by FIND).
Results: A concordance to culture diagnosis of 87% (61/70) for TB positive samples and of 93% (42/45) for smear-positive samples was demonstrated. 37% of samples were from HIV co-infected patients with a concordance to culture diagnosis of 78% (18/23) for TB positive samples and of 89% (16/18) for smear-positive samples. Ongoing studies using near-patient samples with the Lung Institute, University of Cape Town is currently demonstrating significant improvements in sensitivity for low-burden samples with 100% concordance to culture in an initial sample trial (currently n=20) using TaqMan PCR as a molecular read-out.
Conclusions: These results demonstrate the potential of CAPTURE-XT™ to provide a powerful front-end for molecular detection and DST in a true POC setting and in a system suited to low cost testing. This versatile tool could equally be applied as a stand-alone visual detection platform for low cost screening or coupled with on-device culture for phenotypic DST, providing a novel approach to TB Healthcare systems.

SOA-16-1159-02 Performance assessment of two tuberculosis-specific targeted next generation sequencing assays for drug resistance detection

R Colman,[1,2] N Hillery,[1] A Suresh,[1] C Denkinger,[1] T Rodwell,[1,2] [1]Foundation for Innovative New Diagnostics (FIND), Tuberculosis, Geneva, Switzerland, [2]University of California, Medicine, San Diego, CA, United States of America. e-mail: rcolman@ucsd.edu

Background: Acquisition and transmission of drug resistant *Mycobacterium tuberculosis* (Mtb) threatens the WHO goal to end tuberculosis (TB) by 2035. The inability to rapidly detect drug-resistance (DR) profiles in TB patients represents one of the most urgent gaps in TB diagnosis. Targeted next-generation sequencing (tNGS) is a promising approach for comprehensive DR detection direct from sputum.
Methods: We assessed the performance of two TB-specific tNGS assays (TGen's RDST assay and Genoscreen's Deeplex® Myc-TB assay) using blinded, highly-characterized DNA samples extracted from clinical Mtb strains. The selected samples had a variety of phenotypic resistance to rifampin, isoniazid, pyrazinamide, fluoroquinolones, and second-line injectables, with a large diversity of clinically relevant drug resistance associated mutations. We evaluated the performance of the two tNGS assays against both a genotypic reference standard (whole genome sequencing - WGS) and a phenotypic reference standard (liquid culture-based drug susceptibility testing). We also evaluated the assays' dynamic ranges for assay success (calls across all targets, full DR profile) using Mtb DNA dilution curves spiked with human DNA.
Results: Reproducibility of variant calls for blinded triplicates across 50 genetically well-characterized DNAs (including confidence-graded drug resistance associated single nucleotide polymorphisms - SNPs), was 99.1% and 99.9% for RDST and Deeplex Myc-TB respectively.

SNP calls were highly concordant between the tNGS assays and the WGS reference, resulting in high genotypic percent agreement: 95.8-100% and 97.9-100% for RDST and Deeplex Myc-TB respectively for each locus reported.
The addition of human DNA as a potentially interfering agent did not affect either assays' performance significantly, but for RDST increased background noise for detection of minor drug resistant subpopulations.
Conclusions: These findings highlight the accuracy and reproducibility of two tNGS assays used for the detection of clinically relevant resistance-conferring mutations in a diverse set of Mtb strains.

SOA-16-1160-02 The BioNumerics MTBC genotyping plugin: NGS-based lineage determination, in silico spoligotyping, and associations with resistance for the Mycobacterium tuberculosis complex made easy

M Diricks,[1] K De Rauw,[1] M Rodrigue,[2] J Vanderbeke,[1] H Pouseele,[1] K De Bruyne,[1] [1]Applied Maths, bioMérieux, Data Analytics, Sint-Martens-Latem, Belgium, [2]bioMérieux, Global Medical Affairs, Marcy L'Etoile, France.
e-mail: margo.diricks@biomerieux.com

Background: Despite global efforts, the disease burden of tuberculosis (TB) remains very high and the transmission of drug-resistant *Mycobacterium tuberculosis* complex (MTBC) strains is becoming an increasing challenge. Decreasing costs and turn-around-time allow for rapid generation of whole-genome sequencing (WGS) data of MTBC isolates, but there is still a need for user-friendly, high-throughput tools for molecular typing and drug susceptibility analysis. In this study, publicly available WGS data of 1714 isolates were analyzed with the BioNumerics MTBC genotyping plugin.
Methods: The BioNumerics MTBC pipeline includes a SNP-based lineage determination (8 lineages and 55 sublineages); an *in silico* spoligotyping analysis; and a resistance prediction tool for 16 antibiotics based on known resistance mutations. The pipeline is implemented on a high-throughput calculation environment providing results within 15 minutes and allowing for batch analysis of >250 samples/day. Results are stored in a BioNumerics database were they can be easily analyzed, visualized and combined with other data (eg. MIRU-VNTR, wgMLST).
Results: Lineage prediction was in concordance with the described lineage in 100 % of the isolates for lineages 1, 5, 6, and *M. bovis*; and in >98 % for lineage 2, 3, and 4. The *in silico* spoligotyping results correlated with the predicted lineages. In total, 432 octal spoligotypes were detected, with 000000000003771 (sublineage 2 East-Asian Beijing) being the most prevalent (n=422). The plugin predicted 40.0 % of the isolates to be associated with multi-drug resistance (MDR) and 6.8 % to extensive drug resistance (XDR). Resistance mutations were detected in 14 out of 16 antibiotics; resistance against ethambutol, rifampicin, and isoniazid were the most common (45.2 %, 49.9 %, and 53.4 %, respectively).
Conclusions: Starting from WGS data, the BioNumerics MTBC genotyping pipeline allows to easily detect and subtype emerging high-risk XDR or MDR-TB strains, facilitating routine DR-TB diagnosis and surveillance.

SOA-16-1161-02 High-resolution melting curve analysis: a rapid approach for diagnosis and screening of drug resistance directly from CSF sample of tuberculous meningitis patients

K Sharna,[1] M Modi,[2] A Sharma,[3] P Ray,[1] [1]PGIMER, Medical Microbiology, Chandigarh, India, [2]PGIMER, Neurology, Chandigarh, India, [3]PGIMER, Internal Medicine, Chandigarh, India. e-mail: sharmakusum9@yahoo.co.in

Background: The diagnosis of TBM and susceptibility/resistance is difficult as TB MGIT culture lacks sensitivity and timeliness. Timely and accurate diagnosis of the TBM is the need of the hour for initiation of appropriate therapy. We have exploited real time PCR followed by high resolution melt curve (HRM) analysis to detect TB along with associated Multi/extensively drug resistant (MDR/ XDR-TB) directly from Cerebrospinal Fluid (CSF) specimens.
Methods: Real time PCR using IS6110 and MPB64 genes was carried out in 100 cases of TBM and in100 non TB control group. The study group included 30 culture confirmed cases and 70 clinically suspected TBM cases. Phenotypic MGIT liquid culture drug susceptibility was carried out for first and second line anti-tuberculosis drugs. DNA from CSF of all RT PCR positive cases were subjected to HRM analysis with *rpo*B , *kat*G, inhA, gyrA, rrs and eis genes. Sequencing & phenotypic DST (PDST) was used to confirm results of HRM analysis.
Results: The sensitivity of MPB64 and IS6110 RT PCR was 86% and 80%. HRM analysis detected MDR in 7/100 (7%) .Out of 7 MDR cases, one was detected as XDR and was confirmed on PDST& sequencing. Of the 11 cases of isoniazid (INH) resistance detected by HRM analysis, 7(63.66%) were MDR, while 4(36.36%) were isolated INH resistant, and mono floroquinolone (FQ) resistance was detected in 2/100 (2%) cases. In HRM analysis detected additional 2MDR, 2 mono INH resistance and one cases of isolated FQ resistance ,as these were all culture negative cases. Results of HRM analysis were confirmed by sequencing. There was 100% concordance in the results of PDST, sequencing and HRM analysis.
Conclusions: HRM analysis can play a valuable role in reliable and rapid screening of drug resistance in TBM cases in 90 minutes especially in high endemic settings where culture facilities are not available.

SOA-16-1162-02 Direct detection of fluoroquinolone-resistance in sputum samples from tuberculosis patients by high-resolution melt curve analysis

R Gupta,[1] D Anthwal,[1] M Bhalla,[2] J Sivaswami Tyagi,[3,4] S Haldar,[1,4] [1]Post Graduate Institute of Medical Education & Research (PGIMER), Department of Experimental Medicine and Biotechnology, Chandigarh, India, [2]National Institute of Tuberculosis and Respiratory Diseases, Mehrauli, Department of Microbiology, Delhi, India, [3]All India Institute of Medical Sciences, Biotechnology, Delhi, India, [4]Translational Health Science and Technology Institute, Center for Bio-design and Diagnostics, Faridabad, India. e-mail: rakesh23321@gmail.com

Background: Tuberculosis (TB) remains one of the most serious infectious diseases worldwide, causing 1.3 million deaths each year. TB treatment due to multidrug-resistant (MDR) *Mycobacterium tuberculosis* (*M. tuberculosis*) (resistance to isoniazid and rifampicin) requires the use of fluoroquinolones (FLQ). However, the widespread use of FLQ has led to the rise of extensively drug-resistant TB (XDR-TB), which is linked to poor treatment outcomes. FLQ resistance is a major problem and 22% of MDR-TB cases were resistant to FLQ drugs in 2017. This study was carried out to evaluate the utility of high-resolution melt curve analysis (HRM) for the rapid and direct detection of FLQ resistance in *M. tuberculosis* in sputum samples.

Methods: A reference plasmid library was generated for most frequently observed mutations in the resistance determining regions of *gyrA* gene (quinolone resistance-determining region; QRDR) and used as positive controls in HRM. The assay was first evaluated in 20 MDR-*M. tuberculosis* clinical isolates and then validated on DNA isolated from 70 *M. tuberculosis* culture-positive sputum samples that included 56 smear-negative sputum samples, using DNA sequencing as gold standard. Mutants were discriminated from the wild type by comparing melting-curve patterns with those of control plasmids using HRM software.

Results: FLQ resistance was detected in 4 samples by HRM and sequencing (3/4 samples were smear negative). One additional sample was picked up as FLQ mutant by sequencing. The FLQ-HRM assay had sensitivity and specificity of 100% (95% CI 99.3-100) and 96.4% (95% CI 81.65-99.91), respectively. The HRM results showed a 98.5% (κ value=0.97) concordance to DNA sequencing. The HRM assay also detected the presence of the natural polymorphism (S95T mutation) in *gyrA* in 39/70 samples.

Conclusions: The HRM assay was a rapid, cost effective (INR 180/USD 2.8) and closed-tube method for direct detection of FLQ resistance in sputum samples especially for smear-negative sputum samples.

SOA-16-1163-02 Suboptimal thermocycler ramp rate for MTBDR assays negatively impacts the diagnosis of drug-resistant tuberculosis

B Derendinger,[1] M de Vos,[1] S Pillay,[1,2] T Dolby,[2] R Warren,[1] G Theron,[1] [1]DST/NRF Centre of Excellence for Biomedical Tuberculosis Research, SA MRC Centre for Tuberculosis Research, Faculty of Medicine and Health Sciences, Department of Molecular Biology and Human Genetics, Stellenbosch University, Cape Town, South Africa, [2]National Health Laboratory Services, Green Point, TB Department, Cape Town, South Africa. e-mail: brigitta@sun.ac.za

Background: In 2017, 457 560 people were estimated to have multidrug-resistant tuberculosis (MDR-TB) and 8.5% of these, extensively drug-resistant (XDR)-TB. 50% of MDR-TB patients are tested for second-line resistance. We previously showed that performance of MTBDR*plus*, a test usually done prior to MTBDR*sl*, is reduced in smear-negative sputa when a suboptimal thermocycler ramp rate (speed of temperature change during cycles) is used, and that this is a widespread problem.

Methods: We tested 52 smear-negative Xpert MTB/RIF Ultra-positive sputa (17 MDR, 24 pre-XDR, 11 XDR) at a suboptimal ramp rate of 4.0°C/s and 2.2°C/s (manufacturer-recommended). *Mycobacterium tuberculosis*-complex DNA (TUB-band)-detection, accuracy for fluoroquinolone (FQ)- and second-line injectable (SLID)-resistance, indeterminate rates and banding calls were assessed. Separately, on a dilution series of cells [susceptible- and XDR-strain (10^2, 10^3 and 10^4CFU/ml)], inter-reader variability was assessed between two experienced readers at each ramp rate.

Results: Although no improvement was seen in smear-negative sputa for TUB-band detection at 2.2 vs. 4.0°C/s (52/52 vs. 51/52; p=0.32), at 2.2°C/s indeterminate rates improved (0/52 vs. 7/52; p=0.006) and there were less erroneous bands (0/52 strips with an erroneous band vs. 14/52; p< 0.001). These erroneous bands were all false absent bands. Overall, the number of valid results (not TUB-negative, indeterminate or incorrect band; 52/52 vs. 41/52, p< 0.001) hence improved by 21% (95% CI: 8-34%). Of the 189 possible non-control bands in the dilution series of cells (21 bands per strip x 3 dilutions x 3 replicates) for the susceptible strain, readers disagreed on 0.5% (1/189) of bands at 4.0 °C/s but none at 2.2 °C/s (p=0.32). For the XDR strain, there were 2/189 (1.1%) band differences between readers at 4.0 °C/s and none at 2.2 °C/s (p=0.48).

Conclusions: Thermocycler ramp rate contributes to suboptimal performance of MTBDR*sl* on smear-negative sputa. Correction of ramp rate will likely improve the yield of rapid diagnoses for second-line drug susceptibility.

SOA-16-1164-02 Diagnostic sensitivity and time-to-detection (TTD): a direct comparison between the MDR/XDR-TB Colour Test and established liquid and solid culture techniques

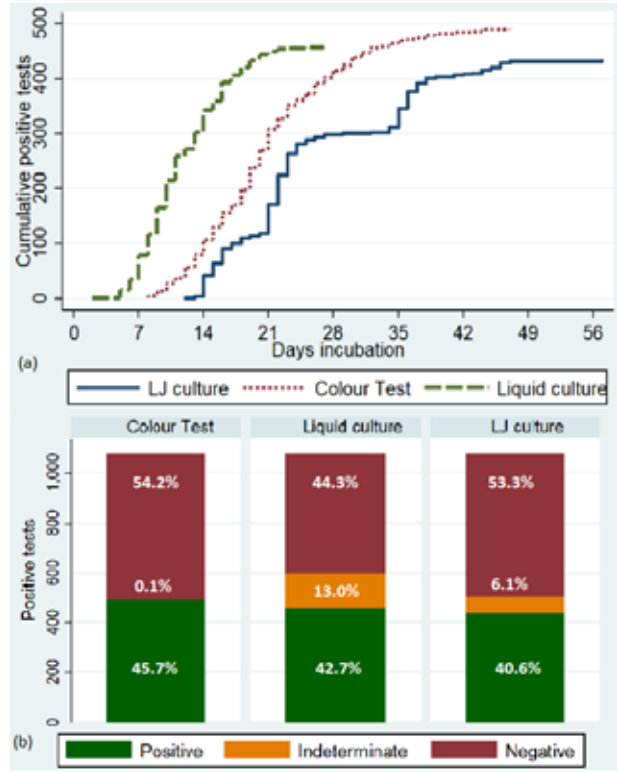
JP Wilson,[1,2] T Valencia,[1,2] R Montoya,[1,2] ES Ramos,[1,2] K Alvarado,[1,2] L Bernaola,[1,2] N Bailon,[1,2] B Herrera,[1,2] S Datta,[1,2,3] CA Evans,[1,2,3] [1]IFHAD - Innovation for Health and Development, Universidad Peruana Cayetano Heredia LID416, Laboratory for Health and Development, Lima, Peru, [2]IPSYD - Innovación por la Salud y Desarollo, Asociación Benéfica Prisma, Lima, Peru, [3]IFHAD - Innovation for Health and Development, Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, London, United Kingdom. e-mail: jpwilson123@outlook.com

Background: Tuberculosis predominantly affects resource-constrained settings where insensitive sputum microscopy remains the primary diagnostic method. Universal access to affordable and timely diagnosis remains a challenge in the global fight against tuberculosis. We evaluated the 'MDR/XDR-TB Colour Test'; a non-commercial thin-layer agar technique that provides simultaneous tuberculosis diagnosis and direct drug-susceptibility testing (DST).

Methods: Diagnostic sputum samples were collected from patients in Peru. Simultaneous culture was performed with: (1) Lowenstein Jenson (LJ) culture, (2) liquid culture (microscopic observation drug susceptibility (MODS) assay), and (3) the Colour Test, for which sputum was disinfected and directly inoculated without centrifugation onto four plate quadrants containing M7H11 growth medium and a colour growth indicator. Three quadrants contained anti-tuberculous drugs for DST. One quadrant remained drug-free for detection. Following inoculation, plates were sealed in an airtight bag and incubated for 6 weeks. Naked-eye screening for detection quadrant colour change occurred twice-weekly, and positive results confirmed by microscopic examination for characteristic colony cording. LJ and liquid cultures were processed as per established protocols with decontaminated and centrifuged sputum. Sensitivity was calculated using a composite gold standard of any positive culture.

Results: Of 1077 sputum samples, 543 (50.4%) grew tuberculosis by any method. TTD is presented in figure 1(a): fastest for liquid (median=11 days, inter-quartile range (IQR)=8-15 days), followed by the Colour Test (20 days, IQR=15-25 days) and LJ (22 days, IQR=18-35 days). Sensitivity was greatest for the Colour Test (90.6%, 95% confidence interval (CI)=87.8-92.9%), intermediate for liquid (84.7%, 95% CI=81.4-87.6%) and lowest for LJ (80.5%, 95%CI=76.9-83.7%). Diagnostic yields are presented in figure 1(b).

Conclusions: We present a study larger than all previous evaluations combined, demonstrating high diagnostic sensitivity of the Colour Test relative to established culture techniques. At USD$1 material costs per test, and providing simultaneous DST, the Colour Test is an inexpensive and relatively bio-safe alternative to established diagnostic techniques.



[Figure 1(a): Comparative time-to-diagnosis. Figure 1(b): Comparative diagnostic yields]

SOA-16-1165-02 Utility of cell-free Mycobacterium tuberculosis DNA for the improved diagnosis of abdominal tuberculosis

P Sharma,[1] D Anthwal,[1] P Kumari,[2] RK Gupta,[1] S Lavania,[2] N Sharma,[3] LK Sharma,[3] RL Taneja,[4] JS Tyagi,[2,5] S Haldar,[1,5] [1]Post Graduate Institute of Medical Education and Research, Department of Experimental Medicine and Biotechnology, Chandigarh, India, [2]All India Institute of Medical Sciences, Department of Biotechnology, New Delhi, India, [3]Dr. Ram Manohar Lohia Hospital, Department of Biochemistry, New Delhi, India, [4]Dr. Ram Manohar Lohia Hospital, Department of Medicine, New Delhi, India, [5]Translational Health Science and Technology Institute, Center for Bio-Design and Diagnostics, Faridabad, India.
e-mail: pratibha.pgimer@gmail.com

Background: Extra-pulmonary TB (EPTB) constitutes ~15-20% of all TB cases worldwide. Abdominal TB (ATB) contributes to 3% of all EPTB cases in India. ATB is a major diagnostic challenge due to its non-specific clinical features and limited yield of standard diagnostic tests. In spite of the development of several molecular assays till date; no single test is suitable for ATB diagnosis.

Here, we for the first time report the detection of cell-free *Mycobacterium tuberculosis* DNA (cMTB-DNA) in ascitic fluid (AF) and its utility in ATB diagnosis.
Methods: A composite reference standard (CRS) comprising of cyto-biochemical, microbiological, radiological parameters and response to therapy was developed to categorize the prospectively enrolled patients (n=67) into 'Definite ATB' (culture positive n=2), 'Probable ATB' (n=15), 'Possible ATB' (n=13) and 'Non-TB' category (n=37). All samples were subjected to liquid culture, cytology, biochemical and molecular assays which included the *devR*-based cMTB-DNA qPCR assay and Xpert MTB/RIF assay (Xpert). The diagnostic accuracy of the molecular assays was assessed using CRS as reference standard.
Results: ROC curves were generated from cMTB-DNA qPCR data of 'Definite+Probable' ATB and 'Non-TB' group and cut-off was set to achieve a ≥ 95% specificity. The cMTB-DNA qPCR assay had a sensitivity of ~ 65% (95% CI:38,86) in 'Definite ATB' and 'Probable ATB' category collectively. The sensitivity of the developed assay increased to 80% (95% CI: 61, 92) on addition of 'Possible ATB' patient group in the evaluation of the assay. Xpert had a poor sensitivity of ~7% (95% CI:0.82, 22) with 100% specificity (95% CI:90.5,100). Fever, weight loss, alcoholism and positive mantoux findings were found to be associated with ATB disease ($p < 0.05$).
Conclusions: The developed cMTB-DNA qPCR assay for ATB meets the sensitivity criterion spelt out in the 'Target product profile' for EPTB samples by UNITAID and has the potential to bridge the existing gap in ATB diagnosis.

SOA-16-1166-02 Cell-free DNA in plasma and urine can be used to diagnose active tuberculosis: preliminary results

A Steadman,[1] S Byrnes,[1] C Bennett,[1] T Motley,[1] A Andama,[2] A Cattamanchi,[3] D Bell,[4] J Connelly,[1] A Somoskovi,[5] D Madan,[1] [1]Intellectual Ventures Laboratory & Global Good, Center for In Vitro Diagnostics, Bellevue, WA, United States of America, [2]Infectious Diseases Research Collaboration, Department of Medical Microbiology, Kampala, Uganda, [3]University of California San Francisco, School of Medicine, Sab Francisco, CA, United States of America, [4]Independent Consultant, N/A, Bellevue, WA, United States of America, [5]Global Good, Global Health Technologies, Bellevue, WA, United States of America. e-mail: asteadman@intven.com

Background: *Mycobacterium tuberculosis* (*Mtb*) cell-free DNA (cfDNA) from plasma and urine may provide a new opportunity for sputum-free diagnosis and follow up of treatment of active tuberculosis (TB), especially in patients with non-productive cough such as children and persons living with HIV. We sought to assess the feasibility of generating a cfDNA-based TB diagnostic suitable for deployment in TB-endemic-region healthcare systems.
Methods: We optimized clinical sample storage conditions, developed automation-compatible DNA extraction and concentration methods, and designed and validated an assay employing non-nested multiplex PCR followed by DNA probe microarray amplicon detection. To assess the starting quantity of each cfDNA *Mtb* target in clinical specimens from Uganda, we designed and validated two tetraplex ddPCR assays.
Results: In early method-optimization-stage research, we detected 21 of 28 (75%) GeneXpert-positive tuberculosis cases using urine cfDNA, and 22/30 (73.3%) GeneXpert-positive tuberculosis cases using plasma cfDNA. Specificity was 76.2% (16 of 21) in urine and 84.2% (16 of 19) in plasma for GeneXpert-negative clinical specimens from Uganda.
Conclusions: Our results from clinical samples suggest *Mtb* cfDNA from plasma and urine is a suitable biomarker providing convenient, extrapulmonary-sensitive, and less-infectious sampling for diagnosis of tuberculosis in regions of prevalence.

SOA-16-1167-02 Pretomanid susceptibility testing of Mycobacterium tuberculosis complex isolates using the BACTECTM MGITTM 960 system

A Bateson,[1] S Andres,[2] S Niemann,[3,4] A Ghodousi,[5] R Groenheit,[6] D Machado,[7] C Köser,[8] A Witney,[9] J Timm,[10] CM Mendel,[10] [1]University College London, Centre for Clinical Microbiology, London, United Kingdom, [2]Research Center Borstel, National Reference Centre for Mycobacteria, Borstel, Germany, [3]Research Center Borstel, Molecular and Experimental Mycobacteriology, Borstel, Germany, [4]Partner Site Hamburg-Lübeck-Borstel-Riems, German Centre for Infection Research, Hamburg, Germany, [5]San Raffaele Scientific Institute (HSR), Emerging Bacterial Pathogens Unit, Milan, Italy, [6]Public Health Agency of Sweden, Supranational Reference Laboratory for Tuberculosis, Stockholm, Sweden, [7]Universidad Nova de Lisboa, Global Health and Tropical Medicine, Instituto de Higiene e Medicina Tropical, Lisboa, Portugal, [8]University of Cambridge, Department of Genetics, Cambridge, United Kingdom, [9]St Georges University, Institute of Infection and Immunity, London, United Kingdom, [10]TB Alliance, Research and Development, New York, NY, United States of America. e-mail: juliano.timm-consultant@tballiance.org

Background: Pretomanid is a new compound under evaluation for the treatment of tuberculosis (TB). Of note, a recent interim analysis of the Nix-TB trial (https://www.tballiance.org/portfolio/trial/5089) showed that treatment for six months with the combination of bedaquiline, pretomanid and linezolid resulted in a favourable response at six months after completion of therapy in 9 out of 10 patients with extensively drug-resistant (XDR), or treatment-intolerant or nonresponsive multidrug resistant (MDR) TB. Because of these promising results, this multi-centre study was conducted to define protocols and quality control (QC) ranges for pretomanid drug susceptibility testing (DST) using the

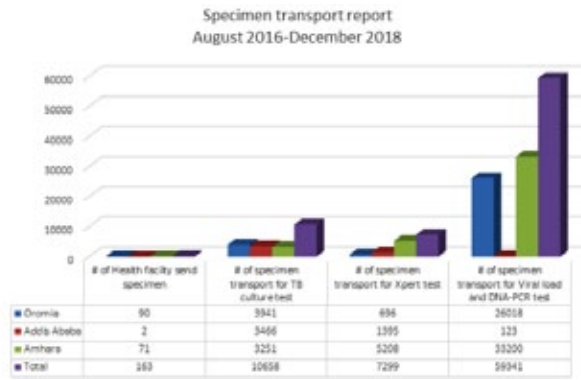
BACTEC™ MGIT™ 960 system, as well as to determine its critical concentration/epidemiological cut-off value (ECOFF).
Methods: The pretomanid minimum inhibitory concentrations (MICs) of 216 *M. tuberculosis* complex (MTBC) clinical isolates were determined in five laboratories using a standardised protocol. Isolates were from pretomanid- and delamanid-naïve patients, included all major phylogenetic MTBC lineages and encompassed a range of resistance phenotypes (drug-susceptible, MDR and XDR). The *M. tuberculosis* reference strain H37Rv was employed for QC purposes. Whole genome sequencing (WGS) was used to correlate MICs with mutations in the known pretomanid resistance genes (i.e. *ddn*, *fdg1*, *fbiA*, *fbiB*, *fbiC*, and *cofC*).
Results: The modal QC value for H37Rv was 0.25 mg/L (range 0.063-0.25 mg/L), demonstrating the high reproducibility of the MGIT™ methodology. *M. tuberculosis* clinical isolates had MICs ranging from 0.016 to 2 mg/L (MIC_{99} = 1 mg/L) except for three isolates which were highly resistant (MIC >8 mg/L) and harboured pretomanid-conferring mutations. Testing of other MTBC species yielded slightly lower MICs (≤0.016 - 0.063 mg/L) except for *M. canettii* which had MICs of 2 mg/L.
Conclusions: A protocol for pretomanid DST using the MGIT™ system was developed and, pending additional genomic and MIC data, 1 mg/L found to represent the likely ECOFF for MTBC.

SOA-17-C10 Finding the missing with TB: many paths to the same truth

SOA-17-1168-02 Integrated van specimen referral from introduction to integration in the Ethiopian health system

D Datiko,[1] G Tibesso,[1] B Sherefedin,[1] J Seid,[1] A Alem,[1] A Alemu,[2] M Melese,[3] P Suarez,[4] [1]Challenge TB (CTB) Project, Management Sciences for Health (MSH), Program, Addis Ababa, Ethiopia, [2]Ethiopian Public Health Institute (EPHI), National TB Reference Laboratory, Addis Ababa, Ethiopia, [3]MSH, Technical Excellence Group, Arlington, VA, United States of America, [4]MSH, Infectious Diseases, Arlington, VA, United States of America.
e-mail: dgemechu@msh.org

Background: Specimen transportation is a key component of the national referral system to access GeneXpert laboratory services and monitor drug-resistant TB. However, maintaining the cold chain system when transporting samples over long distances was problematic. The USAID-funded mechanism dedicated a cold chain vehicle and coordinated testing services in three regions of Ethiopia. We aimed to share the experience of an integrated specimen transportation vehicle service for TB culture, GeneXpert, viral load, and dried blood spotting in Ethiopia.
Methods: The USAID/Challenge TB project, in collaboration with the Federal Ministry of Health (FMOH), deployed eight vehicles designed for specimen transport that could maintain a temperature between 8°C and -20°C. Health facilities were networked with a clear monitoring system. The van sample transport system supported integrated sample transport from 30 TICs and 163 health facilities between 2016 and 2019.
Results: Of the 77,298 specimens collected and transported, 10,658 were for culture/line probe assay, 7,299 were for GeneXpert, and 59,341 were for viral load and dried blood spotting. The average turnaround time dropped significantly, from five to seven days to one day. The specimen rejection rate decreased to 0.3% from a baseline rate of 3.4%. At Adama lab, the contamination rate dropped from 23.3% to 5%.
Conclusions: The introduction of a cold chain vehicle helped the country implement and scale up cold chain specimen transport in the country lab system. We recommend expanding the van specimen transportation system to improve the efficiency of the specimen referral system.



[Graph: Summary results of cold chain vehicle-supported sample transport system, Aug 2016-Dec 2018]

SOA-17-1170-02 Using GXconnectivity to increase DR-TB enrolment rate: experience from Nigeria, 2013-2018

OO Chijioke-Akaniro,[1] A Lawanson,[2] O Omosebi,[2] O Olarewaju,[2] S Onyemaechi,[2] U Ochuko,[2] K Jimoh,[3] C Macek,[4] A Omoniyi,[5] T Odusote,[6] [1]National TB and Leprosy Control Programme, Public Health, Abuja, Nigeria, [2]National TB, Leprosy and Buruli Ulcer Program, Ministry of Health, Public Health Department, Abuja, Nigeria, [3]SystemOne, LLC, GXalert System, Abuja, Nigeria, [4]SystemOne, LLC, SystemOne, LLC, Boston, MA, United States of America, [5]WHO Country Office, Communicable Disease Cluster, Abuja, Nigeria, [6]USAID Nigeria, HIV/AIDS and Tuberculosis, Abuja, Nigeria.
e-mail: ocakaniro@gmail.com

Background and challenges to implementation: Nigeria commenced the implementation of GeneXpert MTB/RIF technology in 2011 with the number of the machines in-country progressively increasing from 7 in 2011 to 394 in 2018. The introduction of this machine contributed to an increase in number of MDR/RR-TB diagnosed from 38 in 2011 to 2275 in 2018. However, despite this progress, the treatment enrolment gap continued to increase, the average time to initiation of treatment was also above two months. The programme in order to address this gap introduced the use of GXAlert system (Systemone) in 2012 in addition to service decentralization.

This study was therefore conducted to evaluate the effect of the Gxconnectivity on the DR-TB enrollment rate and average time of treatment initiation from 2013-2018.

Intervention or response: The GeneXpert machines in the country were connected to GXAlert with the number of machines connected increasing from 45 in 2013 to 392 in 2018. A notification is sent from the GXAlert to the clinician, the DRTB focal person, the State programme and the NTP managers as soon as an RR-TB is diagnosed to ensure and facilitate prompt enrollment. A line-listing tool was also developed and used to monitor time of initiation of treatment.

Results and lessons learnt: The number of diagnosed RR-TB increased from 665 in 2013 to 2275 in 2018. As the coverage of the GxAlert system increases, the proportion of RR-TB enrolled on treatment also increased from 53% in 2013 to 83% in 2018. The average time of initiation of treatment also reduced from over 2 months to less than 14 days.

Conclusions and key recommendations: The enrollment gap is increasingly closing with the use of Gxconnectivity, the time to the initiation of treatment also drastically reduced. As the country advocates for more GeneXpert machines, plans for connectivity to GxAlert should be priority.

SOA-17-1171-02 SITRUST makes GeneXpert testing possible for all presumptive TB patients in hard-to-reach districts in Jayapura City, Papua Province, Indonesia

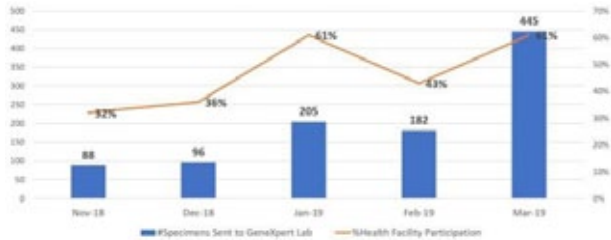
B Wopari,[1] M Rapang,[2] A Mudanang,[3] G Warnares,[2] M Pasangka,[2] M Samsuri,[4] L Stevens,[5] S Ajawaila,[6] N Antari,[7] M Mahsusriyanti,[7] [1]Provincial Health Office Papua, AIDS, TB & Malaria Disease Control, Jayapura, Indonesia, [2]FHI 360 Indonesia, Challenge TB, Jayapura, Indonesia, [3]KNCV Indonesia, Challenge TB, Jayapura, Indonesia, [4]FHI 360, Challenge TB, Jakarta Utara, Indonesia, [5]FHI 360 Asia Pacific Regional Office, Challenge TB, Bangkok, Thailand, [6]Provincial Health Laboratory Papua, Provincial Health Laboratory, Jayapura, Indonesia, [7]District Health Office - Jayapura City, District Health Office, Jayapura, Indonesia. e-mail: beeri.w@gmail.com

Background and challenges to implementation: Papua Province in Indonesia faces geographic challenges, hard-to-reach communities, limited transportation infrastructure and human resource constraints. In 2017, health facilities had difficulty accessing GeneXpert testing for TB diagnosis, despite the new TB diagnostic algorithm calling for GeneXpert testing for all presumptive TB patients. From April to September 2018, there were three GeneXpert machines operating in Jayapura City with a 66% utilization rate.

Intervention or response: In September 2018, the Challenge TB (CTB) project, in collaboration with Yayasan KNCV Indonesia and the Papua Provincial Health Office, piloted an android-based mobile application called SITRUST to improve GeneXpert utilization for TB diagnosis. The application helps the courier request and track specimen from Puskesmas to GeneXpert laboratories. This tracking system together with an appointed courier encouraged TB staff to send specimens for GeneXpert examination. To ensure the pilot was successful, CTB hosted a provincial dissemination workshop, trained all TB staff in Jayapura City, recruited field assistants (for ensuring the system run smoothly and trouble-shoot the application), and conducted regular monitoring and evaluation. The Indonesian Post Office was the courier for shipping specimens for testing, and transportation fees were paid by the Global Fund.

Results and lessons learnt: Between November 2018 and March 2019, GeneXpert utilization in Jayapura City improved to 74%, with 18 (100%) health facilities sending specimens for GeneXpert testing using SITRUST. Between October 2018 and March 2019, 32% of total notified TB patients were diagnosed using GeneXpert, compared to 26% between January and September 2018.

Conclusions and key recommendations: The SITRUST pilot in Jayapura City provides evidence that GeneXpert testing for all presumptive TB patients is possible with good specimen transportation. Further scale-up of SITRUST is needed to reach all 29 districts of Papua, most of which are in remote, hard-to-reach areas. An offline version of SITRUST is needed in areas with limited or unstable internet connection.



[Improvement of Specimens Sent for Xpert Examination Jayapura City November 2018 - March 2019]

SOA-17-1172-02 Operationalising point-of-care TB testing: lessons learnt from a pilot study in a high-burden setting - Buffalo City Metro Health District, Eastern Cape Province, South Africa

C Bezuidenhout,[1] D Bresenham,[1] R Mawarire,[1] P Ngwepe,[1] A Medina-Marino,[1] [1]Foundation for Professional Development, Research, East London, South Africa. e-mail: charlb@foundation.co.za

Background and challenges to implementation: Finding missing cases of Tuberculosis (TB) is imperative to achieve the End TB strategy. Household contact investigations (HHCI) are aimed at finding missing cases. In South Africa, HHCIs have aided in the identification of symptomatic contacts however, barriers to access still impede actual diagnosis. This study aimed to operationalise a new, portable homebased point-of-care TB diagnostic platform to remove such barriers.
Intervention or response: A pilot study was implemented to determine the acceptability and feasibility of home-based TB testing of household contacts using point-of-care diagnostics. Due to the delay in the release of the GeneXpert Omni, a portable battery was used to power the existing GeneXpert-1 device, allowing its use outside the traditional clinical setting. Using tailored carry-bags, the device, portable battery and laptop was transported from house to house. A nebuliser was used to induce sputum and MTB/RIF Ultra cartridges were used for testing. An accompanying real-time electronic data system (EDS) and manual of procedures was designed to guide procedural flows and capture outcome data. Lay health counsellors were trained to conduct homebased screening and testing.
Results and lessons learnt: A total of 97/495 (19.6%) adult household contacts screened positive for TB of which 49 were eligible for point-of-care-testing. Acceptability of homebased testing was proven with 48/49 (98%) providing consent. Producing spot-sputum was a major barrier with 26/48 (54.2%) unable to produce sputum, prompting the introduction of a nebuliser. From the 22 sputum that were collected 3/22 (13.6%) were induced. Successful tests were conducted on 21/22 (95.5%) sputum (1 error), showing that point-of-care TB testing is possible in informal settlement communities.
Conclusions and key recommendations: Point-of-care diagnostics for TB have created much enthusiasm but stakeholders remain unclear of its potential as an in-field diagnostic tool, or the associated operational challenges. Our findings and tools lay the groundwork for new strategies aimed at ending the TB epidemic using portable diagnostic devices.

SOA-17-1173-02 Development of a simple stool processing method for diagnosis of intra-thoracic paediatric tuberculosis using GeneXpert MTB/RIF Ultra testing: results of an in vitro study

M Lounnas,[1] A Diack,[1] M Nicol,[2] S Eyangoh,[3] E Wobudeya,[4,5] O Marcy,[6] S Godreuil,[1,7] M Bonnet,[8] [1]IRD, Infectious Diseases and Vectors: Ecology, Genetics, Evolution and Control (MIVEGEC), Montpellier, France, [2]University of Cape Town Medical School, Division of Medical Microbiology, Department of Pathology, Cape Town, South Africa, [3]Centre Pasteur du Cameroun, Microbiology, Yaoundé, Cameroon, [4]Makerere University Johns Hopkins, Research Collaboration, Kampala, Uganda, [5]Mulago National Referral Hospital, Directorate of Pediatrics and Child Health, Kampala, Uganda, [6]Inserm U 1219, Infectious Diseases in Resource-Limited Countries (IDLIC) - Bordeaux Population Health, Bordeaux, France, [7]University Teaching Hospital of Montpellier, Bacteriology Laboratory, Montpellier, France, [8]IRD, UMI 233 TransVIHMI - UM - INSERM U 1175, Kampala, Uganda. e-mail: manon.lounnas@gmail.com

Background: Stool samples are promising alternatives to respiratory samples for molecular diagnosis of childhood tuberculosis (TB) but they require intensive laboratory processing before molecular testing to remove PCR inhibitors and debris. We aimed to develop a centrifuge-free stool processing method for use at peripheral level in resource-limited settings.
Methods: In an *in vitro* laboratory study, we tested alternative parameters to optimize a sucrose-flotation method that previously showed good sensitivity for childhood TB diagnosis when combined with Xpert. To simplify this reference method using centrifugation, filtration and vortex shaking, we tested modified amount of stool, manual shaking, no filtration, sedimentation and modified dilution ratio. Each alternative parameter was compared head-to-head with the reference method using Xpert MTB/RIF Ultra (Ultra) on stool samples spiked with 10^3 *M. tuberculosis* colony forming units (CFU)/g. We selected the best index methods using a drop-the-loser rule: after 15 tests, methods with invalid/errors > 20% (maximum threshold) were dropped; after 30 tests, methods with invalid/errors < 20% and a sensitivity difference with the reference method < 10% were kept. For final selection, we tested the best parameters combinations at 10^2 CFU/g. We also assessed methods in terms of quantitative Ultra results (cycle thresholds (CTs)) for MTB detection.

Results: Out of 13 different combinations three were tested at 10^2 CFU/g (Table 1). The best combination used 0.5g stool, manual shaking, no filtration, 30-minutes sedimentation, and a 1:5 dilution ratio. It had 10% invalid/error results and a sensitivity of 70% (95% CI 50.4-84.5) and 53% (38.8-78.1) vs 63% (43.9-79.4) and 58% (40.7-79.1) as compared to the reference method, at 10^3 and 10^2CFU/g, respectively.
Conclusions: We identified an optimized centrifuge and vortex-free stool sample processing method with potential to facilitate stool Xpert Ultra testing in high burden and resource-limited settings. It should be further evaluated among children with presumptive TB.

	Manual shaking / Sed 30' / 0.5 g / No filtration / dilution ratio 1:5	Manual shaking / Sed 30' / 1 g / No filtration / ratio 1:5	Manual shaking / Sed 30' / 0.5 g / Gauze filtration / ratio 1:5
Invalid (Index vs reference method)	10% vs 6%	11% vs 0%	10% vs 6%
Errors (Index vs reference method)	0% vs 0%	0% vs 0%	0% vs 0%
Sensitivity (Index vs reference) method	53% vs 58%	11% vs 22%	30% vs 58%
Mean CTs IS6110-1080 (Index vs reference method)	25.9 vs 27.4	27.2 vs 29.1	26.4 vs 27.4
Mean CTs SPC (Index vs reference method)	28.6 vs 29.1	29.1 vs 29.2	29.1 vs 29.1

[Performances of the three methods tested at 102 CFU/g using Xpert MTB/RIF Ultra compared with the reference method]

SOA-17-1174-02 Frequency of and adherence to guidelines for "trace-positive" Xpert MTB/RIF Ultra results in routine care in Uganda

M Natalie Nantale,[1,2] T Nalugwa,[1,2] D Oyuku,[1,2] A Nakaweesa,[1,2] P Shete,[3,4] D W Dowdy,[5] E Kendall,[6] A Cattamanchi,[3,4] A Katamba,[1,2] [1]Makerere University, College of Health Sciences, Department of Medicine, Kampala, Uganda, [2]Uganda Tuberculosis Implementation Research Consortium, Research, Kampala, Uganda, [3]University of California, Curry International Tuberculosis Center, San Francisco, CA, United States of America, [4]University of California, Division of Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [5]Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, MD, United States of America, [6]Johns Hopkins Bloomberg School of Medicine, Division of Infectious Diseases, Baltimore, MD, United States of America.
e-mail: mariamnantale2013@gmail.com

Background and challenges to implementation: Xpert® MTB/RIF Ultra (Ultra) has recently been rolled out as a next-generation cartridge for detection of *Mycobacterium tuberculosis* and rifampicin resistance using the GeneXpert® platform. A new semi-quantitative category, 'MTB detected trace', can be reported for samples with low bacillary load. Guidelines recommend that patients with trace-positive results be treated if HIV-positive and retested if HIV-negative. There is limited information about the frequency of and practices related to "trace-positive" results in routine care.
Intervention or response: We conducted a cross-sectional study at 6Xpert testing sites in Uganda between September 2018 and March 2019.We extracted test result data from GeneXpert platforms and reviewed TB treatment registers to determine 1) the frequency of, and patient characteristics associated with, trace-positive results, and 2) whether patients with trace-positive results were re-tested (if HIV-negative) or initiated on treatment (if HIV-positive).
Results and lessons learnt: 2611 patients were tested using Ultra and 223(8.5%) had positive results. Of these, 20(9%) patients had trace-positive results and 12/20 (60%) were among HIV-infected patients. Ultra testing was repeated in 2/8 (25%) HIV-negative and 1/12 (8.3%) HIV-positive patients with an initial trace-positive result. The second tests were again trace-positive in all three patients. Of the 12 HIV-positive individuals, 3 (25%) were treated (2 after the initial and1 after the second trace-positive result). Of the 8 HIV-negative individuals, 6 (75%) were treated (4 after the initial and 2 after the second trace-positive result).
Conclusions and key recommendations: "Trace-positive" Ultra results were relativelycommon among all positive test results, and guidelines for repeat testing versus treatment initiation are not being followed in routine care. Further studies should investigate barriers to guideline implementation, and assess outcomes of patients with trace-positive Ultra results to inform future guideline revisions.

SOA-17-1175-02 Optimising the Xpert MTB/RIF network in Ho Chi Minh City, 2017-2018

TPC Nguyen,[1] VH Nguyen,[2] TKT Nguyen,[2] TH Pham,[3] TTN Khieu,[2] KU Quach,[4] TTH Bui,[1] VA Ho,[1] A Finlay,[1] [1]Center of Disease Control and Prevention, Division of Global HIV/AIDS and Tuberculosis, Hanoi, Viet Nam, [2]National Tuberculosis Program of Vietnam, National Reference TB Laboratory, Hanoi, Viet Nam, [3]Pham Ngoc Thach Lung Hospital, Microbiology, Ho Chi Minh, Viet Nam, [4]Ho Chi Minh Provincial AIDS Center, TB/HIV, Ho Chi Minh, Viet Nam. e-mail: ogk7@cdc.gov

Background: Vietnam dramatically expanded the Xpert MTB/RIF (MTB/RIF) testing network between 2012 and 2017. We assessed utilization and factors influencing optimal use of MTB/RIF laboratory sites in Ho Chi Minh City (HCMC), the highest tuberculosis (TB) and rifampin-resistant TB province in Vietnam.
Methods: We reviewed MTB/RIF testing volume at each site (Q1-Q3 2017) and calculated annual capacity assuming program standard instrument operation (3 batches/

Site name	Total tests (n)	GeneXpert Instrument (n)	Theoretical module (n)	Theoretical batch (n)	Working day (n)	Actual module (n)	Actual batch basing on staffing (n)	Theoretical utilization (%)	Actual utilization (%)
PNT Lung hospital	9,602	5	20	3	189	17	3	85%	100%
DTU 6	3,407	1	4	3	189	4	3	150%	150%
DTU 8	2,937	1	4	3	189	4	3	130%	130%
DTU 9	570	1	4	3	105	3	2	45%	90%
DTU 12	815	1	4	3	147	4	3	46%	46%
DTU Binh Thanh	1,671	1	4	3	189	3	3	74%	98%
Pediatric 1 hospital	219	1	4	3	189	4	3	10%	10%

[SOA-17-1175-02 Table 1. Xpert MTB/RIF Utilization at seven sites in Ho Chi Minh City]

day × number of modules × working-days), and utilization (100% x total tests/capacity). We conducted on-site assessment on the specimen referral network, identify factors influencing utilization, and estimate MTB/RIF turnaround time (TAT), defined as time from sputum collection to the return of results to the clinician.

Results: The MTB/RIF network comprised 44 modules (11 instruments) at 7 sites in HCMC serving 24 district TB units (DTU). The theoretical utilization ranged 10-150% (Table 1). Five of seven sites had high testing demand (the utilization exceeds 75% set by National TB Program). Operational barriers (i.e. inadequate laboratory staff to run tests, cartridges out of stock, module failures with delayed replacement, and CPU malfunction) varied by site, which intensified utilization. For example, DTU 9 experienced module failure at the beginning and part-time staff, so actual utilization was 90% compared to theoretical one, 45%. Overall TAT was long, ranging 9-15 days. Long TAT was driven by paper-based system for returning lab results and substandard TAT tracking practices.

Conclusions: Our findings showed high testing demand within MTB/RIF network and long TAT of MTB/RIF test results in HCMC, suggesting the program re-align the MTB/RIF network to meet the need of accessing MTB/RIF tests. Existing capacity could be enhanced by developing standard procedures to transmit verified test results electronically, monitoring TAT, improving inventory management, using historic maintenance records to budget for anticipated downtime, and ensuring adequate human resources at each MTB/RIF site.

SOA-17-1176-02 Factors hindering Xpert MTB/RIF potential in improvement in patient-level outcomes

T Agizew,[1,2] U Mathebula,[3] [1]Centers for Disease Control and Prevention Botswana, HIV Services, Gaborone, Botswana, [2]University of Botswana, Department of Family Medicine and Public Health, Gaborone, Botswana, [3]Centers for Disease Control and Prevention Botswana, HIV Programs, Gaborone, Botswana. e-mail: hoa6@cdc.gov

Background: After the World Health Organization endorsed the use of Xpert MTB/RIF (Xpert), countries are shifting from smear microscopy to Xpert-based tuberculosis diagnostic algorithms. Current evidence indicates that despite improved diagnostic ability, Xpert showed no discernible impact on patient-level treatment outcomes. We reviewed recent literatures and aim to find out why Xpert has not improved tuberculosis treatment outcomes eight years after implementation in many low- and middle-income countries.

Methods: We summarized recent narrative reviews, systematic reviews, and Meta-analyses on the diagnostic and therapeutic impact of Xpert versus smear microscopy and investigated factors affecting treatment outcomes. In addition, we reviewed enhanced care (defined as intensified TB case finding with additional staff to actively trace patients who missed clinic appointments), sputum quality, and patients with Non-tuberculous mycobacterium (NTM) who received anti-TB treatment as potential factors affecting treatment outcome.

Results: We included eight intervention trials from the narrative review, 13 citations from systematic reviews and meta-analyses from four clustered trials. We identified three potential factors that contribute to tuberculosis treatment outcomes more than replacing smear microscopy with Xpert. First, enhanced care that traces patients who miss clinic appointments contributed to substantial reductions in mortality rates. Second, suboptimal sputum quality negatively affected Xpert test results in microbiologically confirming TB. Third, patients with non-tuberculous mycobacterium (NTM)-positive culture who tested negative for tuberculosis via Xpert were treated with anti-tuberculosis drugs.

Conclusions: Patient-related factors (retention in care), the quality of sputum samples, and healthcare worker factors appear to affect tuberculosis treatment outcomes more than the testing technology. High-income countries achieved population-level tuberculosis control long before molecular testing was introduced. Our findings show that tuberculosis control in low-income countries requires systematic changes beyond replacing smear microscopy with Xpert.

SOA-17-1177-02 Accuracy of Xpert Ultra in the diagnosis of pulmonary TB among children in Uganda

W Ssengooba,[1,2] S Mujumbi,[1] E Wobudeya,[3] R Mboizi,[3] F Cresswell,[4,5] D Meya,[4] L Choo,[6] A Crook,[6] M Joloba,[1] A-M Demers,[7] [1]Makerere University, College of Health Sciences, Department of Medical Microbiology, Kampala, Uganda, [2]Makerere University, College of Health Sciences, Lung Institute, Kampala, Uganda, [3]Makerere University, John Hopkins University, Research Collaboration, Pediatrics, Kampala, Uganda, [4]College of Health Sciences Makerere University, Infectious Diseases Institute, Kampala, Uganda, [5]London School of Hygiene and Tropical Medicine, Clinical Research, London, United Kingdom, [6]University College London (UCL), MRC Clinical Trials Unit, London, United Kingdom, [7]Stellenbosch University, Desmond Tutu Tuberculosis Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Cape Town, South Africa. e-mail: willyssengooba@gmail.com

Background: Childhood pulmonary tuberculosis (PTB) presents a significant diagnostic challenge, due to the paucibacillary nature of disease, requiring more sensitive testing and invasive specimen collection. We determined the accuracy of the Xpert MTB/Rif Ultra (Ultra; Cepheid, Sunnyvale, CA) for diagnosis of PTB.
Methods: This sub-study was performed in Uganda as part of the SHINE trial, a randomized trial evaluating 4 vs. 6 months of standard treatment for children with minimal TB disease. At least two samples were collected for smear, Xpert, Lowenstein Jensen (LJ) and liquid (MGIT) culture.
We randomly selected one uncontaminated respiratory sample for Ultra testing on frozen pellets. We determined the diagnostic accuracy of Ultra compared to XpertMTB/Rif (Xpert) and culture using two reference standards:
1) LJ and/or MGIT (culture-based RS)
2) composite reference standard (RS) of 'any positive TB test'.
Results: Of the 398 children evaluated, 353 (89%) with valid culture, Xpert and Ultra results were included. The median age was 2.8-years (IQR 1.3-5.3), 8.5% were HIV-positive and 56% were male.
Using the culture-based RS, 31 (8.8%) were positive. The sensitivities were 58% (18/31) for Ultra, and 45% (14/31) for Xpert. Eighteen Ultra-positive patients tested negative by the culture-RS. Twenty-two Ultra-positive samples were Xpert-negative of which 20 were trace-positive and 16/20 were negative by culture.
The composite RS was positive in 50 (14.4%) of which 36 (72%) were positive by Ultra, 16 (32%) by Xpert, 30 (60%) by MGIT, 20 (40%) by LJ. Against the composite RS, Ultra offers 40% (72% vs 32%; $P < 0.001$) sensitivity over Xpert and 12% (72% versus 60%; $P < 0.001$) over MGIT culture.
Conclusions: Among young children screened for non-severe PTB in Uganda, Ultra has a higher sensitivity compared to Xpert and potentially also culture for the diagnosis of PTB. Further studies to investigate Ultra trace-positive children are needed.

SOA-17-1178-02 Diagnostic accuracy of stool Xpert MTB/RIF for active tuberculosis detection in children: a systematic review and meta-analysis

E Maclean,[1,2] G Sulis,[1,2] CM Denkinger,[2,3,4] JC Johnston,[5] M Pai,[1,2] F Ahmad Khan,[2,6,7] [1]McGill University, Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]McGill International TB Centre, Faculty of Medicine, Montreal, QC, Canada, [3]FIND, TB Programme, Geneva, Switzerland, [4]University of Heidelberg, Faculty of Medicine, Heidelberg, Germany, [5]University of British Columbia, Respiratory Medicine, Vancouver, BC, Canada, [6]Research Institute of the McGill University Health Centre & Montreal Chest Institute, Respiratory Epidemiology & Clinical Research Unit, Montreal, QC, Canada, [7]McGill University, Medicine, Montreal, QC, Canada.
e-mail: emily.maclean@mail.mcgill.ca

Background: Obtaining samples for microbiologic evaluation of children with presumptive pulmonary tuberculosis (PTB) is often difficult, particularly in children under 5, as invasive sampling techniques are required. Such techniques may not be widely available and are challenging to implement. Nucleic-acid amplification testing of simpler-to-collect stool samples could be a non-invasive method of diagnosing PTB. We conducted a systematic review and meta-analysis to evaluate the diagnostic accuracy of testing stool with the Xpert MTB/RIF assay ('stool Xpert') for childhood PTB.
Methods: Four databases were searched for publications from January 2008 to June 2018. Studies assessing the diagnostic accuracy amongst children of stool Xpert compared to a microbiological reference standard of conventional specimens tested by mycobacterial culture or Xpert were included. Bivariate random-effects meta-analyses were performed to calculate pooled sensitivity and specificity of stool Xpert against the reference standard. Where available, meta-analyses were also performed to calculate stool Xpert performance compared to a clinical reference standard.
Results: From 1589 citations, 9 studies (n=1681) were included. Median participant ages ranged from 1.3 to 10.6 years. Protocols for stool processing and testing varied

substantially, with differences in reagents and methods of homogenization and filtering. Against the microbiological reference standard, pooled sensitivity and specificity of stool Xpert were 67% (95%CI:52-79) and 99% (95%CI:98-99), respectively. Sensitivity was higher among children with HIV (79%; 95%CI:68-87; versus 60%; 95%CI:44-74 among HIV-uninfected). Compared to the clinical reference standard, stool Xpert sensitivity was 22% (95%CI:9-44) and specificity was 99% (95%CI:98-99). Heterogeneity was high. Data were insufficient for subgroup analyses in children under age 5, the most relevant target population.
Conclusions: Stool Xpert could be a non-invasive method of ruling-in PTB in children, particularly those with HIV. However, studies specifically focused on children under 5 are needed, and generalizability of the evidence is limited by the lack of a standardized stool preparation and testing protocol.

SOA-18-C3 Insights into the DR-TB epidemics

SOA-18-1179-02 Extensively drug-resistant tuberculosis genomic characterisation in Peru

D Santos Lázaro,[1] Z Puyen,[1] [1]Instituto Nacional de Salud, Public Health, Lima, Peru. e-mail: zpuyeng@gmail.com

Background: XDR-TB represents one of the most severe forms of tuberculosis. It has an increasing number of cases and the lowest treatment success rate. In this study, we carried out a genomic characterization of Peruvian XDR-TB strains.
Methods: The study included 66 Peruvian XDR-TB strains isolated from 2011 to 2015. Reference assembly was performed using BWA v0.7.12. 'Variant calling' and 'Hard filtering' (DEPTH ≥ 10; QUAL ≥ 30; AF ≥ 0.75) was made with GATK v4.0.12. Bayesian inference of transmission chains was done with adegenet v2.1.1, ape v5.3 and outbreaker v1.1-8 packages, all implemented in R v3.5.3. *In silico* Spoligotyping was performed using SpoTyping v2.0 and SITVIT2 database. Finally, an evolutionary tree was made using RAxML v2.8.10 with 221 XDR-TB strains from different parts of the world (external strains).
Results: Peruvian XDR-TB strains comprise 4840 SNVs and a lesser nucleotide diversity (ϖ = 0.0001660022) than external strains (ϖ = 0.0002004494). 56 strains (84.9%) were isolated in the capital city (Lima). According to Bayesian analysis, there was two *imported cases*, which gave rise two genomic clusters (cases 14 and 57, **Figure 01A**). However, the analysis of 'secondary cases generation' does not determine the existence of any case of XDR-TB infection focus (bar chart, Figure 01A). The analysis of collection dates showed a progressive increase in genetic differentiation between strains (SNV accumulation) through years (**Figure 01B**). Finally, Peruvian XDR-TB strains belong mainly to Euro-American lineage (89%), and evolutionarily they are more related to strains belonging to South Africa and Belorussia cladres (**Figure 01D**).
Conclusions: Peruvian TB strains mainly acquired the XDR phenotype in an independently way. There is no evidence of representative infection focus of XDR-TB. In addition, there is a clear predominance of Euro-American Lineage in Peruvian XDR-TB strains and a lower diversity than similar strains in the rest of the world.

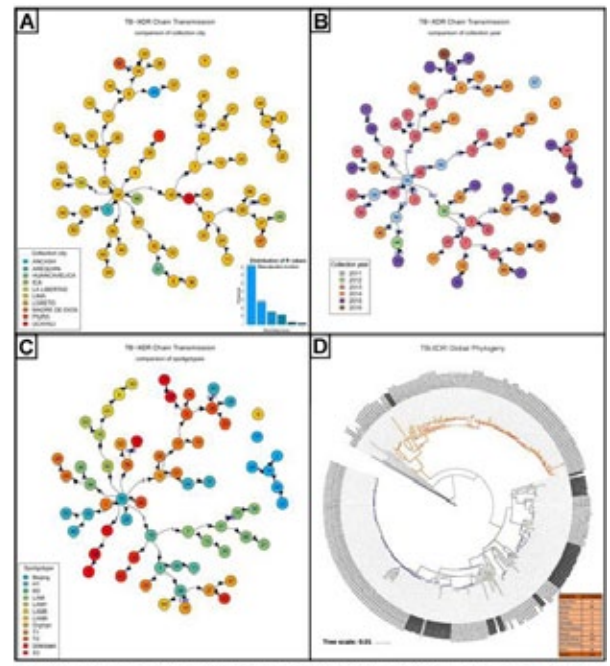


Figure 01. TB-XDR transmission trees generated by Bayesian inference (A-C). Number of MCMC iterations = 2 x 10^7 (sampled every 500 iterations). Trees generated using 4840 polymorphic sites throughout the entire XDR-TB genomes. Each XDR-TB case is represented by an individual vertex. All trees (A-C) show vectors with posterior probability support greater than 0.9. A) Transmission tree compared to the 10 sample collection cities. The bar graph (bottom right corner) shows the frequency of the numbers of secondary cases generated. The edges show posterior probability values. B) Transmission tree compared with the years of sample collection. The edges show the difference in the number of SNVs between each case. C) Transmission tree compared with the spoligotypes of each strain. The edges show posterior probability values. From A to C there are two imported cases (14 and 57), while case 9 is grouped with the larger cluster but with a posterior probability lower than 0.9. D) Global phylogeny of 271 TB-XDR strains. 20451 SNVs and 1000 bootstraps were used for evolutionary reconstruction. The clades shaded in red belong to the East-Asiatic lineage, while the clades shaded in blue belong to the Euro-American Lineage. Peruvian TB-XDR strains have the name shaded on a black background. The tree was rooted at Lineage 7 strain.

[Figure 1]

SOA-18-1180-02 Detailed molecular epidemiological studies of multidrug-resistant Mycobacterium tuberculosis (MDR-TB) isolates identify local transmission of MDR-TB in Kuwait

S Ahmad,[1] N Al-Mutairi,[1] E Mokaddas,[1] [1]Kuwait University, Microbiology, Jabriya, Kuwait. e-mail: suhail_ah@hsc.edu.kw

Background: Increasing incidence of multidrug-resistant tuberculosis (MDR-TB) is hampering efforts to control TB. Kuwait is a low (25/100,000) TB incidence country and ~1% of Mycobacterium tuberculosis strains are resistant at least to rifampicin and isoniazid (MDR-TB). This study performed molecular characterization

of MDR-TB strains by detecting resistance conferring mutations in seven loci. Sequence data were combined with spoligotyping for detecting local transmission of MDR-TB in Kuwait.

Methods: MDR-TB strains (n=131) from 88 newly diagnosed TB patients and 50 susceptible strains were used. Susceptibility testing was done by MGIT 960 system, gMTBDRplus assay and PCR-sequencing of three regions of rpoB, katG codon 315 (katG315) + inhA regulatory region (inhARR), embB (embB306/embB406/embB497 regions), rpsL + rrs-500-900 regions and pncA for rifampicin, isoniazid, ethambutol, streptomycin and pyrazinamide, respectively. Concatenated sequences were used to construct phylogenetic tree by MEGA7 software. Spoligotypes were identified by SITVIT2 and phylogenetic tree was made by MIRU-VNTRplus software.

Results: Pansusceptible isolates contained wild-type sequences. Mutations were detected in most isolates in rpoB, katG+inhARR, embB, rpsL+rrs and pncA which confer resistance to rifampicin, isoniazid, ethambutol, streptomycin and pyrazinamide, respectively. Phylogenetic analysis of multi-locus concatenated sequences showed unique patterns for 51 patient's isolates while 37 patient's isolates grouped in 14 clusters. Spoligotyping identified 35 patterns (19 unique patterns and 69 patients's isolates in 16 patterns) including 11 orphan patterns. Beijing genotype was most common (28/88). Sixteen isolates recovered within two years yielded 6 clusters (each containing 2-5 isolates) by both fingerprinting methods.

Conclusions: Our study provides first insight into molecular epidemiology of MDR-TB in Kuwait and identified six potential cases of local transmission of MDR-TB involving 2-5 subjects (including 5 Kuwaiti patients) which had escaped detection by routine surveillance studies. Detailed molecular fingerprinting studies identify possible cases of local transmission of MDR-TB in low TB incidence countries for contact tracing.

SOA-18-1181-02 Mycobacterium tuberculosis whole-genome sequencing provides insights into the Manila strain and drug-resistant mutations in the Philippines

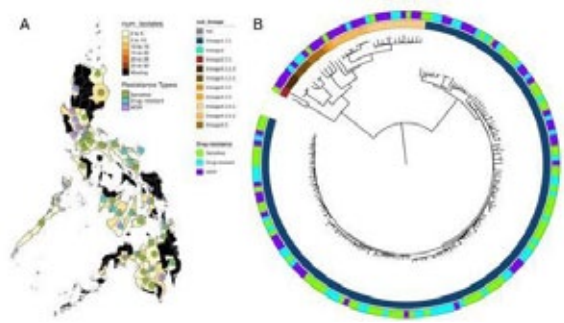
JE Phelan,[1] DR Lim,[2] S Mirarai,[3] P Florez de Sessions,[4] MA Tujan,[5] JC Hafalla,[6] ML Hibberd,[1] S Kato,[7] MCG Ama,[2] TG Clark,[8] [1]London School of Hygiene & Tropical Medicine, Infection Biology Department, London, United Kingdom, [2]Research Institute for Tropical Medicine, National Tuberculosis Reference Laboratory, Muntinlupa City, Philippines, [3]Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Department of Mycobacterium Reference and Research, Tokyo, Japan, [4]Genome Institute of Singapore, GERMS, Singapore, Singapore, [5]Research Institute for Tropical Medicine, Molecular Biology Laboratory, Muntinlupa City, Philippines, [6]London School of Hygiene & Tropical Medicine, Department of Immunology and Infection, London, United Kingdom, [7]Research Institute of Tuberculosis (RIT), Japan Anti-Tuberculosis Association (JATA), RIT-JATA, Tokyo, Japan, [8]London School of Hygiene & Tropical Medicine, Department of Infectious Disease Epidemiology, Faculty of Epidemiology and Population Health, London, United Kingdom. e-mail: dodge.lim@gmail.com

Background: The Philippines has a very high incidence of tuberculosis (TB), with an increasing prevalence of multidrug-resistant (MDR-TB) *Mycobacterium tuberculosis (Mtb)* strains making its control difficult. Although the *Mtb* "Manila" genotype is thought to be prevalent in the country, little is known about the genetic diversity of circulating strains.

Methods: A total of 178 *Mtb* isolates were whole genome sequenced (WGS) at the Genome Institute of Singapore and Research Institute of Tuberculosis, Japan from the Philippines National Drug Resistance Survey on Tuberculosis (2012).

Results: By WGS, we found the majority (143/178; 80.3%) belonged to the Indo-Oceanic Manila lineage, with the minority belonging to lineages 4 (European-American; n=33) and 2 (East Asian; n=2). A high proportion were found to be multidrug-resistant (34/178; 19.1%), established through highly concordant laboratory drug susceptibility testing and *in silico* prediction methods. Some MDR-TB isolates had near identical genomic variation, providing potential evidence of transmission. By placing the Philippine isolates within a phylogeny of global *Mtb* (n>17,000), we established that they are genetically similar to those observed outside the country, including a clade of Manila-like strain-types in Thailand. An analysis of the phylogeny revealed a set of ~200 SNPs that are specific for the Manila strain-type, and a subset can be used within a molecular barcode. Sixty-eight mutations known to be associated with 10 anti-TB drug resistance were identified in the Philippine strains, and all have been observed in other populations. Whilst nine putative streptomycin resistance conferring markers in *gid* (8) and *rrs* (1) genes appear to be novel and with functional consequences.

Conclusions: Overall, this study provides an important baseline characterisation of *M. tuberculosis* genetic diversity for the Philippines, and will fill a gap in global datasets and aid the development of a nation-wide database for epidemiological studies and clinical decision making including molecular barcoding for detecting Manila strains.



[Figure 1. The 178 M. tuberculosis isolates: (A) A phylogenetic tree constructed using 17,522 SNPs; (B) Map of the Philippines annotated with the source and drug-resistance of the isolates]

SOA-18-1182-02 Increased moxifloxacin dosing among MDR-TB patients with low-level resistance to moxifloxacin did not improve treatment outcomes in a tertiary care centre in Mumbai, India

JA Tornheim,[1] I Gajjar,[2] SVBY Shivakumar,[3] AN Gupte,[1] G Kishore,[4] M Karane,[2] C Rodrigues,[5] A Gupta,[1] ZF Udwadia,[4] [1]Johns Hopkins University School of Medicine, Division of Infectious Diseases, Baltimore, MD, United States of America, [2]P.D. Hinduja National Hospital and Medical Research Centre, RePORT Project, Mumbai, India, [3]Johns Hopkins University - India Office, CCGHE, Mumbai, India, [4]P.D. Hinduja National Hospital and Medical Research Centre, Pulmonary Medicine, Mumbai, India, [5]P.D. Hinduja National Hospital and Medical Research Centre, Microbiology, Mumbai, India. e-mail: tornheim@jhu.edu

Background: *Mycobacterium tuberculosis* strains resistant to isoniazid and rifampin ("MDR-TB") are increasingly identified worldwide, requiring renewed focus on the nuances of drug resistance. Patients with low-level moxifloxacin resistance may benefit from moxifloxacin doses >400mg daily, but limited outcomes data are available. To assess the impact of moxifloxacin 600mg daily ("high-dose") on treatment outcomes, we analyzed data from a cohort of MDR-TB patients with moxifloxacin resistance.

Methods: We reviewed records from an ongoing cohort of MDR-TB patients at a tertiary care center in India from October 2015-April 2019. Participants with moxifloxacin resistance at 0.5μg/mL in liquid culture were categorized according to treatment regimens of ≥4 drugs with or without high-dose moxifloxacin based on drug susceptibility test results. Logistic regression was used to measure the association between high-dose moxifloxacin and good treatment outcomes, defined as successful completion of 24 months of MDR-TB treatment or cure without relapse after 36 months of observation.

Results: We identified 334 MDR-TB patients with resistance to moxifloxacin, 273 (81.7%) of whom received high-dose moxifloxacin and 61 (18.3%) of whom did not. Treatment outcomes were similar between groups (60.3% vs. 59.2% with good outcomes, p=0.85). Univariable analysis found that good outcomes were associated with extrapulmonary disease, earlier initiation of treatment, smear positivity, lesser extent of radiographic lung involvement, susceptibility to moxifloxacin at 2.0μg/mL (low-level resistance only), and resistance to linezolid, but not with high-dose moxifloxacin treatment (odds ratio 1.12, 95% confidence interval 0.58-2.11, p=0.73).

Multivariable analysis did not show an association between high-dose moxifloxacin and good treatment outcome after controlling for these factors and concomitant treatment (adjusted odds ratio 0.89, 95% confidence interval 0.34-2.28, p=0.81).

Conclusions: In a large observational cohort, the addition of moxifloxacin 600mg to a DST-based treatment regimen was not associated with better treatment outcomes among MDR-TB patients with moxifloxacin resistance at 0.5μg/mL.

SOA-18-1183-02 Baseline predictors of unfavourable outcome in the short MDR-TB regimen: exploratory analyses from the STREAM trial

S Ahmed,[1] R Goodall,[1] P Phillips,[2] S Meredith,[1] A Nunn,[1] STREAM Trial Collaboration [1]University College London (UCL), Medical Research Council Clinical Trials Unit at UCL, London, United Kingdom, [2]University of California, School of Medicine, UCSF Center for TB, San Francisco, CA, United States of America.
e-mail: saiam.ahmed@ucl.ac.uk

Background: STREAM Stage 1 was a randomised non-inferiority phase 3 trial comparing a 9-11 month "short regimen" to the WHO 2011 20-24 month "long regimen" for MDR-TB patients. The proportion of participants with an unfavourable outcome on the short regimen was shown to be non-inferior to that on the long regimen. We investigated baseline factors associated with unfavourable outcome in the short regimen.

Methods: The modified intention-to-treat population included 245 participants who received the short regimen. Baseline variables (demographics, bacteriological, resistance, clinical/laboratory assessments, treatment history) were included in univariable analyses to identify factors significantly associated with unfavourable outcome ($p < 0.1$). Multivariable stepwise logistic regression models (backwards elimination, exit probability $p=0.05$) were used to identify which of these factors were independently associated with unfavourable outcome.

Results: Among 245 participants, 52 (21%) had an unfavourable outcome. HIV co-infection, phenotypic susceptibility to ethambutol or isoniazid, low haemoglobin and extensive opacification on chest x-ray were associated with increased odds of an unfavourable outcome in univariable analyses (all $p< 0.05$). In multivariable analyses, participants with ethambutol resistance at baseline had reduced odds of an unfavourable outcome compared to those who were ethambutol susceptible [OR 0.42 (0.20, 0.88)], whilst odds of an unfavourable outcome were increased in those with HIV co-infection [OR 2.95 (1.46, 5.98)]. The model discrimination, measured using the area under receiver operator characteristic curve, was 0.68.
Conclusions: Fewer favourable outcomes in HIV co-infected participants on both trial arms have been previously reported, yet HIV co-infected trial participants did better than expected with a lower proportion having an unfavourable outcome than reported by WHO. The finding that ethambutol susceptibility at baseline is associated with a poor outcome is challenging to explain and further work is needed to recognise if this is other than a chance finding.

SOA-18-1184-02 Successful outcome for patients switched from kanamycin to linezolid in a modified oral short regimen for MDR-TB in Niger

MB Souleymane,[1] A Piubello,[2,3] IM Lawan,[1] S Morou,[1] I Boukary,[1] MM Assao Neino,[4] [1]Damien Foundation Niger, TB, Niamey, Niger, [2]International Union Against Tuberculosis and Lung Disease (The Union), MDR-TB, Paris, France, [3]Damien Foundation Belgium, MDR-TB, Brussels, Belgium, [4]National Tuberculosis Program, TB Control, Niamey, Niger. e-mail: bachirsoul@gmail.com

Background: The short regimen is implemented in Niger since 2008 with excellent outcomes. However, ototoxicity secondary to injectable is a concern and data on modified oral short treatment regimens (STR) are lacking.
Methods: A prospective longitudinal study was conducted on a modified STR replacing kanamycin with linezolid (600 mg/d) in case of hearing loss (grade 1) at baseline or during treatment. WHO definitions were used for outcomes and adverse events were assessed according to French National Agency for Research on AIDS.
Results: A total of 173 patients were treated with STR for pulmonary MDR-TB from 2016 to 2018. Among them, 22 (12.7%) had a modified STR, switching from kanamycin to linezolid during treatment (14) or starting with linezolid (8).
Fourteen (63.6%) were males, 2 (9.1%) were HIV positive, the median age was 37.5 years (range 21-71) and the median BMI was 16.5 kg/m^2 (range 13-24.2). No patients had strains resistant to fluoroquinolones and/or injectables.
The median time from treatment start to switch kanamycin to linezolid was 2 months (range 0-3) and the median duration of treatment with linezolid was 2 months (range 1-5).
All patients had smear and culture conversion (median: 1 month, range 1-6 and 2 months, range: 2-4 respectively).
Nineteen patients (86.4%) were cured and 3 died of respiratory failure (2) and severe immunosuppression (1). Nine patients assessed for follow-up 6 months after cure remained culture negative.
Severe adverse events were anaemia in 5 cases (22.7%) with a median onset of 1 month
(range 1-3) and thrombocytopenia in 1 case (4.5%). These patients received blood transfusion, linezolid was reintroduced at the same dosage with no further problems.
Seven patients (31.8%) had a reversible mild to moderate peripheral neuropathy. No patients had optic neuritis.
Conclusions: A modified STR with linezolid may achieve high cure rates with manageable adverse events.

SOA-18-1185-02 Good end-of-treatment outcomes for patients receiving standardised short MDR-TB treatment in a high HIV-prevalence setting in Mozambique

M Bastard,[1] M Arago Galindo,[2] L Molfino,[2] C Mutaquiha,[3] P Zindoga,[3] I Manhiça,[3] E Ardizzoni,[4] B Rusch,[5] A Telnov,[6] [1]Epicentre, Research, Geneva, Switzerland, [2]Médecins Sans Frontières (MSF), Medical, Maputo, Mozambique, [3]Ministry of Health, National TB Program, Maputo, Mozambique, [4]Institute of Tropical Medicine, Mycrobacteriology, Antwerp, Belgium, [5]Médecins Sans Frontières (MSF), Operations, Geneva, Switzerland, [6]Médecins Sans Frontières (MSF), Medical, Geneva, Switzerland.
e-mail: mathieu.bastard@geneva.msf.org

Background: The STREAM trial has shown that a short MDR-TB regimen was noninferior to a long regimen. Although HIV-infected patients were included in this trial and randomization was stratified according to HIV status, additional evidence of the effectiveness of the short regimen in HIV-infected population is needed.
Methods: A prospective study was conducted in Maputo, Mozambique, providing standardized short MDR-TB treatment for patients diagnosed with active pulmonary rifampicin resistant TB and previously not exposed to second-line drugs. We reported the final treatment outcomes and compared treatment success according to HIV status and resistance profile.
Results: In total, 162 patients started short MDR-TB regimen: 58% were males, median age was 32 [IQR 25-40], median BMI was 18.3 kg/m^2 [IQR 16.6-20.0] and 104 (64.2%) were HIV-positive with a median CD4 of 220 cells/μL [IQR 122-366]. At treatment initiation, 47.3% were resistant to ethambutol, 55.0% to pyrazinamide, 45.4% to ethionamide, 3.4% to fluoroquinolone

and 5 to one injectable drug. End of treatment outcomes were: 123 (75.9%) success, 9 (5.6%) died, 13 (8.0%) failed treatment and 15 (9.3%) lost to follow-up. Success rate was 71.8% (95%CI 62.1-80.3%) in HIV-positive and 85.9% (95%CI 74.2-93.7%) in HIV-negative patients. In multivariate analysis, the odd of success in HIV-positive patients was lower than in HIV-negative (aOR=0.43, 95%CI 0.16-1.11). Additionally, treatment success was similar in patients resistant to ethambutol, pyrazinamide or ethionamide as compared to patients susceptible to these drugs. Resistance to fluoroquinolones was strongly predictive of treatment failure.

Conclusions: The short MDR-TB regimen (including second-line injectable drugs recently excluded from group A drugs) implemented in programmatic conditions in a setting with high prevalence of both HIV and resistance to pyrazinamide, shows a good success rate, comparable to STREAM trial results. We believe that this regimen has a potential for further development especially with replacement of injectable drugs with new drug.

SOA-18-1186-02 The effect of different indicators of extensive disease on multidrug-resistant tuberculosis treatment outcomes: an individual patient data meta-analysis

JR Campbell,[1,2] SK Brode,[3] M Bonnet,[4] L Guglielmetti,[5] R Kempker,[6] R Laniado Laborin,[7] R Singla,[8] A Trajman,[9] P Viiklepp,[10] D Menzies,[2] The Collaborative Group for the Meta-Analysis of Individual Patient Data in MDR-TB Treatment 2019 [1]McGill University, Department of Epidemiology, Biostatistics and Occupational Health, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, McGill International TB Centre, Montreal, QC, Canada, [3]University of Toronto, Department of Medicine, Toronto, ON, Canada, [4]Epicentre, Médecins Sans Frontières, Kampala, Uganda, [5]Sorbonne Université, Université Pierre et Marie Curie 06, Unité 1135, Team E13 (Bactériologie), CR7 INSERM, Centre d'Immunologie et des Maladies Infectieuses, Paris, France, [6]Emory University, School of Medicine, Atlanta, GA, United States of America, [7]Universidad Autonoma de Baja California, School of Medicine, Tijuana, Mexico, [8]National Institute of TB and Respiratory Diseases, Department of Tuberculosis and Respiratory Diseases, New Delhi, India, [9]Federal University of Rio de Janeiro, Internal Medicine Post-Graduate Program, Rio de Janeiro, RJ, Brazil, [10]National Institute of Health Development, Estonian Tuberculosis Registry, Tallinn, Estonia. e-mail: jonathon.campbell@mail.mcgill.ca

Background: Treatment decisions for multidrug-resistant tuberculosis (MDR-TB) are multifaceted. Presence of extensive tuberculosis disease is one such factor that influences treatment. We sought to determine the effect that both radiological and bacteriological extent of disease indicators had on treatment outcomes in MDR-TB patients treated with individualized longer regimens.

Methods: Individual patient data for 13,104 MDR-TB patients from 53 studies in 40 countries were compiled. We conducted meta-analyses for the effect on outcomes (**Table**) of three indicators at treatment start: acid fast bacilli smear positivity, bilateral disease, and lung cavitation. Studies where an indicator of interest was reported for < 50% of patients were excluded. Propensity-score based adjustment was made for country income group, treatment year, age, HIV, antiretroviral therapy, past and present treatment, and drug resistance, with a study-level random effect. Within each meta-analysis, adjustment was also performed on the other two indicators of disease extent to limit potential confounding. Adjusted odds ratios (aOR) and 95% confidence intervals (95%CI) were calculated, referenced to groups without the disease extent indicator.

Results: Of the 13,104 patients, 11,697 (89.3%) were included in at least one analysis. Included patients were less likely to be from upper-middle-income countries, and more likely to have extensively drug resistant tuberculosis and receive new MDR-TB drugs. Smear positivity was associated with the highest risk of treatment failure or relapse (aOR 2.2; 95%CI 1.6-2.8) and bilateral disease had the highest risk of death (aOR 2.0; 95%CI 1.4-2.7). Lung cavitation appeared to be the weakest predictor of unfavourable outcome (**Table**).

			Adjusted odds ratios (95% confidence interval)	
Extent of Disease Indicator At Treatment Start	Patients Included (Number of Studies)	% Patients with Indicator	Treatment failure or relapse vs. success	Death vs. success
Acid Fast Bacilli Smear-Positive	10,259 (47)	71.7%	2.2 (1.6-2.8)	1.5 (1.3-1.8)
Bilateral Disease	5403 (30)	68.9%	1.7 (1.2-2.4)	2.0 (1.4-2.7)
Lung Cavitation	6543 (40)	61.0%	1.2 (0.9-1.6)	1.5 (1.1-1.9)

[Risk of Unfavourable Outcomes in Patients with Indicators of Extensive Disease]

Conclusions: Smear positivity and bilateral disease were most associated with unfavourable outcomes. This analysis highlights the importance of considering both of these factors when making MDR-TB treatment decisions. Future analyses should evaluate patient factors associated with these disease presentations and possible interactions between the indicators.

SOA-18-1187-02 Is transmission of drug-resistant tuberculosis changing? Investigating temporal trends using age-disaggregation

CF McQuaid,[1] T Cohen,[2,3] A Dean,[4] G Knight,[5] R Houben,[5] R White,[5] [1]London School of Hygiene and Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [2]Yale School of Public Health, Global Health Concentration, New Haven, CT, United States of America, [3]Yale School of Public Health, Public Health Modelling Concentration, New Haven, CT, United States of America, [4]World Health Organisation, Global TB Programme, Geneva, Switzerland, [5]London School of Hygiene and Tropical Medicine, Department of Infectious Disease Epidemiology, London, United Kingdom. e-mail: finn.mcquaid@lshtm.ac.uk

Background: The global Review on Antimicrobial Resistance (AMR) projected that by 2050 a quarter of deaths due to AMR would be due to drug-resistant tuberculosis (DR-TB), but there remains uncertainty over the current trend in burden. Here we infer changes in the DR-TB transmission burden by considering trends in the age-disaggregated disease incidence rate.
Methods: We use the odds ratio (OR) for DR-TB vs. drug-sensitive TB (DS-TB) in children (< 15 years) compared to adults (≥15 years) as an indicator for recent transmission, assuming a higher proportion of adult cases are likely to be a result of reactivation of latent infection. We compare the OR for 2000-2011 vs 2012-2018 using national DR-TB surveillance data reported to the World Health Organization (WHO) to test for any observable change.
Results: Sixteen countries had sufficient quality data to allow for comparison, primarily found in the WHO European Region. There is strong evidence that the OR decreased between 2000-2011 and 2012-2018 in three countries; Germany (1.64 [95% confidence interval CI 1.12-2.39] - 0.26 [CI 0.07-1.07]), Kazakhstan (1.03 [CI 0.71-1.5] - 0.38 [CI 0.31-0.45]) and the USA (2.35 [1.45-3.80] - 0.63 [CI 0.28-1.42]). There is very weak evidence for a declining OR in Uzbekistan (1.28 [80% CI 0.40-4.12] - 0.29 [CI 0.21-0.39]) and no evidence for a changing OR in the remaining countries.
Conclusions: A declining OR in Kazakhstan and potentially Uzbekistan may be an indication of a recent reduction in DR-TB transmission, while any link between declining ORs and burden in Germany and the USA may be confounded by migration. Our analysis suggests that despite the relatively long term and comprehensive surveillance of DR in TB, we still cannot definitively say whether or not DR-TB transmission is being controlled at a national and global level.

SOA-18-1188-02 Spread of drug-resistant tuberculosis at Brazilian border with Paraguay and Bolivia

M Tatara,[1] KE da Silva,[1] K Walter,[2] D Ferrari,[1] F Sacchi,[3] PC dos Santos,[1] F Moreira,[1] E Cunha,[4] J Andrews,[2] J Croda,[5] [1]Universidade de Federal da Grande Dourados, Laboratório de Pesquisa em Ciências da Saúde, Dourados, MS, Brazil, [2]Stanford University, Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Palo Alto, CA, United States of America, [3]Municipal Health Secretary, Referent Center of Tuberculosis and Leprosy, Dourados, MS, Brazil, [4]Central Laboratory of Public Health of Mato Grosso do Sul, State Secretary of Health, Campo Grande, MS, Brazil, [5]Oswaldo Cruz Foundation, Department in Public Health, Campo Grande, MS, Brazil. e-mail: juliocroda@gmail.com

Background: The objective of the present study was to describe the molecular characteristics and risk factors associated with recent transmission of tuberculosis (TB) drug-resistant cases isolated from a central-western Brazilian state bordering Paraguay and Bolívia.
Methods: From January/2014 to April/2017, we enrolled in a prospective study all confirmed diagnostic of TB cases. The patients answered a standardized questionnaire and variables obtained included sociodemographic and TB history data. All sputum specimens were examined by microscopy or GeneXpert® MTB/RIF. Drug susceptibility tests (DST) were performed using BACTEC MGIT 960 and the genetic relationship of *Mycobacterium tuberculosis* (MTB) isolates was evaluated using IS*6110*-RFLP. Strains were also subjected to whole genome sequencing (WGS) using via Illumina NextSeq (2 x 151-bp).
Results: Genotyping showed that 102 (58%) isolates were grouped into 26 clusters and 64 (36%) isolates had unique RFLP patterns. A high rate of recent resistant transmission was observed (30%); in addition, 78% of TB resistant cases were classified as new cases, indicating a high rate of primary resistance. Our study highlighted that alcoholism was associated with the acquisition of TB drug-resistant in patients with genomically unique strains. Incarceration ($P = < 0.01$; OR 7.05; 95CI 1.25-39.84) was identified as a major contributor to the spread of TB, especially MDR-TB. In addition, 46.1% of clustered cases comprised patients from community and prison settings evidencing the dissemination between these populations. Genetic relatedness among isolates and predictions of drug-resistance were largely consistent between WGS, genotyping and phenotypic methods.
Conclusions: Our findings showed that the population movements might be related with the introduction of new strains. In addition, our findings emphasize an urgent need to develop effective control strategies to interrupt the MTB transmission chain, especially among prisoners and community residents, thus preventing potential outbreaks of resistant TB.

SOA-18-1189-02 Systematic review and meta analysis of the proportion of relapses or reinfections among TB recurrent episodes

V Vega,[1] S Rodriguez,[1] P Van der Stuyft,[2] C Seas,[1,3] L Otero,[1,3] [1]Universidad Peruana Cayetana Heredia, Facultad de Medicina, Lima, Peru, [2]Faculty of Medicine, Ghent University, Department of Public Health, Ghent, Belgium, [3]Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru. e-mail: victor.vega.z@upch.pe

Background: The proportion of relapses and reinfections among recurrent tuberculosis (TB) episodes as measured by molecular biology techniques provides information to guide TB prevention and care activities. We analyzed the pooled proportion of relapses and reinfections among TB recurrences.

Methods: We searched Medline, Cochrane, LILACS and SciELO for cohort studies and clinical trials published from January 1980 until February 2018 in English, French and Spanish. Study selection and data extraction were done independently by two reviewers. We selected studies using molecular techniques to differentiate relapses and reinfections.

We assessed risk of bias using the Newcastle-Ottawa scale for observational studies and the Cochrane risk of bias tool for clinical trials. Meta-analysis of proportions using random effects model was done with RStudio Version 1.1.463.

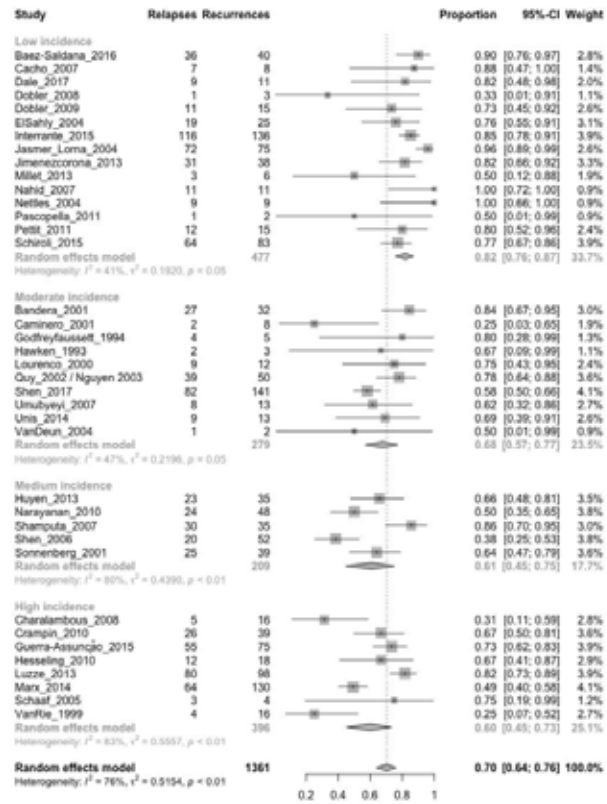
We tested for heterogeneity with the I^2statistic. We conducted subgroup analysis according the country-level incidence of TB as estimated by the World Health Organization for the year the study was conducted. TB incidence per 100,000 population was defined as low if less than 30 cases, moderate if between 30 and 100 cases, medium if between 100 and 300 cases and high if more than 300 cases. The protocol was registered in PROSPERO.

Results: Of 238 studies reporting TB recurrences, 38 differentiated relapses and reinfections. The overall pooled proportion of relapses was 0.70 (95% CI 0.64-0.76).

The pooled proportion of relapses in low incidence settings was 0.82 (95% CI 0.76-0.87), 0.68 (95% CI 0.57-0.77) in moderate incidence settings, 0.61 (95% CI 0.45-0.75) in medium incidence settings and 0.60 (95% CI 0.45-0.73) in high incidence settings.

The figure shows the proportion of relapses according to incidence level and the heterogeneity analysis.

Conclusions: Relapses were the most frequent mechanism of recurrence in low incidence settings. Heterogeneity between studies, especially in medium and high incidence settings was considerable, however, reinfection seems to play an important role.



[Forest plot: Proportion of relapses according TB incidence]

E-POSTER SESSION (EP)

EP-11-D1 Addressing TB in vulnerable populations

EP-11-197-02 Global burden of tuberculosis in incarcerated populations: a meta-analysis and statistical model

L Martinez,[1] O Cords,[1] K Walter,[1] J O'Marr,[1] J Zheng,[1] N Patkar,[1] J Croda,[2] J Warren,[3] T Cohen,[4] J Andrews,[1]
[1]Stanford University, Department of Infectious Disease and Geographic Medicine, Stanford, CA, United States of America, [2]Federal University of Mato Grosso do Sul, School of Medicine, Campo Grande, MS, Brazil, [3]Yale School of Public Health, Department of Biostatisitics, New Haven, CT, United States of America, [4]Yale School of Public Health, Department of Epidemiology of Microbial Diseases, New Haven, CT, United States of America.
e-mail: leomarti@stanford.edu

Background: More than 11 million people were incarcerated globally in 2018, and tuberculosis is a major cause of morbidity and mortality in this population. Despite this, the number of incarcerated individuals with tuberculosis globally is unknown. We conducted a meta-analysis of tuberculosis prevalence studies among incarcerated populations and used country-level incarceration data to estimate the tuberculosis burden in prisons globally and regionally.
Methods: We conducted a systematic search to identify studies published between 1980-2018 reporting prevalent tuberculosis in incarcerated populations, and two reviewers independently extracted information from eligible publications. We used random-effects modeling to pool tuberculosis prevalence estimates globally and by World Health Organization region. Using reported incarceration data from the World Prisons Brief, and drawing upon estimates of prevalence-to-incidence ratios, we then estimated the number of tuberculosis cases occurring in prisons for each region.
Results: In total, TB prevalence was reported in 136 studies from 31 countries, with a pooled prevalence of 1.6% (95% CI: 1.2-1.9%). Prevalence was highly heterogeneous, ranging from 0% to 33%.
The estimated incidence of tuberculosis (per 100,000 inmates) in prisons by region was: Africa, 2,100 (95% CI: 1,800-3,400); Americas, 800 (95% CI: 500-1,900); Eastern Mediterranean, 1,600 (95% CI: 1,100-4,600); Europe, 500 (95% CI: 300-1,100); South-East Asia, 700 (95% CI: 600-1,800); Western Pacific, 2,400 (95% CI: 2,300-4,700). The proportion of all tuberculosis cases occurring in prisoners ranged from 0.3% in the South-East Asia, 5% in the Western Pacific, to 12% in the Americas.
Conclusions: Globally, over 130,000 prisoners develop tuberculosis every year, with the majority occurring in the Western Pacific (41%) and Americas (21%) region, and incidence rates are consistently many fold higher than the general population. There is a need for increased focus on tuberculosis control strategies in prisons to address the excessive burden in this population and achieve global tuberculosis reduction targets.

EP-11-198-02 RefuScreen-TB: evaluation of improved TB screening algorithms in refugees using novel diagnostics

L Kübler,[1,2] L Olbrich,[1,2] K Avsar,[3] U Behrends,[2,4] U von Both,[2,5] M Seilmaier,[6] H Hoffmann,[7] C Geldmacher,[1,2] M Hölscher,[1,2] N Heinrich,[1,2] [1]Ludwig Maximilians University, Division of Infectious Diseases and Tropical Medicine, Munich, Germany, [2]German Centre for Infection Research (DZIF), Partner Site Munich, Munich, Germany, [3]Ludwig Maximilians University, Asklepios Klinik, Munich, Germany, [4]Technical University of Munich, Children's Hospital Schwabing, Munich, Germany, [5]Ludwig Maximilians University, Hauner Children' s Hospital, Munich, Germany, [6]Ludwig Maximilians University, Klinikum München Schwabing, Munich, Germany, [7]IML Red, WHO-Supranational Reference Laboratory of Tuberculosis, Munich, Germany.
e-mail: lisa.kuebler@liwest.at

Background: Tuberculosis (TB) remains one of the top ten causes of deaths worldwide. One of the populations most at risk for developing active TB are refugees. Since current screening and diagnostic algorithms perform sub-optimally, even in settings with satisfactory resources, more efficient tools for mass-testing and confirmation of disease are needed.
Methods: Since 2017, children and adults were enrolled in RefuScreen-TB, an observational diagnostic study at 4 hospitals in Munich, assessing a variety of new tests for active TB. Inclusion criteria were suspicion of active TB or recent TB contact history. The screening and diagnostic workup included specimen collection for TB culture and further investigations for active TB as determined by the clinicians. Patients were classified as having confirmed TB, unconfirmed TB and unlikely TB based on microbiological, radiological and clinical findings. New test performance is currently being evaluated.
Results: Until now, 357 patients were recruited, 69% of those underwent TB testing due to clinical suspicion based on symptoms, while only 15% due to abnormal admission examination. In total, 57 nationalities were included, 36% were refugees, 25% migrants from safe countries and 36% German/EU citizens; the highest number of patients enrolled were of German nationality, followed by Nigerian, Somalian, Romanian and Eritrean. 174/357 (49%) were diagnosed as having active TB and started on anti-TB treatment. TB was microbiologically confirmed in 135/174 (78%) by PCR and/or culture.

Conclusions: RefuScreen-TB is a unique study setup that allows to enrol a significant number of patients for a TB diagnostic study in a well-resourced setting with a considerable number of Germans/EU-citizens. Analysis is still ongoing with further results to be presented, including correlation of demographics such as flight routes with TB status. With this well-characterized cohort the ongoing evaluation of new tests with different detection-approaches will generate findings of high interest.

EP-11-199-02 Improving the diagnosis of tuberculosis in Cameroon prisons in 2018 through mass tuberculosis campaigns

A Kuate Kuate,[1] V Mbassa,[2] A Etoundi Evouna,[3] F Bekang Angui,[4] E Belinga,[2] A Wandji,[5] A Mintop,[6] H Bava,[7] M Manga Ze,[8] [1]Cameroon National Tuberculosis Program, Case Management, Training and Researc Unit, Yaounde, Cameroon, [2]Cameroon National Tuberculosis Program, Management, Yaounde, Cameroon, [3]Cameroon National Tuberculosis Program, Monitoring and Evaluation, Yaounde, Cameroon, [4]German Society for International Cooperation, IT Department, Yaounde, Cameroon, [5]Cameroon National Tuberculosis Program, Littoral Regional Office, Douala, Cameroon, [6]Cameroon National Tuberculosis Program, East Regional Office, Bertoua, Cameroon, [7]Cameroon National Tuberculosis Program, Far North Regional Office, Maroua, Cameroon, [8]Cameroon National Tuberculosis Program, South Regional Office, Ebolowa, Cameroon. e-mail: akuate2001@yahoo.com

Background: On average 23 times higher than in the general population, tuberculosis (TB) situation in Cameroon prisons is a major public health problem. In 2018, mass TB campaigns were organized there to diagnose and manage pulmonary tuberculosis (PTB) cases missed by routine screening and identify PTB case cells/neighborhoods for contact tracing.
Methods: In 2018, mass campaigns were organized in 39 prisons. Were considered as tuberculosis suspects, the inmates who had been coughing since ≥1 week. The other symptoms of tuberculosis were also checked. A questionnaire to collect demographic data and information about TB symptoms was submitted to them. A sputum test by Genexpert or TB Lamp was used for the detection of Mycobacterium tuberculosis (those who were positive for TB Lamp had a GenExpert test). They were also offered a voluntary HIV test.
Results: In all, 50% (39/78) of prisons were involved in 2018 mass tuberculosis campaigns. Approximately 67.7% (20772/30701) of inmates throughout the country were screened. 16.5% (3423/20772) of which 96.6% were male and 3.4% female suspected of tuberculosis. 4% (136) of bacteriologically proven pulmonary tuberculosis (BPT) cases were reported and managed 1.02% (35) of suspected cases were reported as HIV positive, 3% were TB/HIV co-infected. No multi drug resistant tuberculosis case was found.
Conclusions: These mass campaigns revealed that despite an effective TB control program in prisons, undetected PTB cases remain high. Besides, regular TB mass campaigns, combined with better prison conditions, could reduce the incidence of the disease in prisons and in the general population.

EP-11-200-02 Effect of urban DOTS on tuberculosis case finding among prisoners in Kabul prisons - a document review

SM Sayedi,[1] A Hamim,[1] D Safi,[1] MK Rashidi,[1] N Tareen,[1] G Qader,[1] MN Samadi,[1] L Manzoor,[2] P Suarez,[3] N Ahmadzada,[2] [1]Management Sciences for Health (MSH), Challenge TB (CTB) Project, Kabul, Afghanistan, [2]Ministry of Public Health (MoPH), National Tuberculosis Program, NTP, Kabul, Afghanistan, [3]MSH, MSH, Arlington, VA, United States of America. e-mail: mrashidi@msh.org

Background and challenges to implementation: In 2018, there are about 12,500 inmates within two prisons in. Before 2015, no complete tuberculosis (TB) services or reporting systems existed in Kabul prisons, which resulted in low TB case findings. Only 37 cases of all form TB within prisons was reported in 2014. The National TB Program (NTP) with support from the USAID-funded Challenge TB (CTB) project expanded the urban DOTS approach, which involves public and private health care providers in TB control efforts, to two main prisons in Kabul to address this gap
Intervention or response: After signing a memorandum of understanding with the appropriate ministries and conducting a baseline assessment, CTB created a targeted intervention to combat TB in prison populations. The CTB project trained 22 medical staff on: TB case management; proper recording and reporting processes; improved supervision, monitoring, and feedback loop to prison TB clinics; and conducting active screening through mobile X-ray. The NTP and CTB technical teams reviewed data collected from 2015-2018 using standard NTP reporting tools and compared the information with existing surveillance data.
Results and lessons learnt: In 2018, 229 all form TB cases were identified in prisons, compared to 37 cases in 2014 (P Value < 0.0000001). Out of 229 cases, 90 of them were bacteriologic confirmed TB cases in 2018, in 2014 it was 31 cases. In five years a total of 30,588 all form of TB cases were identified in Kabul, 893 (3%) of them were in prisons. Of the total 9,596 bacteriologically confirmed TB cases in Kabul, 391(4%) were from prisons. The incidence of TB among inmates was 1823/100,000 population, while it was 146 in general populations of Kabul.
Conclusions and key recommendations: Urban DOTS services in Kabul prisons made significant improvements to case finding among inmates and recommend engaging other prisons in TB services as high risk vulnerable groups.

Indicator	2014	2015	2016	2017	2018	Total
# of Outpatient Attendance	17100	18,461	35,450	47,050	50,447	151,408
# of Presumptive TB patients	320	534	820	754	881	3309
# of bacteriologically confirmed TB cases notified	31	77	106	87	90	391
# of all forms TB cases notified	37	115	212	300	229	893

[Table 1: Yearly cascade data for number of TB case notified and confirmed in Kabul prisons, 2015 - 2018]

EP-11-201-02 Tuberculosis in women and children among internally displaced population in North-Eastern Nigeria

S Abdulkarim,[1] S John,[2] M Smelyanskaya,[3] E Ubochioma,[4] [1]Gombe State Agency for Control of AIDS, Public Health, Gombe, Nigeria, [2]Adamawa State Agency for Control of AIDS, Public Health, Adamawa, Nigeria, [3]Stop TB Partnership, TB REACH, Geneva, Switzerland, [4]National Tuberculosis, Leprosy and Buruli Ulcer Control Programme, Public Health, Abuja, Nigeria. e-mail: surajkwami@yahoo.co.uk

Background and challenges to implementation: Insurgent activities of "Boko Haram" in North-Eastern Nigeria in the past 6 years led to the displacement of over 2 million persons with a high number of women and children.

Internally displaced populations (IDPs) are at high risk of tuberculosis (TB) due to overcrowding, poor ventilation, poor access to health services and high prevalence of HIV among other factors. Malnutrition and harmful gender norms confer additional risk of TB among displaced women and children.

Intervention or response: Trained Volunteers conducteddoor to door TB education and screening, mass community outreach and TB contact examinations from 23thJune 2017 to 30thAugust 2018 in 12 of 48 Local Government areas of Adamawa, Gombe and Yobe States in IDP Camps and Host Communities. Sputum samples were collected, transported and analysed using GeneXpert equipment while childrenunder six years were transported for clinical evaluation at designated health facilities.

Results and lessons learnt: Of the 323,936 verbally screened IDPs, 202,245 (62%) were women and 16,529 (5.1%) were children; out of which 16,340 (8.1%) and 1,401 (8.3%) women and children were TB symptomatic respectively. 78% (12,784) of TB symptomatic women were detected through door to door screening while 55% (768) of the children were detected through outreach; 869 (53%) women and 126 (7.7%) children were detected with all form of TB.

Conclusions and key recommendations: A high proportion of TB cases among IDPs identified were women and children. Door to door TB education and screening are effective in detecting TB cases among women compared to mass community outreach while both approaches are effective in detecting children.

EP-11-202-02 Patchwork epidemiological strategy for the active search of pulmonary tuberculosis in marginalised communities: first Latin America overview

N Romero-Sandoval,[1,2] H Sánchez-Pérez,[2,3] O Horna-Campos,[2,4] M Martin,[1,2,5] Latin America and Africa Research Network-GRAAL [1]Universidad Internacional del Ecuador, School of Medicine, Quito, Ecuador, [2]Grups de Recerca d'Amèrica i Àfrica Llatines' Research Network, GRAAL, Barcelona, Spain, [3]El Colegio de la Frontera Sur - ECOSUR, Salud y Sociedad, San Cristóba de Las Casas, Mexico, [4]Universidad de Chile, Escuela de Salud Pública, Santiago, Chile, [5]Universidad Autonoma de Barcelona, Medicina Preventiva, Barcelona, Spain. e-mail: nromero@uide.edu.ec

Background and challenges to implementation: The control and prevention of pulmonary tuberculosis (PTB) is a great challenge in rural or marginalized communities, with limited geographic and cultural access, lack of resources, and non-representation in population censuses. The macro indicators of health (incidence, prevalence and mortality rates) do not represent their reality. We show evidence of hidden prevalence of PTB and chronic cougher (CC) in marginalized communities from three Latin America countries through patchwork strategy, and illustrate the difference regarding official data, through likelihood analysis.

Intervention or response: In our inter-college research network, namely the "Latin America and Africa Research Network-GRAAL", we have been working on PTB matters with indigenous communities and other marginalized communities for 15 years. We implement the active search of CC throughout the participation of whole community (Patchwork strategy), considering their worldview, in coordination with health systems.

Results and lessons learnt: In Mexico, Ecuador and Peru (Figure 1) patchwork studies revealed hidden 7-8% prevalence of CC, in comparison with the official 4% anticipated. A general hidden prevalence of 12% of PTB much higher to the official rates (Table 1). When joint efforts are made with the communities and discrimination against people with PTB is avoided, the application of the direct observed treatment strategy achieves full compliance, when supervised by the community itself.

Conclusions and key recommendations: Patchwork strategy is a tool to fight against the inequalities in the PTB. The joint efforts of academics, health services and the communities lead to greater adherence rates and cure, in the short term and maintained over time.

Country	Place	N	CC (CC rate - %) [Valuable samples]	PTB (Positive Ziehl-Nielsen smear test) - frequency	Positive rates (%) on valid samples (95% CI)	Estimated prevalence rate over population and contrast test	Official notification rate in the country or area studied
Mexico	Chiapas / Secondary health care (1 marginalized region)	Spontaneous demand of medical attention (hospital secondary level)	221 (NA) [219]	46	21 (15.5 - 26.5)	71-124*10-5 G2 >7.9§	34.2 *10-5
	Chiapas / Primary health care (6 marginalized indigenous communities)	2203	573 (26%)* [153]	17	11.1 (6.1-16.5)	71-124*10-5 G2 >7.9§	34.2 *10-5
	Chiapas / Home survey (32 marginalized indigenous communities)	11274	340 (3.1%) [227]	17	7.5 (3.5-12.5)	71-124*10-5 G2 >7.9§	34.2 *10-5
Ecuador	Central Andean Region (2 marginalized indigenous communities)	640	172 (26.9%)* [92]	44	47.8 (37.4-58.2)	No data to contrast	No data to contrast
	South-Eastern(d) Amazonia (12 marginalized indigenous communities	1598	123 (7.7%)* [118]	2	1.7 (0.8-4.2)	1.25*10-3 G2=11.8§	34 * 10-5
	South Andean(d) Region 2 marginalized neighborhood)	2149	107 (4.9%) [107]	3	2.8 (0.9-6.5)	1.4 *10-3 G2=18.3§	34* 10-5
Peru	Lima / Primary health care (1 marginalized neighborhood)	Spontaneous demand of medical attention	150 (NA) [142]	17	11.9 (10.3-17.7)	No data to contrast	No data to contrast
	Lima / Primary health care (1 marginalized neighborhood)	Public transportation workers hospital records	NA	NA	NA	21.3*10-3 G2=21.3§	7.5*10-3

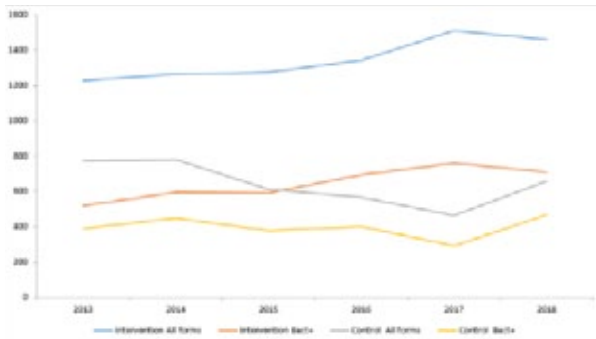
NA Not applicable.
*Proportion of CC. G^2 were significant, $p < 0.001$, under the official hypothesis of 4% of CC. §Conformity contrast ($p < 0.001$). The contrast between the observed rates and those recorded in official statistics (local rate for CC and national rate for PTB) was performed using likelihood ratio contrasts and the corresponding statistic (G2).

[EP-11-202-02 Table 1. CC, PTB, prevalence rates and contrast between observed rates and those recorded in official statistics by sites where patchwork strategy was applied]

EP-11-203-02 District-level combination interventions lead to significant increase in tuberculosis case detection rates among mining workers in Ethiopia

B Reshu,[1] DJ Dare,[2,3] S Negash,[1] D Bekele,[4] N Hiruy,[1] D Datiko,[1] M Melese,[5] P Suarez,[5] [1]Management Sciences for Health, USAID/Challenge TB Project, Addis Ababa, Ethiopia, [2]KNCV Tuberculosis Foundation, Technical Division, The Hague, Netherlands, [3]Formerly, Management Sciences for Health, USAID/Challenge TB Project, Addis Ababa, Ethiopia, [4]Oromia Regional Health Bureau, Disease Prevention and Control, Addis Ababa, Ethiopia, [5]Management Sciences for Health, Infectious Diseases Cluster, Arlington, VA, United States of America.
e-mail: degu.dare@kncvtbc.org

Background and challenges to implementation: Artisan mining workers are at significantly higher risk of getting infected and developing TB disease due to high prevalence of other lung diseases, overcrowded living conditions, high rates of HIV infection, and frequent alcohol and tobacco use. Since most of the miners are migratory workers, they often have limited access to established health services. Our aim was to improve TB case finding among mining workers through targeted interventions.
Intervention or response: We identified six mining districts in two zones of Oromia region. In each district, we deployed a district project coordinator who closely worked with the government counterpart. The district coordinator trained health extension workers, sensitized and mobilized community volunteers, and facilitated slide fixing and referral. Moreover, the project provided motor bikes to facilitate transportation of staff and specimen samples and organized district-level quarterly review meetings. We collected routine notification data and compared TB case notification rates between control and intervention districts both for the pre-intervention (2013-2015) and post-intervention (2016-2018) periods. We selected six control districts from non-adjacent, mining zones.
Results and lessons learnt: Notified all forms (AF) TB cases declined from 2,162 to 1,692 over the intervention period in the control districts, yielding a 22% reduction in the number of AF TB cases. On the other hand, there was a 14% increase in AF TB cases in the intervention districts, making the overall effect of the intervention 36%. Bacteriologically confirmed (Bact+) TB case notification declined by 5% in the control districts, from 1,221 to 1,162, while there was a 27% increase in intervention districts, from 1,708 to 2,163. The overall effect of the intervention on Bact+ case notification rate was 32%. See Figure.
Conclusions and key recommendations: Targeted district level interventions led to significant increase in TB case notification rates. Such interventions should be integrated within the local health system to ensure sustained impact on the TB epidemic.



[TB case notification rates in intervention and control sites, Oromia, Ethiopia: 2013 - 2018]

EP-11-204-02 TB case finding in vulnerable populations in Navoi Region, Uzbekistan

K Mukhamedov,[1] N Parpieva,[2] I Liverko,[2] J Ismoiliva,[3] M Volik,[4] S Tashkhodjaeva,[4] M Saipova,[4] [1]Regional TB Dispensary Navoi Region, Republican of Uzbekistan, MOH Uzbekistan, Navoi, Uzbekistan, [2]Republican Specialized Scientific-Practical Medical Center of Tuberculosis and Pulmonology, MOH Uzbekistan, Tashkent, Uzbekistan, [3]Project HOPE - People-to-People Health Foundation, Inc., USAID TB Control Program, Dushanbe, Tajikistan, [4]Project HOPE - People-to-People Health Foundation, Inc., USAID TB Control Program, Tashkent, Uzbekistan.
e-mail: navoi8861@mail.ru

Background and challenges to implementation: Tuberculosis (TB) is associated with a range of medical and social factors that are often concentrated in specific vulnerable, hardly accessible populations. The USAID TB Control Program, together with National TB Program (NTP) of Uzbekistan considered the following key determinants of vulnerability: HIV infection, injecting drug use, imprisonment, and labor migration. To improve access to health services, the Program piloted a model of a multidisciplinary team (MDT) in Navoi region, Uzbekistan.
Intervention or response: The MDT (included: TB specialist, HIV specialist, psychologist, nurse, outreach workers) linked TB services with local communities, identified people at-risk from vulnerable populations and provided them with access to TB diagnosis, treatment and psychosocial support. At first, an outreach worker screened people at risk for presumptive TB and referred them for testing according to national regulations. Referrals were made through a voucher system, ensuring confidentiality and proper registration. During intervention implementation (June 2015 to October 2018), the MDT referred 9496 beneficiaries. 7982 persons (84%) reached testing. 69 cases were detected (0.9%) and 66 (95%) started treatment. 1093 TB cases were reported in the region (6.3% identified through MDT) during the same period. As population, covered by Navoi MDT, represents 2% of the country's population, the extrapolation would demonstrate considerable impact.
Results and lessons learnt: Achievement of the new UN targets on TB and goals of the Decree of the President of the Republic of Uzbekistan on "Measures to improve the provision of TB and pulmonary care" is impossible without addressing vulnerable groups. The MDT model in Navoi region showed promising results with high referral and treatment initiation.
Conclusions and key recommendations: The MDT model needs new approaches to ensure its sustainability during the country´s transition to self-financing. Based on the model, the Ministry of Health and NTP plan to add psychologists' positions in TB facilities and enhance case management services.

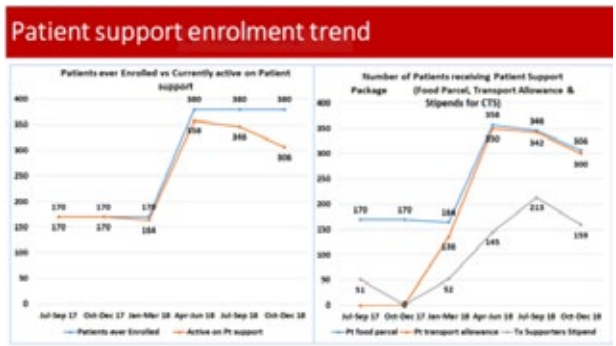
EP-11-205-02 Successful implementation of a comprehensive support package for patients with drug-resistant tuberculosis in Eswatini

D Vambe,[1] N Dlamini,[2] S Masuku,[3] T Dlamini,[4] F Msibi,[1] P Mndzebele,[5] M Nkambule,[2] B Kerschberger,[6] [1]National TB Program, PMDT, Manzini, Eswatini, [2]National Tuberculosis Program, PMDT, Manzini, Eswatini, [3]National TB Control Program, Monitoring and Evaluation, Manzini, Eswatini, [4]National Tuberculosis Program, TB Program Management, Manzini, Eswatini, [5]National Tuberculosis Program, DOTs, Manzini, Eswatini, [6]Médecins Sans Frontières (Operational Centre Geneva), Research, Mbabane, Eswatini.
e-mail: dvambe@gmail.com

Background and challenges to implementation: Treatment of drug resistance TB is challenging in many resource poor settings. The long duration of treatment, high pill burden and catastrophic costs for patients poses challenges for treatment adherence. From 2011-2016, Eswatini piloted the provision of a comprehensive patient support package (cPSP) with enhanced nutritional, economic and adherence support. We describe the national scale-up of this intervention thereafter.
Intervention or response: The national TB control programme (NTCP) received additional funding through the Global Fund for the nationwide scale-up of cPSP. In 2017, one focal person was recruited to coordinate the implementation. TB health care workers, implementing partners and the community were sensitized about the new patient support package. A food package for nutritional support was defined and agreements were signed with supermarkets near the 13 treatment sites. Standard operating procedures were developed followed by onsite training of health care workers for the provision of cPSP. CTS were trained to provide direct-observed therapy, patient support and monthly reports.
Results and lessons learnt: By December 2018, 306 patients were active on treatment. All of them (100%) received the food packages, 300 (98%) received transport allowance and 159 (52%) had a CTS receiving a stipendum. A lesson learnt was that the administrative part of the programme needed a focal person for implementation. Advocacy was needed to ensure that all stake-

holders are on-board and understands the programme. Transparent communication by health workers to both patient and CTS is required to avoid misunderstanding related to the financial benefits. Submission of reports by CTS was most challenging, which could be solved by an electronic reporting system.

Conclusions and key recommendations: Effective coordination across stakeholders and transparent communication are key to successful implementation of CPSP. This package has improved collaboration between patients and care givers. Continued supportive supervision with monitoring systems in place is important to ensure good progress in implementation.



[Patient support enrolment trend]

EP-11-206-02 Association of nutritional factors with tuberculosis treatment outcomes

H Gupta,[1] S Kant,[2] Dr. Amita Jain Dr. S.M. Natu [1]King George's Medical University, Pediatric Oncology, Lucknow, India, [2]King George's Medical University, Respiratory Medicine, Lucknow, India. e-mail: skantpulmed@gmail.com

Background: Malnutrition increases the risk of progression of Tuberculosis (TB) infection to active TB disease and further leads to weight loss. Lack of adequate weight gain with TB treatment is associated with an increased risk of death and TB relapse and can be an indication poor treatment response. The aim of this study is to assess the nutritional factors associated with tuberculosis treatment outcome.

Methods: A prospective follow-up cohort study was conducted at the two urban Directly Observed Treatment Short-course (DOTS) centers of Lucknow. Assessment of nutritional status was performed by anthropometric measurements and dietary intake computations by 24-hour Dietary Recall Method. The paired student t-test was used to compare the nutritional changes from baseline to six-month treatment. Multivariate logistic regression analysis was used to determine the factors associated with treatment outcomes.

Results: A total of 370 newly diagnosed pulmonary tuberculosis patients were recruited. Out of these, 28 patients were lost to follow-up after treatment and remaining 342 patients were analyzed. The mean(±SD) age of the study population was 29(±12) years. At baseline, total nutrient intake was less than 50% as compare to Recommended Dietary Allowances. Significant ($p< 0.0001$) increase was observed in nutrients intake with the clinical, radiological and bacteriological outcomes at six month treatment. Protein ($p=0.04$) and retinol ($p=0.01$) intake were significantly associated with the conversion of clinical outcomes, i.e. symptomatic to asymptomatic. Intake of energy ($p=0.04$), protein ($p=0.04$) and fat ($p=0.008$) were significantly associated with complete radiological clearance. In drug-related outcomes, energy ($p=0.01$) and protein ($p=0.02$) intakes were associated significantly with drug resistance. Among all the nutrients, protein intake was closely associated with clinical, radiological and bacteriological outcomes.

Conclusions: Protein intake was related with different clinical, radiological and bacteriological outcomes. Increased intake of protein was probably associated with rapid clinical recovery and weight gain, complete radiological clearing and early bacteriological conversion.

EP-12-C10 Diagnostic laboratory quality and integration

EP-12-207-02 Improving tuberculosis diagnosis using an integrated TB-HIV intra-district courier system in Kasama district, Zambia

J Mulenga,[1] F Chibinga Mwiinga,[1] L Nachilembo Mulenga,[1] J Bwembya,[1] K Mwape,[2] J Sikazwe,[2] L Kabango,[3] M Malukutu,[1] D Phiri,[1] J Nikisi,[1] [1]USAID Eradicate Tuberculosis, TB, Lusaka, Zambia, [2]Ministry of Health, Public Health, Kasama, Zambia, [3]USAID EQUIP, Laboratory, Kasama, Zambia. e-mail: jmulenga@path.org

Background and challenges to implementation: Diagnosis of tuberculosis (TB) in resource-limited settings like Zambia is hampered by weak and usually fragmented sputum specimen courier systems. To improve TB diagnosis in Kasama District of Zambia, the USAID Eradicate TB (ETB) project integrated sputum specimen couriers into an existing HIV courier system supported by another partner—EQUIP Zambia.

Intervention or response: This intervention was implemented between July and December 2018 in the two GeneXpert® hubs in Kasama District, where EQUIP Zambia was already operating a courier system for HIV viral load testing and early infant diagnosis. Following a proposal from ETB, sputum sample referral was integrated into the existing HIV courier system. ETB trained two laboratory personnel as trainer of trainers in sputum collection and packaging, who later oriented

other staff and motorbike riders. Two Motorbike riders collected viral load samples together with sputum samples on a weekly basis from 41 non-diagnostic sites and transported them to GeneXpert hubs. Routine program data were collected retrospectively from laboratory registers and sputum tracking forms and analyzed in January 2019.

Results and lessons learnt: The number of sputum samples delivered to GeneXpert hubs increased by 76% (from 400 in the period January-June 2018 to 703 in the period July-December 2018). The number of patients diagnosed with bacteriologically confirmed TB at GeneXpert hubs also increased by 143% (from 23 in the period January-June 2018 to 56 in the period July-December 2018). Percentage rejection rate was 5 % (38 out of 703 samples).

Conclusions and key recommendations: This intervention has demonstrated the feasibility and potential of integrating sputum and HIV viral load courier systems to improve access to TB diagnostic services in resource-limited settings. This integrated approach may also help promote rational use of resources by both the TB and HIV programs through avoidance of duplicated trips to health facilities and improve TB screening among people living with HIV.

EP-12-208-02 Tuberculosis sample transportation using Indian postal services in Delhi, India

M Hanif,[1] KK Chopra,[2] A Khanna,[3] KS Sachdeva,[4] N Kumar,[4] S Anand,[5] S Raman,[6] Z Sidiq,[1] N Babbar,[3] S Chandra,[5] [1]New Delhi TB Centre, Intermediate Reference Laboratory Delhi, New Delhi, India, [2]New Delhi TB Centre, State TB Training and Demonstration Centre, New Delhi, India, [3]Government of NCT of Delhi, State TB Control Office, New Delhi, India, [4]Government of India, Central TB Division, New Delhi, India, [5]Office of World Health Organization India, Tuberculosis Division, New Delhi, India, [6]Municipal Corporation of Delhi, District TB Office, New Delhi, India. e-mail: irldlndc@rntcp.org

Background and challenges to implementation: Universal Drug Sensitivity Testing (UDST) requires Tuberculosis (TB) sample transport availability at the nearest peripheral diagnostic facility for the benefit of patient treatment. In order to escalate the UDST flow in Delhi, an operational framework was designed between State TB program and Indian Postal Service for sputum sample transportation from peripheral diagnostic centres to Culture and Drug Sensitivity (CDST) Laboratories. The study aims to understand the feasibility of the operational framework deployed under programmatic conditions for sputum transport in Delhi.

Intervention or response: East Delhi District of Karawal Nagar was selected based on randomization of laboratory workload and distance from CDST laboratory. Primary TB specimens were packaged according to requirements for Category B substances. Between September 2018-October 2018, samples were picked from peripheral diagnostic centre by representative of Indian Postal Service. Each peripheral diagnostic centre had India Postal Service branch in their area. Feasibility of the pilot was assessed based on predefined indicators:
(a) Sample turnaround time
(b) Number of samples rejected due to leakage
(c) Timely reporting of sample results
(d) Cost per sample transport through India Post versus cost through courier mechanism.

Results and lessons learnt: A total of 89 sputum samples were transported during the study period. All the samples were delivered to the CDST Laboratory within one day of dispatch. No breakage of the samples was observed and results could be communicated to the respective centers within the permissible turn-around-time. Cost per sample through India Post was reduced by half and 1/4th when compared to cost of sample transportation with help of patient's relative and private courier agency, respectively ($p< 0.01$).

Conclusions and key recommendations: Sample transport through Indian Postal service is an excellent example of public sector collaboration under programmatic conditions. The services are cost effective and extensively decentralised for country wide roll out in diverse settings.

EP-12-209-02 Improving lab testing among presumptive TB and pulmonary TB adult patients in, Moresby South, Papua New Guinea

S Murithi,[1] S Gacheri,[1] I Naraman,[2] W Tepori,[3] E Edimani,[4] F Kaemala,[1] D Tesfaye,[4] [1]FHI 360, Health-TB, Port Moresby, Papua New Guinea, [2]National Capital District, TB, Port Moresby, Papua New Guinea, [3]Badili BMU, TB Clinic, Port Moresby, Papua New Guinea, [4]FHI 360, Health, Port Moresby, Papua New Guinea. e-mail: smurithi@fhi360.org

Background and challenges to implementation: Papua New Guinea (PNG) has a high burden of tuberculosis (TB), multidrug-resistant TB, and TB/ HIV co-infection. Considerable proportion of TB cases are not bacteriologically confirmed (69%). National Capital District (NCD) is one of the three TB-hot spots in PNG. In 2017, 27% of pulmonary TB patients in NCD never received sputum testing due to limited access to diagnostic services; few staff and inadequate documentation of laboratory results resulting in patients being reported as clinically diagnosed. To address these gaps, TB project introduced various interventions at Badili Clinic in January-December 2018.

Intervention or response: Interventions at Badili included establishing a triage corner where all presumptive TB patients are screened before being sent for sputum testing; establishing an in-house microscopy laboratory with an in-built quality assurance system; designating

full-time staff to manage presumptive patients & ensure sputum test results are recorded in the register; and assigning a van to support sample shipment for GeneXpert testing to nearest reference laboratories. GeneXpert results are transmitted online via emails to clinicians.

Results and lessons learnt: During the intervention period, 803 (81%) presumptive patients received a sputum test compared to 386 in 2017. The percentage of pulmonary patients receiving a sputum test at diagnosis increased from 75% in Q1, 80% in Q2, 93% in Q3 & to 100% in Q4. During same period, sputum conversion for smear-positive patients at two months improved from 67% in Q1 to 85% in Q4. An in-house microscopy laboratory contributed to improved turnaround time for testing from two weeks to 24 hours.

Conclusions and key recommendations: Increasing access to quality-assured laboratory diagnostics; establishing an efficient sputum transportation system and mechanism for reporting results; and having designated staff to screen presumptive patients can reduce barriers to quality TB laboratory testing.

EP-12-210-02 Improving laboratory quality management systems for TB diagnostics services in Mukono District, Central Uganda

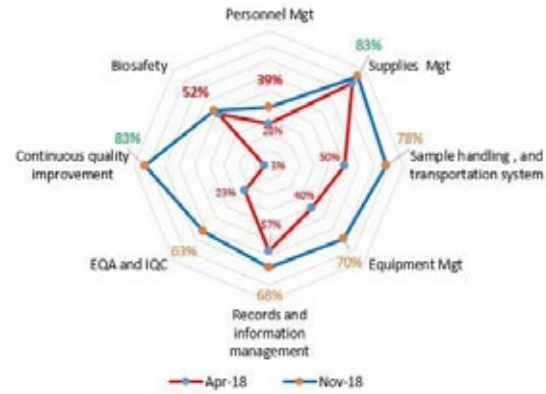
R Mangeni,[1] K Mutesasira,[1] A Nkolo,[1] M Joloba,[2] E Birabwa,[3] H Nabawanga,[4] [1]University Research Co., LLC (URC), USAID Defeat TB Project, Kampala, Uganda, [2]National Tuberculosis & Leprosy Control Program, National Tuberclosis Reference Laboratory, Kampala, Uganda, [3]USAID, USAID/Defeat TB Project, Kampala, Uganda, [4]Mukono District Local Government, District Health Department, Kampala, Uganda. e-mail: mangenironald63@gmail.com

Background and challenges to implementation: Medical laboratories have an essential role in determining clinical decisions and providing clinicians with information that assists in the diagnosis and management of Tuberculosis. The TB laboratory infrastructure and test quality is still in the nascent stages in most districts in Uganda. WHO-AFRO established the Stepwise Laboratory Quality Improvement Process towards Accreditation (SLIPTA) framework in developing countries to achieve ISO 15189 standards. Therefore it was valuable for USAID Defeat TB project to establish a process by which laboratories can improve TB diagnostic quality of services following the SLPITA framework.

Intervention or response: Nine (9) public health facilities in Mukono in central Uganda were assessed for baseline in April 2018 and reassessed for improvement in November 2018. Assessors used a customized WHO-AFRO SLIPTA checklist comprised of seven elements. Onsite monthly mentorship were conducted using quality improvement approaches to close gaps.

Results and lessons learnt: There was improvement across the quality essentials through as monitoring results TAT, monthly cleaning of genexpert machines filters, quarterly EQA participation, and use of backup hub riders to improve sample transportation. Least performing essentials were Biosafety (59%) and Personnel (39%) mainly due to poor infrastructure and inadequate staff respectively.

Conclusions and key recommendations: This stepwise mentorship support and periodic assessment highlights the priority areas for technical assistance to optimize laboratory performance as the laboratories aim at achieving international accreditation. Biosafety and human resource capacity still remain a big challenge in Laboratory TB services, thus calls for urgent attention to address the areas.



[Average score for laboratory quality management components in 9 health facilities in Mukono district]

EP-12-211-02 Increasing tuberculosis case detection rate through the public private mix: a progressive and productive Nigeria experience

E Adibo,[1] E Onyeje,[1] I Okekearu,[2] [1]El-Lab Limited, Pathology, Lagos, Nigeria, [2]USAID SHOPSPlus Project, SHOPSPlus, Abuja, Nigeria. e-mail: adibo_elo@yahoo.com

Background and challenges to implementation: Nigeria is a high tuberculosis, TB, burden country where, annually, over 300,000 new cases go undetected or unreported. The National Tuberculosis Programme (NTP) in March 2016 adopted Xpert MTB/Rif assay for the diagnosis of all presumptive cases. The technology is barely employed in the Nigerian private sector sought by approximately 60% of Nigerians.

Intervention or response: The Federal Ministry of Health, in September, 2018 made the first ever donation of a Genexpert GX4 machine to a private organization, El-lab Limited. El-lab has demonstrated commitment and proficiency by ensuring a 24hour 7days a week testing of sputum received from across the densely populated Lagos state. El-lab created private-private networks with other private laboratories and hospitals in Lagos state for ease of sample referrals to its Genexpert Site and employed the services of 2 dispatch riders for sputum samples pick up and keyed into the NTP reporting system.

Results and lessons learnt: Within 6 months of operations, El-lab Genexpert Site have run about 3,960 sputum samples, a huge progress when compared with the obtainable average of 1440 tests for the same period from a typical Genexpert site on the National Tuberculosis Programme (NTP). Within this period, about 374 samples/persons were diagnosed with Drug Susceptible TB, while 24 persons were diagnosed with Rifampicin Resistant TB. Test results were promptly released and over 90% of cases commenced treatment due to the ease of referral within the network of facilities as promoted by the USAID funded SHOPS Plus project.

Conclusions and key recommendations: Deployment of advanced methods of TB diagnosis into the private sector is key to increasing rate of TB case finding; tested and proven private practitioners should be identified and supported by the NTP in this direction. Formation of network of facilities aids referral and ease of communication with government to commence treatment using the government provided free TB drugs.

EP-12-212-02 Introduction of Cartridge-Based-Nucleic-Acid-Amplification-Test (CBNAAT) proved a boon to NTP; increased DR-TB and RifRes cases improved UDST status in Odisha, India

G Mallick,[1] B Panda,[2] PK Hota,[2] MS Munir,[2] S Mishra,[2] B Patnaik,[2] R Tarelakar,[3] S Mohanty,[4] [1]The Union, TB, New Delhi, India, [2]Government of Odisha, TB, Bhubaneswar, India, [3]World Health Organisation, TB, Bhubaneswar, India, [4]The Union South East Asia, TB, New Delhi, India. e-mail: gmallick@theunion.org

Background and challenges to implementation: Drug-Resistant TB(DRTB) continues to be a public health crisis with 558,000 people (range, 483,000-639,000) developed TB which is Resistant to Rifampicin (RR-TB). 8.5% (95% confidence-interval, 6.2-11%) were estimated to have extensively drug-resistant TB(XDR-TB) worldwide in 2017. India accounts for 24% of the global burden and tops among the three listed high burden countries (China 13% & Russian Federation 10%).

Sputum smear microscopy under NTP still holds good and is the *golden standard* to diagnose TB in India.

But accessing and diagnosing DRTB, XDRTB and TB among the PLHIVs (whose sputum tests are continuously negative due to lack of caseous necrosis) that need WHO endorsed rapid diagnostics (WRD) has been a challenge in Odisha. A CBNAAT test that ensures cutting transmission through early detection, provide correct treatment through early DST to prevent antimicrobial resistance that decreases morbidity and mortality was introduced in the state during 2018.

Intervention or response: Aspiring to achieve the commitments made under Universal Health Coverage (UHC) and the End TB Strategy Milestones for 2025 (*estimated Fall of TB incidence by 10%; & death 6.6%*), Odisha state implemented UDST by establishing 38 exclusive DRTB Centres at districts, medical colleges and IRL & NRL facilities where all TB diagnosed cases received a minimum of RR testing.

State level program managers, District TB Officers and their supervisory staff, district PMDT Coordinators and its committee members were given extensive training on the revised/updated PMDT guidelines and Delamanid & Bedaquilin (the newly introduced drug).

39 CBNAAT machines (including one mobile facility that reaches out to the hard to reach pockets/populations) were supplied to these DRTB Centres for patients' convenience and decentralized molecular testing for TB and RR cases. Buffer stock of cartridges and lab consumables were maintained and supply to the centres was ensured.

CBNAAT diagnostic facilities was offered free of cost to all TB patients who initiated on re-treatment, those remained smear positive on any follow up with failures of first line treatment, people with high risk group contacts of DRTB cases and key populations like PLHIV, children, EPTB cases including referrals from the private sector. Three tier quality assurances of all diagnostic procedures was followed and ensured by the NRL, IRL, Nodal DRTB Centres and the District DRTB Centres routinely.

Results and lessons learnt: CBNAAT added around 60,000 tests during the year. Against 284,284 smear microscopy tests of presumptive TB cases, CBNAAT contributed additional 20.86% by examining 59,303 cases, making the total as 343,587 tests for the period. UDST was offered to 7440 (24%) diagnosed cases against 31,117 total TB notification that ensured early diagnosis. An average of 150 tests were done per centre/month while 18 centres crossed >200 tests mark/month.

Out of 483 DRTB/RR cases, 210 initiated shorter regimen while 241 got the conventional therapy that makes 93% treatment initiation achievement mark. 85% H-mono/poly regimen cases initiated treatment (113 treated of 133 diagnosed). 15 cases were diagnosed with 2nd line drug resistance(MDR+any SU, XDR, Mixed pattern). Table 1

No. of MDR/RR patient diagnosed	No. of patient initiated on Shorter MDR-TB regimen	No. of patient initiated on Conventional regimen	% of DR/RR TB patient initiated on treatment	No. mono/poly patient diagnosed	No. of H mono/poly patient initiated on treatment	% of patient initiated on H mono/poly-regimen	No. diagnosed with 2nd line drug resistance (MDR+any SU,XDR, Mixed pattern)
230	100	22	54	2	28	11	3

[EP-12-212-02 Table: 1; Case detection and treatment of DR/RR TB Patients for 2018]

Conclusions and key recommendations: CBNAAT test represented a major milestone for TB diagnosis and care. Evidence to date indicates that implementation of this test could result in a three fold increase in the diagnosis of patients with drug resistant TB and a doubling in the number of HIV associated TB cases diagnosed in areas with high rates of TB and HIV.
However, critical gaps in TB diagnosis *remains*. Despite CBNAAT's success, its scope remains limited by its cost and infrastructure requirements. Simpler, more robust, accessible and easy to use tests (TRUNET piloted in India) are required to maintain the desired performance characteristics in routine clinical settings and particularly at the lower levels of care by improving supply chain management, quality assurance of laboratories (particularly at peripheral sites), training of health care workers and referral of specimens for more intensive testing, (second line DST).
Operational research and policy guidance to shape novel strategies are needed to improve the implementation of existing tools and develop new approaches.

EP-12-213-02 Tackling TB in Indonesia: diagnostics alone isn't enough, holistic approaches are needed

RK Dewi,[1] SK Meharwal,[2] D Aulia,[1] D Papworth,[2] A Armimi,[1] L Mursida,[1] N Nurjannah,[1] [1]Ministry of Health, Subdirectorate Tuberculosis, Jakarta, Indonesia, [2]Chemonics International, Jakarta, Indonesia.
e-mail: retnokd@gmail.com

Background: Indonesia ranks 2nd in top 10 TB burden countries. Tremendous progress has been made in expanding laboratory capacity across the archipelago to enhance the testing volumes and improve access to services in a geographically challenging country. 839 GeneXpert, 21 quality assured culture, 11 drug susceptibility testing (DST), and seven Second Line- Line Probe Assay (SL-LPA) laboratories have been established.
Methods: the aim of the study was to assess the impact of expanded diagnostic capacity on the number of tuberculosis cases detected and treated. Data mining into national TB digital information system was used to extract retrospective data from 2016 through 2018. GeneXpert utilization data was collected separately from monthly reports. We also analyzed the number of rifampicin-resistant individuals who received follow on SL-LPA from January 2017 to December 2018, as well as percentage of treatment success.
Results: a total of 1,386,348 TB cases were detected from January 2016 to December 2018. Only 140,594 (10.14 %) were diagnosed by GeneXpert, utilized only 29% of existing GeneXpert capacity. 16,638 rifampicin resistant cases were detected however, only 38.6% received phenotypic DST. Data from July to December 2018 showed that only 26% of the rifampicin-resistant cases received a follow-on SL-LPA leaving a huge capacity unutilized. Additionally, treatment success of drug resistant TB was only 44% between 2016 to 2017.
Conclusions: In spite of rapid roll out of GeneXpert network and establishment of DST laboratories, utilization of diagnostic capacity remains low. Treatment of drug resistant TB was also far below expectations, indicating a holistic approach to TB care needs to be adopted.

EP-12-214-02 Testing diagnostic algorithm for community-based case finding strategies: India

P Bhat,[1] PC Bhatnagar,[1] [1]Voluntary Health Association of India (VHAI), Community Health, New Delhi, India.
e-mail: apmvhaiaxshyadelhi2@gmail.com

Background and challenges to implementation: Globally, community-based case finding strategies have always discussed about diagnostic algorithms to be incorporated into guidelines. The National TB Programme of India, has revised the algorithms through a consultative process in general in line with global. According to revised algorithm identified Presumptive TB patient may be tested for sputum smear microscopy and chest X-ray simultaneously. Following the results as positive, all need to be confirmed through Xpert/CBNAAT tests. The current algorithm was adopted into community-based case finding strategy.
Intervention or response: The Voluntary Health Association of India under Project Axshya is implementing community-based case finding strategies in 25 districts across high TB burden districts of India. The activities - Active case finding, Active community surveillance units, Health camps and fast tracking PTBPs in high workload hospitals were conducted by trained community volunteers and were monitored by trained district co-ordinators.
Results and lessons learnt: The community-based activities reached over a 5 million populations through trained volunteers over a period on one year from Jan 2018 to Dec 2018. During this period 44,000 presumptive TB patients were identified and 86% of them were tested through sputum smear microscopy. Among those who were tested 9% of them were sputum-smear positive. Out of all sputum-smear negative, 3% gave the sputum samples for CBNAAT. MTB was detected in 24% of 1030 tested and sputum of 211 were rifampicin sensitive and 34 were rifampicin resistant. Higher proportion of Rifampicin resistant was found in Active case finding exercise.
Conclusions and key recommendations: The community-based activity needs to incorporate methods to follow-up on all sputum smear negative PTBPs and ensure they complete the diagnostic algorithms. The results show additional yield of TB patients including rifampicin resistant cases when diagnostic algorithms are completed.

EP-12-215-02 HealthCare provider initiated demand creation: a veritable approach to address gaps in TB case detection, treatment and referrals in high TB-prevalence, low-detection states

E Adibo,[1] I Okekearu,[2] E Onyeje,[1] V Ibeziako,[3] [1]El-Lab Limited, Pathology, Lagos, Nigeria, [2]USAID SHOPS Plus Project, SHOPS Plus, Abuja, Nigeria, [3]Institute of Human Virology Nigeria, Office of the Chief Executive Officer, Abuja, Nigeria. e-mail: ifeanyi_okekearu@shopsproject.com

Background and challenges to implementation: Genexpert assay has been adopted as the first line Tuberculosis, TB test for more than 3 years in Nigeria, yet published data indicates that the roll out of the machine has not made the desirable impact on TB control in the country. The National Tuberculosis Programme, NTP continues to note that many of the over 400 machines installed across Nigeria are underutilized.
Intervention or response: El-lab Limited, a Private Medical Laboratory in Lagos, Nigeria, became a Genexpert site in September, 2018, when the Federal Ministry of Health installed a Genexpert machine in the facility. El-lab created awareness on this service availability within and across many private hospitals/clinics, nursing homes, private standalone laboratories, community pharmacies and the general public through series of meetings and print media. Adequate measures to ensure optimization of the machine, which include training more personnel on the use of the machine, to ensure a 24hours, seven days a week testing, steady electric power supply, short turnaround time, employment of dispatch riders for sample pick up and result return, organization of outreaches to high TB burden areas and leveraging on existing network meetings were put in place. The laboratory have received technical support from the USAID SHOPS Plus project on staff training/mentorship and, the Institute of Human Virology Nigeria, IHVN, through the global fund support, have ensured uninterrupted supply of cartridges and other consumables.
Results and lessons learnt: Efforts at creating community awareness and collaboration with other health facilities enhanced the number of sputum samples received by the center with averagely, 700 samples tested each month. More healthcare providers and individuals continue to access the Genexpert assay through its efforts.
Conclusions and key recommendations: Many of the Genexpert machines in Nigeria are domiciled in public facilities. It is important that these centers be strengthened to not only test but to contribute to demand creation through feasible methods.

EP-12-216-02 Application of IFN-γ/IL-2 FluoroSpot assay for distinguishing active tuberculosis from non-active tuberculosis: a cohort study

L Zhang,[1,2,3] S Wan,[1] S Ye,[1] X Cheng,[1] Y Zhang,[1] X Shi,[1,2] B Zhou,[1] X Sun,[1] X Liu,[1,2,3] [1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Department of Infectious Diseases, Beijing, China, [2]Chinese Academy of Medical Sciences and Peking Union Medical College, Center for Tuberculosis Research, Beijing, China, [3]Peking Union Medical College, International Clinical Epidemiology Network, Clinical Epidemiology Unit, Beijing, China. e-mail: lifanzhang1982@126.com

Background: Currently available Interferon-γ release assay cannot reliably differentiate active TB (ATB) from non-active TB (non-ATB). This study aimed to evaluate the diagnostic accuracy of the IFN-γ/IL-2 FluoroSpot assay, which can simultaneously detect IFN-γ and IL-2 secretion, for differentiating ATB from non-ATB.
Methods: All patients with suspected ATB from the clinic and ward of infectious diseases and general medicine in Peking Union Medical College Hospital (PUMCH, a 2000-bed tertiary general hospital) between January 2016 and September 2017 were consecutively enrolled. The inclusion criteria included age≥16 years old, HIV-negative, positive T-SPOT.*TB* (Oxford Immunotec, Abingdon, UK) results. Based on patients' clinical manifestations, imaging findings, microbiological or histopathological results and patient′s response to the treatment of TB, diagnosis was independently made by two physicians blinded to the results of IFN-γ/IL-2 FluoroSpot assay. Laboratory technicians who conducted the assays were blind to the final diagnoses.
Results: 191 suspected ATB patients with positive T-SPOT.TB results were consecutively recruited. 64 (33.5%) participants had ATB, including 22 (34.4%) microbiologically or histologically confirmed TB and 42 (65.6%) clinically diagnosed TB. 119 (62.3%) cases were non-ATB and 8 (4.2%) were clinically indeterminate. After being stimulated with ESAT-6 and CFP-10 antigens, the median frequency and proportion of IFN-γ+IL-2- T cells were significantly higher in the ATB group than the non-ATB group ($P< 0.001$). The areas under the ROC curves of IFN-γ+IL-2- T cells were larger than those of total IFN-γ+ T cells (0.788 vs. 0.739, $p=0.323$). With a cutoff value of 25 SFCs/250,000 PBMCs for frequency, sensitivity and specificity of this assay were 73.4% and 69.8% respectively. When combining the frequency and proportions of IFN-γ+IL-2- T cells, the sensitivity and specificity were increased to 95.3% in parallel testing and 83.2% in serial testing respectively.
Conclusions: In conclusion, IFN-γ/IL-2 FluoroSpot assay is conducive for the diagnosis of ATB in patients with positive T-SPOT.TB results.

EP-13-C8 PPM across different settings: models, outcomes & sustainability

EP-13-217-02 Landscape of private healthcare providers notifying TB patients in India

B Vadera,[1] R Rao,[2] KS Sachdeva,[3] A Karad,[1] K Rade,[4] [1]Central TB Division, Govt of India, WHO RNTCP Technical Assistance Project, New Delhi, India, [2]Ministry of Health & Family Welfare, Central TB Division, New Delhi, India, [3]Ministry of Health and Family Welfare, Govt. of India, Central TB Division, New Delhi, India, [4]WHO Country Office, TB, New Delhi, India. e-mail: dr.vadera@gmail.com

Background and challenges to implementation: India has a large and diverse private health sector. At least half of an estimated 2.7 million TB patients presumed to seek care in private sector. Notification of patients from these providers, extent of notifying provider´s network is key to reach large number of patients outside public health system. We described coverage and the landscape of private health care establishments notifying TB patients to the national programme.
Intervention or response: In 2012, TB has been made notifiable disease and the system for case notification was established. The District Programme units map private health care providers, prioritize, register them and repeatedly sensitize, motivate and support to notify TB patients. In order to expand network of engaged providers, innovative interface agencies have been used to establish linkages and networking activities. Recently, incentives for private providers for notification and strengthening of regulatory measures have been undertaken.
Results and lessons learnt: From 2014 to 2018, we found a four-fold annual increase in the annual notification of TB patients by private providers, 132 to 558 thousand annually. Till date, 164,752 private health establishments have been registered with RNTCP, approximately 40% of the estimated 4 lakh private providers nationwide. Of the registered providers, 53,744 (33%) providers have notified at least one case ever and 32,115 (16%) providers notified patients in 2018. The number of private providers notifying annually increased more than four times, from 7833 to 32115. In 2018, three states had ~40% of notifying providers and contributed to 40% of notification. 80% of private notifications in 2018 came from the 20% of private providers.
Conclusions and key recommendations: Since the inception of notification system for private health care providers, there is four-fold increase in notifying private providers. Less than one fifth providers notifying TB patients annually, represents potential to expand the network of providers for increasing notification of TB.

EP-13-218-02 Joint effort to end TB in India: twofold increase in TB case notification; one-year implementation data analysis

RK Gandhi,[1] B Kalottee,[2] S Raj,[3] C Thakur,[3] [1]PATH India, TB Portfolio, Mumbai, India, [2]CHRI, TB Portfolio, Delhi, India, [3]CHRI, TB, Delhi, India. e-mail: rgandhi@path.org

Background and challenges to implementation: India, world's highest TB burden country has resolved to End-TB by 2025. Realizing the need for active involvement of private health-sector, National TB Program calls for Joint Effort to End-TB (JEET), to reach out to missing millions of TB patients, supposed to be treated by private-sector. We report the implementation data of 29 districts where PATH India supported this initiative.
Intervention or response: JEET was implemented through a Patient Provider Support Agency (PPSA) which provided free diagnostics, drugs, logistical and administrative support to engage private-sector. Private providers were studied and prioritized providers were engaged based on predesigned criteria to optimally increase the TB notifications. These private providers were strategically connected with referral networks, laboratory networks and chemist networks, periodically followed up, strategically sensitized and supported for necessary logistical and technical requirements to diagnose and treat TB for free. These patients were digitally notified to National TB Program.
Results and lessons learnt: From April 2018 to March 2019, PPSA implemented by PATH mapped 6549 private providers, of which 3646 (56%) providers were prioritized for engagement. Of these prioritized providers, 1800 (49%) were actively engaged. In one implementation year, PPSA contributed to 53000 TB case notification, which increased the total TB case notification (public and private combined) by 70%.
Conclusions and key recommendations: JEET has been proved successful so far to actively involve many private practitioners in End-TB efforts. This initiative has remarkably contributed to TB notification and thereby for public health actions.

EP-13-219-02 Private sector TB notification increased 2.6 times within 2 years with involvement of private providers and pharmacies in Jharkhand, India

R Dayal,[1] S Nayak,[2] R Yeole,[3] R Sahay,[4] [1]State TB Cell, Health, Medical Education & Family Welfare, Ranchi, India, [2]The Union South East Asia, Tuberculosis, Ranchi, India, [3]WHO RNTCP Technical Assistance Project India, Tuberculosis, Ranchi, India, [4]Drug Directorate, Health, Medical Education & Family Welfare, Ranchi, India. e-mail: stojh@rntcp.org

Background and challenges to implementation: India reports ~1.6 Million(60%) TB cases per annum against WHO estimates of 2.7million. Cases from majority of Private Health facilities and Pharmacies remains unre-

ported despite of orders/rules regarding TB notification and up-keeping of records of all patients and providers by pharmacies for 46 enlisted Schedule H1 drugs including Anti TB Treatment(ATT) Drugs. India has more than 850000 pharmacies; however, only 9% were reporting by 2016. Jharkhand, a tribal state reported only 4211(10%) private sector TB cases during 2016 against target of 40,000.

Intervention or response: The TB control program in collaboration with Drug Directorate started a private sector engagement framework in 2017 to enhance notification and care of private patients in Jharkhand. ATT Drug sale data of two major suppliers for Jharkhand were analyzed district wise. During 2017-18, 2182 Private Health Establishments (665 clinics, 452 hospitals, 950 pharmacies, 115 laboratories) were engaged through training and sensitization. Pharmacies were specially targeted and engaged through Drug Inspectors to enforce Schedule H-1 provisions.

Results and lessons learnt: Private TB notification in 2018 enhanced to 10931(160%) against 4211 in 2016. During that period, public sector notification increased by 4% (36452 to 37919). Private TB Notification from 11 per 100000 population in 2016 enhanced substantially to 28 in 2018. Pharmacies reporting zero cases in 2016, contributed 2553(25%) to total private Notifications in 2018. 12 districts identified from drug sale data had a share of 90%. The intervention resulted in increasing case notification substantially, i.e. 2.6 times in two years.

Conclusions and key recommendations: Early detection, notification, standard regimen and follow-up are the mainstays of TB program. The intervention certainly opens the door to scale-up, that government and international donors should take forward, with a structured and long term approach. Further pharmacies can play the role in bridging the gap in notification, counseling and universal access to TB care.

EP-13-220-02 Differential performance of networked private sector facilities conducting active case finding for tuberculosis in Lagos, Nigeria: the SHOPS Plus experience

I Okekearu,[1] A Iroko,[2] C Obanubi,[3] T Odusote,[3] B Olusola-Faleye,[2] F Nwagagbo,[2] C Chukwuemeka,[2] M Toriola,[2] E Ekanem,[4] E Baruwa,[5] [1]Abt Associates/ SHOPS Plus, International Development Division, Abuja, Nigeria, [2]Abt Associates/ SHOPS Plus, International Development Division, Lagos, Nigeria, [3]United States Agency for International Development, Office of HIV/ AIDS and Tuberculosis, Abuja, Nigeria, [4]Abt Associates, International Development Division, Rockville, Nigeria, [5]Abt Associates, International Development Division, Rockville, MD, United States of America.
e-mail: ifeanyi_okekearu@shopsproject.com

Background and challenges to implementation: The USAID funded SHOPS Plus program is scaling up a model of active case finding for tuberculosis (TB) in Lagos Nigeria. In collaboration with Lagos State TB Program this multi-cadre model of private providers consists of hospitals, laboratories, community pharmacists (CPs) and patent medicine vendors (PMVs). SHOPS Plus provides network support to enhance screening, referrals, TB testing and treatment. This analysis assessed the differential performance/contribution of the various cadres.

Intervention or response: A retrospective review of outpatient department (OPD) attendances, screening logs, presumptive registers and facility registers across the SHOPS Plus networks in Lagos between 1 October 2018 to 28 February 2019.

Results and lessons learnt: 372 facilities were reviewed: 58.3%, 15.3%, 6.7% and 19.6% were hospitals, laboratories, CPs and PMV respectively. Of the total patients seen the percentage screened for TB was 18.6%, 10.8%, 4.4% and 12.9% at hospitals, laboratories, CPs and PMVs. Of the 8,817 presumptive TB identified and tested for TB, 68.1%, 15.9%, 3.7% and 12.3% came from hospitals, laboratories, CPs and PMVs respectively. The number needed to screen (NNS) to diagnose a TB case was highest for the PMVs (22.6) and lowest for the hospitals (7.5). Of 992 TB cases diagnosed, 805 (81.1%) were from hospitals while CPs contributed the least (2.4%). The TB cases diagnosed per facility within the 5-month review period was 3.7 per hospital, 2 per laboratory, 0.1 per CP and 0.7 per PMV.

Conclusions and key recommendations: Screening levels were low across provider cadres. Hospitals accounted for most TB case notification across the network. The assumption that CPs, laboratories and PMVs can drive patients to hospitals does not yet hold but these data identify where bottlenecks exist. There is urgent need to evaluate the barriers to screening of clients (currently less than 15%) attending private providers in Lagos to achieve gains from active TB case finding.

EP-13-221-02 The engagement of private healthcare providers contributed to reaching out to the missing TB cases in Kampfumo district of Maputo City, Mozambique

B Macuacua,[1] S Mukhopadhyay,[2] J Jone,[1] I Manhiça,[1]
[1]Ministry of Health of Mozambique, National Tuberculosis Program, Maputo, Mozambique, [2]Universal Health Services, TB, New Delhi, India.
e-mail: bachir.macuacua@gmail.com

Background: The City of Maputo, one of Mozambique´s 11 provinces, has the largest network of private health care providers in the country, formally licensed. They provide health services to substantial number of clients (including low-income people) including those with TB symptoms who seek these services as their first point of contact.

In Kampfumo District, the National TB Program engaged three formal private health facilities and one military hospital. The TB service collaboration comprises of regular referrals of TB presumptive cases from private health facilities to public health facilities for early diagnosis of TB, provision of DOTS by private providers, collaborative TB / HIV activities, preventive treatment for high-risk people and eligible children contacts, air-borne infection control and case notification.

Methods: A cross-sectional study was carried out to identify the proportion of the TB cases notified in 2018 by engaging private and other public TB services providers in Kampfumo District as part of NTP's PPM initiative. The analyzed data was extracted from the National Health Information System database.

Results: In 2018, 207 (corresponding 184 per 100,000 population) additional TB cases (all forms) were notified by engaging private sector, which was around 19% of total 1091. The notification rate increased from 888.2 (in 2017) to 969.2 per 100,000 population. Of these 207 cases, 84 were female and 123 male (corresponding to 18% and 19% of the total cases reported gender-wise respectively). Disaggregated by age groups, 6 (2.9%) children (1 of 0-4 years and 5 of 5-14 years) and 201 (97.1%) adults (>14 years), which corresponds to 9.38% and 19.57% of the total cases age-group wise, respectively.

Conclusions: Engagement of private sector has contributed significantly to notification of TB cases in Kampfumo District. Therefore, scaling up of the approach should be considered, in Mozambique, as one of the key strategies of reaching out missing TB cases.

EP-13-222-02 Finding missing people with tuberculosis (TB): the role of traditional healers in finding missing TB cases in Tanzania

G Munuo,[1] L Ishengoma,[2] J Lyimo,[3] A Nyirenda,[1] A Maro,[1] [1]Amref Health Africa in Tanzania, Disease Control and Prevention, Dar es Salaam, Tanzania, United Rep., [2]Ministry of Health Community Development Gender Elderly and Children, National TB and Leprosy Tanzania, Dar es Salaam, Tanzania, United Rep., [3]Management and Development for Health, GF TB Project, Dar es Salaam, Tanzania, United Rep.. e-mail: gmunuo@gmail.com

Background and challenges to implementation: Tanzania is among the 30 high burden countries with Tuberculosis (TB) in the world among 13 countries accounting for 75% of missed TB cases globally. According to 2018 WHO report, Tanzania in 2017 missed 56% cases of TB from the estimated 154 000 cases, only 44% (68,500) were detected by the program, with treatment success of 90% percent. The challenge of finding the missing people with TB calls for the engagement of others who are the first encounters with community like traditional healers (THs) and drug dispensing outlets among others.

Intervention or response: Amref health Africa in collaboration with national TB and leprosy through GF grant engaged community providers including traditional healers in finding missing people with TB in 8 regions. The team identified the traditional healers which are mostly the first encounter for illness people before reaching the public health facility. A total of 275 traditional healers were sensitized and trained on TB screening and referrals of presumptive cases. The program was able to follow up with 46 of the trained traditional healers last quarter reporting period 2018. The referral data and those diagnosed with TB was collected at the facility and were entered in Electronic TB reporting System.

Results and lessons learnt: For the period of October - December 2018, 46 Traditional healers were able to refer 107 presumptive TB cases of which 12 were confirmed TB patients and were initiated TB treatment . This is missing opportunities in finding TB cases in Tanzania and other countries where Traditional Healers are common.

Conclusions and key recommendations: Engaging Traditional healers where they are the first encounter with patients before reaching the formal health facility is crucial intervention in increasing case detection. it's of paramount importance for the programs to include Traditional Healers in their strategies for finding all missing people with TB in their countries.

EP-13-223-02 Role of graduate private providers in urban TB control programme: BRAC experience in Chattogram City Corporation

F Khatun,[1] MA Islam,[1] S Islam,[1] S Reja,[1] SMG Raihan,[1] A Islam,[1] [1]BRAC, Communicable Disease Control (TB), Dhaka, Bangladesh. e-mail: fatema.kh@brac.net

Background and challenges to implementation: Bangladesh is one of the high burden TB countries in the world. According to Bangladesh National TB prevalence survey TB is more in urban setting than in rural. To address this issue BRAC under leadership of National Tuberculosis Control Programme (NTP) strengthen its effort to identify missing TB cases in urban areas.
Intervention or response: In Chottagram City Corporation BRAC directly works in 24 wards with population coverage of 17, 26,076.In these areas potential Graduate private providers (GPP) are mapped, listed and networking was established with them. They were oriented on national algorithm of TB, introducing with new diagnostic tool like gene xpert, assess to free digital x-ray , address of NTP designated TB centres ,free diagnostic support for poor TB presumptive, system of DOT for treatment adherence. These encourage GPPs to refer TB presumptive and diagnosed TB cases to NTP designated centres which ultimately help to identify missing TB cases in urban communities.
Results and lessons learnt: In 2017, 695 GPPs were oriented through 34 networking meetings and in 2018, 100 were oriented through 5 meetings. In 2017 and 2018, 3231 and 4390 TB cases were registered in BRAC centres in Chottagram City Corporation respectively. Among them 1263 (39%) TB patients 1751(40%) TB patients and were referred by GPPs. In 2017 and 2018, 2, 44,201 and 2, 68,596 TB cases were notified under National Tuberculosis Control programme. Among them 51,282(21%) and 56,715(21%) TB cases were referred by GPP in 2017 and 2018 respectively.
Conclusions and key recommendations: Private providers play an important role in providing health care services to a large proportion of patients with tuberculosis. There is a need for innovative measures to increase participation of the private sector in the national TB control program which helps to identify missing TB cases in the country specially in urban settings.

EP-13-224-02 Factors influencing uptake of TB service delivery in private sector

NN Hanson-Nortey,[1] MN Mensah,[1] J Anaman,[1] R Osih,[2] S Charalambous,[2] G Churchyard,[3] [1]Aurum Institute Ghana, Ghana Operations, Accra, Ghana, [2]Aurum Institute, Aurum Global, Johannesburg, South Africa, [3]Aurum Institute, Head Office Management, Johannesburg, Ghana. e-mail: janaman@auruminstitute.org

Background and challenges to implementation: National TB case notification rates in Ghana have consistently declined over the past 5 years. TB control activities have remained largely in the public sector without recourse to opportunities within the private sector. Systematic engagement of private sector has been shown to contribute to national case notifications, not without challenges. We show that previous involvement in public health interventions and the process of engagement contributes significantly to the performance and sustenance of private providers in TB control activities.
Intervention or response: Aurum Institute Ghana and partners conducted a baseline assessment of targeted private hospitals and clinics in Accra and Kumasi Metros to assess their capacity and willingness to provide TB services including intensified case finding among OPD attendants, key and vulnerable populations within a TB REACH Wave 6 project using a checklist.
Results and lessons learnt: Among 56 facilities assessed, 6 refused to participate in the project. Of the remainder, 41 (82%) had previously participated in public health interventions; 44 (88%) provided national health insurance services; 21 (42%) had previous experience with PPM-DOTS and 14 (25%) did not conduct TB diagnosis though they had functioning laboratories resulting in lower case detection rates than those with functioning lab with TB diagnostic capacity and screened more people.
Facilities with the top 5 yields from presumed cases utilised their laboratory diagnostic capacity whilst those with the 5 lowest yields had no TB diagnostic capacity.
Conclusions and key recommendations: Facilities with previous experience implementing public health programmes were more receptive to the intervention, screened more persons and delivered quality services than those who did not. Previous involvement in a public health intervention contributed to ease of adoption and quality of TB service delivery. Availability of a functioning laboratory with TB diagnostic capacity led to increased TB case detection rates.

EP-13-225-02 Patient provider interface agency to patient provider support agency: a story of integration from NGO to government

D Shah,[1] S Surendran,[2] V Puri,[1] U Waghmare,[1] S Talekar,[1] A Kothari,[1] [1]Municipal Corporation of Greater Mumbai (MCGM), Tuberculosis, Mumbai, India, [2]PATH, Health Systems, Mumbai, India.
e-mail: dtomhbmc@rntcp.org

Background and challenges to implementation: In India, surveys indicate 50% of TB patients are diagnosed and treated in the private sector, but not necessarily notified. From 2014-2017, PATH implemented the Private Provider Interface Agency (PPIA) in Mumbai- an entity to engage with private health care providers and patients to improve case notification and treatment adherence. With this intervention, annual notification jumped from 2000 (2014) to 24,000 (2017). This pilot project is a good example of Build -Operate - Transfer Model to the Municipal Corporation of Greater Mumbai (MCGM). Since February 2018, the public health system has been financing and monitoring the implementation of this interface agency - renamed as Patient Provider Interface Agency (PPSA).
Intervention or response: In 2017, the MCGM contracted two NGOs as PPSAs to provide the end-to end gamut of services. Dedicated coordinators were recruited as the crucial link between the government and private sector. The transition of ownership from a private to public entity was challenging on the policy, perception and operations fronts. MCGM designed new work-flows; conducted multiple stakeholder meetings and built institutional mechanisms to manage the program.
Results and lessons learnt: The PPSA has performed fairy well in terms of sustaining the TB notification numbers from the private sector and instrumental in demonstrating that Public Health Systems can successfully integrate NGO led programs

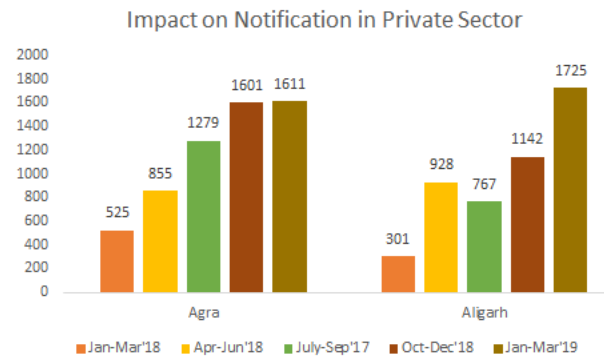
[Case notification trend from October 2016 to December 2018: From PPIA to PPSA]

Conclusions and key recommendations: The alignment of political and administrative, leveraging of market forces and ongoing stakeholder engagement were essential for the integration. PPSA's first year has seen hits and misses. The Public Health System acknowledges the need for internal change management and sustained dialogue with the private sector to strengthen the program. Based on learnings, the PPSA has been sanctioned additional funding and a larger mandate to ensure quality services. As a proof of concept, it demonstrates how an integrated platform like PPSA maybe be used to engage with private sector for Universal Health Care.

EP-13-226-02 Joint efforts for effective private sector engagement in the urban settings of two cities in of Uttar Pradesh, India

B Kalottee,[1] S Vijayan,[2] C Thakur,[3] S Raj,[3] A Rehman,[4] R Sharma,[4] EK Vinayakan,[5] [1]Centre for Health Research and Innovation, TB-HIV, New Delhi, India, [2]PATH, TB-HIV, New Delhi, India, [3]Centre for Health Research and Innovation, TB, New Delhi, India, [4]MAMTA Health Institute for Mother and Child, TB, New Delhi, India, [5]MAMTA Health Institute for Mother and Child, Chronic Diseases, New Delhi, India. e-mail: bkalottee@chri.org.in

Background and challenges to implementation: The Joint Effort for Elimination of Tuberculosis (JEET) project for private sector engagement is being implemented by CHRI under the guidance of the Central Tuberculosis Division, Government of India (GoI) and funded by The Global Fund to Fight AIDS, TB and Malaria (GFATM).
Agra and Aligarh, the two most populous cities in Uttar Pradesh, have an urban population of 1.91 and 1.22 million respectively. The estimated Tuberculosis (TB) cases annually in Agra and Aligarh are 9792 and 8160 respectively.
Under-reporting, diagnostic delays, non-standardized regimens and catastrophic health expenditure to TB patients in the private sector is a challenge in these cities.
Intervention or response: A multitasking approach is adopted to find and treat the "missing cases". CHRI hires staff for mapping, identifying, engaging potential providers and notifying patients to the National TB program (NTP) and trains them with program support. An interface agency (MAMTA),extends patient support for collection and transportation of sputum samples, treatment adherence and facilitating provision of incentives through NTP. The NTP provides access to free drugs and diagnostics (CBNAAT test) and Direct Beneficiary Transfer (DBT) in the form of provider and patient incentives for notifications and nutritional support respectively.
Results and lessons learnt: Within 9 months of implementation starting July 2018, a 3 to 5 fold increase in notifications has been recorded.
211 Private providers are engaged, 577 sputum samples transported for CBNAAT testing, 166 patients put on Government drugs and 1758 patients provided DBT.



[Trend in Private Sector Notifications (Jan'18-Mar'19)]

Conclusions and key recommendations: The success of the intervention is linked to the Government led additional logistics support which served as an incentive for both providers and patients. Building a private -private collaboration for patient provider support with minimal public sector interaction helped increase the access to TB services and notifications from the private sector. The Government can build on such models with support from domestic funding to ensure sustainable private sector engagement.

EP-13-227-02 The additional financial burden of care seeking for TB symptoms in South Africa's private sector

J Boffa,[1,2] A Daftary,[1,3] J Chikovore,[4] A Salomon,[1] T Mkhombo,[5] B Daniels,[6] A Kwan,[7] S Wu,[1] M Pai,[1,8] S Moyo,[5] [1]McGill University, McGill International TB Centre, Montreal, QC, Canada, [2]University of KwaZulu-Natal, Centre for Rural Health, Durban, South Africa, [3]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa, [4]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Durban, South Africa, [5]Human Sciences Research Council, HIV, AIDS, STIs, and TB Unit, Cape Town, South Africa, [6]World Bank, Development Research Group, Washington, DC, United States of America, [7]University of California, Health Policy, Berkeley, CA, United States of America, [8]Manipal McGill Centre for Infectious Diseases, Manipal Academy of Higher Education, Manipal, India.
e-mail: tnmkhombo@hsrc.ac.za

Background: South Africa offers TB testing free from user-fees through the national public health system; however, an estimated 29% of people with TB symptoms first report to private providers. Utilising data from a study of standardised patients (SPs) - healthy patient actors - we estimated the financial burden borne by patients presenting with TB symptoms to private general practitioners in KwaZulu-Natal.
Methods: Data was derived from 220 initial cash-paying interactions with private providers undertaken in 2018. We summarised the cost of patient interactions and compared cost drivers for those who were referred and not referred to the public health sector for TB testing or treatment.
Results: The average fee for private consultation was ZAR305.65 (USD21.86)(range ZAR0-530). In 85% of interactions this fee included the dispensing of one or more medications. A total of 88/220 interactions (40%) ended with referral back to a public clinic. Fees were waived in 5/220 interactions (3%), all of which involved referral to the public sector. While not statistically significant, providers who referred to clinics were less likely to ask SPs to return for follow-up (25% vs 47%, p=0.07) compared to non-referring providers. No difference was found with referral to private laboratories for diagnostic tests (1% vs 9%, p=0.78), the average consultation fee (ZAR305 vs ZAR306, p=0.94), and prescription for additional medication (9% vs 9%, p=1).
Conclusions: In addition to opportunistic costs, 97% of SPs presenting to private providers with TB symptoms incurred out-of-pocket costs. Patients were referred to the public system in 40% of interactions. Those who were not referred were more often asked to return to the provider, implying further costs. Additional costs for both those referred and not referred included prescription medications and diagnostic tests which would be freely available in the public sector. A National Health Insurance scheme is expected to reduce these cost burdens.

EP-14-B1 Digital CXRs: screening and diagnosis

EP-14-228-02 Evaluating the addition of digital chest radiography to routine symptom screening for diagnosing TB within correctional facilities

K Velen,[1] F Sathar,[1] C Hoffmann,[2] H Hausler,[3] A Fononda,[3] S Govender,[4] M Lerefolo,[4] A Govender,[4] S Charalambous,[1] [1]The Aurum Institute, Implementation Research Department, Johannesburg, South Africa, [2]John Hopkins University, Department of Medicine, Baltimore, MD, United States of America, [3]TB/HIV Care Association, Research, Cape Town, South Africa, [4]Right to Care, Research, Johannesburg, South Africa.
e-mail: velenk06@yahoo.com

Background: Key populations such as inmates will need to be prioritized to achieve the Global Plan to End TB. We evaluated TB yield when supplementing symptom-screening with digital chest radiography (d-CXR) with automated computer-aided detection (CAD) among inmates in a routine programme in South Africa.
Methods: We consecutively enrolled adult inmates (new admissions and sentenced) from five facilities in three provinces. All participants were symptom and d-CXR screened for TB and any person with ≥1 symptom or CAD score of ≥50, provided two sputa, each for MGIT

culture and GeneXpert MTB/RIF Ultra (Xpert Ultra) testing. In addition, to determine whether the screening strategies would miss any cases, we tested 800 inmates asymptomatic with CAD< 50. A TB diagnosis was defined as positive Xpert Ultra or MGIT culture.

Results: We enrolled 3,576 participants; 99.6% male, median age 34 years(IQR: 28-41), and 584(16.3%) HIV-infected on self-report. We identified 867(24.2%) participants requiring investigation [394(11.2%) on symptoms alone, 685(19.1%) on d-CXR alone and 867(24.2%) with either symptoms or d-CXR]; 747(86.2%) provided sputa and we had at least one result for 738(98.8%). We diagnosed 28(0.78%) new TB cases. TB yield was 0.36%(13/3576) if testing was on symptoms alone and 0.70%(25/3567) on d-CXR alone. Adding d-CXR to symptom screening, identified 15 additional TB cases. Amongst those with results for both tests (n=562, 75.2%), Xpert Ultra and Culture had similar TB yield (0.56% vs 0.48%, p=0.21). Amongst the 800 inmates asymptomatic with normal CAD scores, 781(98.2%) tested, and 5(0.63%) TB cases diagnosed.

Conclusions: During a routine screening programme among inmates, addition of d-CXR identified two times more undiagnosed TB than patients investigated on symptoms alone. Xpert Ultra performed well against culture in an ambulatory, potentially pauci-bacilliary population. Complimentary use of d-CXR may potentially overcome subjectivity inherent in symptom screening alone for identifying TB in this population.

EP-14-229-02 The accuracy of computer-aided detection for tuberculosis (CAD4TB) for digital chest X-rays in mass screening for tuberculosis in Brazilian prisons

C Celina Ribeiro da Silva,[1] A da Silva Santos,[2] E Lemos,[1] C Goncalves,[3] J Andrews,[4] J Croda,[3,5] [1]Federal University of Grande Dourados, Medicine, Dourados, Brazil, [2]Federal University of Grande Dourados, Medicine, Campo Grande, Brazil, [3]Federal University of Mato Grosso do Sul, Medicine, Campo Grande, Brazil, [4]Stanford University, Division of Infectious Diseases and Geographic Medicine, Stanford, United States of America, [5]Oswaldo Cruz Foundation, Research, Campo Grande, Brazil.
e-mail: juliocroda@gmail.com

Background: While the World Health Organization recommends systematic screening for tuberculosis in prisons, it is not widely performed in low- and middle-income countries due to cost constraints. We aimed to evaluate the accuracy of computer-aided detection for tuberculosis (CAD4TB) in the context of mass screening in Brazil, and to determine whether radiographic abnormalities correlated with sputum bacillary burden.

Methods: We performed systematic tuberculosis screening in the three largest prisons in Mato Grosso do Sul, Brazil. All prison inmates, irrespective of symptoms, were invited to participate and were screened by X-ray, sputum culture and sputum Xpert, performed on a mobile diagnostic unit in which an X-ray digitizer was used together with CAD4TB software. We assessed CAD4TB score accuracy by receiver operating characteristic analysis, and compared with CAD4TB score with Xpert semiquantitative load by Spearman's correlation measure.

Results: Among 7,246 inmates screened by chest radiograph, 246 (3.4%) had tuberculosis confirmed by sputum Xpert or culture. CAD4TB had high overall accuracy (AUC 0.89) in identifying cases. At the Youden's optimal threshold, sensitivity was 80% and specificity was 86%. At a more liberal threshold, sensitivity was 88% and specificity was 73%. CAD4TB score was positively associated with quantity of MTB detected by Xpert, with the following median scores by Xpert level: not-detected, 46 (IQR: 32-59); very low, 77 (IQR: 62-89); low, 86 (IQR: 63-96); medium, 91 (IQR: 78-97); high, 96 (IQR 87-97) (p< 0.0001). At the optimal threshold, sensitivity for medium or high semiquantitative load was 90%.

Conclusions: In systematic screening for tuberculosis in prisons, CAD4TB performed very well, achieving high sensitivity (88% at 73% specificity), which could focus resources for confirmatory sputum testing. Additionally, CAD4TB scores were positively associated with semi-quantitative Xpert load in sputum, suggesting that it may be useful in identifying individuals with the greatest bacillary burden.

EP-14-230-02 AI in the real world: performance analysis of AI-powered TB screening tool vs. radiological and bacteriological confirmatory tests

T Raj,[1] R Suresh,[1] J Triñona,[2] R Nalda,[2] P Putha,[1] M Tadepalli,[1] B Reddy,[1] A Jagirdar,[1] M Gune,[3] J Anthony,[4] [1]Qure.ai Technologies Pvt Ltd, Research, Mumbai, India, [2]Access TB Project, TB Care and Prevention, Manila, Philippines, [3]Gune Medical Center, Radiology, Ambernath, India, [4]St John's Research Institute, Division of Epidemiology and Population Health, Bangalore, India.
e-mail: tarun.raj@qure.ai

Background: In this study, we prospectively evaluate the performance of an AI algorithm deployed through mobile vans for TB screening in a high prevalence country. We also evaluate the possibility that AI can be trained to identify signs of microbiological positivity from chest X-rays.

Methods: A deep learning algorithm was trained to detect signs of tuberculosis on chest X-rays, using radiologist opinions and the WHO-recommended DNA-based confirmatory sputum test (GeneXpert). The algorithm was deployed for 90 days in 2 mobile vans as part of a TB screening program conducted by a program in Philippines. As part of this program, all X-rays were reviewed by the algorithm and by radiologists. Subjects who screened positive on the X-ray, either by AI or through the radiologists′ read were recommended a

confirmatory GeneXpert test. We compare the performance of our algorithm and reporting radiologists on 448 cases for which GeneXpert results are available. 298 patients are registered as Female, 144 as Male and 6 as other. Mean age of patients was 52.92 years and standard deviation was 16.52 years. 421 of these cases were reported as GeneXpert negative and 27 cases are GeneXpert positive.
Results: The algorithm showed similar sensitivity 0.81(0.62-0.94) and higher specificity 0.76(0.72-0.80) compared to radiologists 0.81(0.62-0.94) and 0.74(0.69-0.78) when detecting microbiologically confirmed TB. Algorithm AUC was 0.87 versus the GeneXpert ground truth. The algorithm identified 12 fewer false positives and 12 more true negatives compared to the radiologists. Agreement % and cohen's kappa between the radiologists and algorithm is 78.4% and 0.434 respectively.
Conclusions: AI algorithms can accurately screen chest X-rays for tuberculosis in a high prevalence population. Real-world evidence paves the way for the use of AI for cost-effective TB screening with quicker turnaround times.

EP-14-231-02 Finding additional TB cases through improving chest X-ray reading by clinicians at hospitals

C Eang,[1] N Song,[1] S Oun,[2] B Team,[1] M Chea,[2] L Stevens,[1] [1]FHI 360, Public Health, Phnom Penh, Cambodia, [2]National Center for Anti-Tuberculosis and Leprocy, Public Health, Phnom Penh, Cambodia.
e-mail: songngak@yahoo.com

Background and challenges to implementation: Cambodia has a TB incidence of 326/100,000. It is estimated that more than a third of TB patients remain undiagnosed or untreated, leading to ongoing transmission of the disease. Many clinicians at referral hospitals (RH) do not have sufficient training in chest X ray (CXR) reading and interpretation, leading to missed diagnoses. To find these missing patients, the Challenge TB (CTB) project took action to improve clinicians' capacity to read and interpret CXRs.
Intervention or response: CTB trained and provided on-site coaching on CXR reading and interpretation for 40 clinicians in 11 RHs. During the on-site coaching, the team collected the CXR films of presumptive TB patients and re-read them with RH clinicians. The project also developed and introduced a smartphone-based online communication platform where clinicians can post presumptive TB patients' CXRs and receive comments and advice from peers. The platform is monitored by a CXR monitoring team of certified professionals with extensive CXR interpretation experience.
Results and lessons learnt: Over six months, 2,563 CXR films for presumptive TB patients were taken at the 11 RHs. 1,114 (43%) of the films were reviewed by the CXR monitoring team. Among those, 970 (87%) of the films showed no sign of active TB, which was confirmed by both trained RH clinicians and the monitoring team. However, 133 (13%) of the films that were interpreted as "no active TB" by RH clinicians were confirmed as active TB by the CXR monitoring team. Those patients who were found to have been previously misdiagnosed were called back for treatment.
Conclusions and key recommendations: CXR training followed by systematic review of CXR films and online communication that allows feedback and advise from peers and experts can improve clinicians' CXR interpretation knowledge and skills. This type of multi-faceted capacity-building intervention can help find missing people with TB and connect them to treatment.

EP-14-232-02 The results of mobile screening teams as active case finding activities in Turkey: which groups should be screened?

H Ilter,[1] E Kabasakal,[2] S Ozkan,[3] SM Mutlu,[2] S Gogen,[2] S Ozkara,[4] [1]Ministry of Health, General Directorate of Public Health, Ankara, Turkey, [2]Ministry of Health, General Directorate of Public Health, Department of TB, Ankara, Turkey, [3]Ministry of Health, Ankara Provincial Health Directorate, Yenimahalle Camlica Family Health Center, Ankara, Turkey, [4]Ataturk Chest Diseases Hospital, Tuberculosis Clinic, Ankara, Turkey.
e-mail: suozkan@gmail.com

Background: Early diagnosis and treatment of tuberculosis (TB) patients are essential for successful TB control. Generally used passive method for TB cases detection based on application to health services with disease complaints. Active method is detection of patients by screening especially in specific risk groups. Results of radiological TB screenings conducted by Mobile Screening Teams (MST) in Turkey analyzed retrospectively.
Methods: Radiological screening data of MSTs in 2015, 2016 and 2017 are collected and analyzed. MSTs in 20 provinces assigned to screen close and designated provinces; active screenings performed at least once a year for risk groups in all 81 provinces. MSTs carry out programs including risk groups such as prisons, nursing homes and kindergartens. Other institutions screened for contact examinations in case of index case or upon request. X-rays performed by mobile vehicles, evaluated by TB control unit physicians, further investigations performed for suspicious cases. TB disease investigated by clinical, radiological and bacteriological methods.
Results: Total 704,208 people had chest X-rays taken by MSTs as, 239,932 in 2015, 233,874 in 2016, 230,432 in 2017 and 145 TB patients newly diagnosed. Approximately 60% of screenings performed in prisons, 106 TB patients detected. TB patient detection prevalence in 3 years by mobile screenings is 20.6 per 100,000. Highest rates of TB diagnosis by active screening are in nursing homes and health facilities, followed by prisons.TB patient detection rates are very low in schools, dormitories and military screenings (Table 1).

Site of screening	Number of Institutions Screened	Number of people scheduled to screen	Number of People Screened	Screening target achievement rate (%)	Number of Radiologically suspicious TB	Number of TB patients detected during Screening	TB disease prevalence at Screening (per 100,000)
Prison	1,158	519,608	420,367	80.9	10,008	106	25.2
Nursing home	566	46,941	33,926	72.3	2,503	15	44.2
Kindergarten	132	8,550	6,786	79.4	73	1	14.7
Military	195	105,810	85,621	80.9	448	4	4.7
Health facility	138	14,917	12,489	83.7	613	5	40,0
School, student dorm	500	82,903	65,922	79.5	924	4	6,1
Other	377	91,390	79,097	86.5	1,395	10	12,6
TOTAL	3,066	870,119	7042,08	80.9	15,964	145	20,6

[EP-14-232-02 Table 1. TB Screenings performed by mobile screening teams in the years, 2015 to 2017]

Conclusions: Considering TB incidences in Turkey respectively in these years, about 1,5 times more patients are determined by MST screenings. TB patient contacts screenings which is the most important risk group, performed by registered TB units and not evaluated in this study. Since TB incidence continues to decrease annually and TB elimination targeted in Turkey, finding cases by active method in high risk groups should be continued.

EP-14-233-02 Factors associated with chest X-ray uptake in a household contact screening initiative in Ho Chi Minh City, Viet Nam

NTT Nguyen,[1] AJ Codlin,[1] RJ Forse,[2] LNQ Vo,[3,4] GC Do,[5] HV Le,[6] HB Nguyen,[6] TN Vu,[7] GT Le,[7] NV Nguyen,[6] [1]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [3]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [4]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [5]Pham Ngoc Thach Lung Hospital, Quality Assurance, Ho Chi Minh City, Viet Nam, [6]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [7]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam.
e-mail: nga.nguyen@tbhelp.org

Background: Viet Nam is currently rolling out a "Double X" diagnostic algorithm: screening with chest X-ray (CXR), followed by Xpert testing for people with CXR abnormalities. However, there is limited evidence on how best to operationalize this testing approach, particularly in the context of active TB case finding.
Methods: A large-scale household contact (HHC) screening initiative has been ongoing across seven districts of Ho Chi Minh City since 2017. Community health workers (CHWs) visit the homes of index TB patients to complete a household asset survey, enumerate HHCs and verbally screen them. All HHCs are referred for CXR regardless of their symptom status. Project data were used to assess CXR uptake across 24 clinical and demographic variables of the HHCs and their index TB patients using a multivariate logistic regression model.
Results: 13,339 household contacts were referred for CXR in 2018. Of these, only 3,731 (28.0%) were screened by CXR and the remaining 72.0% of referrals did not materialize. The following demographic and clinical factors were associated with non-participation: male gender (aOR 1.20 [1.1-1.3]), a lack of a cough (aOR 2.56 [2.3-2.8]), a lack of chest pain (aOR 1.66 [1.3-2.1]), not having diabetes (aOR 2.28 [1.7-3.1]) and not having social health insurance (aOR 1.22 [1.1-1.4]). HHCs with a lower household asset score were also less likely to participate, particularly among individuals with an asset score between 0-5 points (aOR 2.24 [1.5-3.3]). Finally, HHCs referred by community volunteers were less likely to get a CXR than those referred by salaried/employed community workers (aOR 2.51 [2.2-2.7]).
Conclusions: CHWs should provide targeted counselling, particularly to asymptomatic males, to explain the benefits of CXR screening for HHCs. Since low socioeconomic status is associated with non-participation, additional research should be conducted on indirect and other hidden costs of "free" TB screening, along with the effectiveness of social protection interventions.

	HHCs with no CXR result, n(%)	aOR (95% CI)
Male gender	4,205 (73.9%)	1.20 (1.1-1.3)
No cough	8,864 (79.2%)	2.56 (2.3-2.8)
No chest pain	9,430 (72.6%)	1.66 (1.3-2.1)
No diabetes	9,490 (72.1%)	2.28 (1.7-3.1)
No health insurance	1,749 (76.1%)	1.22 (1.1-1.4)
Asset score		
0 - 5 points	687 (77.3%)	2.24 (1.5-3.3)
6 - 11 points	6,856 (72.5%)	1.90 (1.4-2.7)
12 - 17 points	1,973 (69.5%)	1.80 (1.3-2.5)
18 - 22 points	92 (59.4%)	Ref
CHW employment model		
Volunteer districts	4,419 (82.6%)	2.51 (2.3-2.7)
Employee districts	5,189 (64.9%)	Ref

[Parameters associated with lack of CXR uptake]

EP-14-234-02 "Missing million": a study to assess the potential of offering chest X-rays for sputum smear negative TB cases to reduce this gap

GC Mallick,[1] J Kuwatada,[1] [1]MAMTA Health Institute for Mother and Child, Chronic Disease, New Delhi, India.
e-mail: gcmallick@mamtahimc.org

Background and challenges to implementation: The WHO has found that India tops the list of the world's missed tuberculosis (TB) cases. The objective of this pilot study is to assess impact of offering chest X-Ray (CXR) to sputum smear negative (SN) cases in preventing new smear negative (NSN) cases getting missed otherwise. In 34 districts of 6 states (Haryana, Rajasthan, Bihar, Uttar Pradesh, Himachal Pradesh and Chhattisgarh) in India on a pilot basis, we offered CXR upfront to SN presumptive TB Patients (PTBP) during January - March 2019.

Intervention or response: Project Axshya in collaboration with district TB cell offered CXR to sputum smear negative patients symptomatic of TB by linking them with CXR facility made available at their convenient places. During intervention period, in 34 districts, where Axshya is working, sputum of 22'595 PTBP was tested. If sputum was found negative, the person was advised to get CXR done. Thereafter a comparative analysis was done with state and national level to assess utility of CXR for SN cases in an easily accessible manner.

Results and lessons learnt: Positivity rate of new sputum positive (NSP) is found close to 11% (2'494 out of 22'595 cases) among selected group. 6% of total SN cases (20'101 cases) was availed CXR. Positivity rate in these SN patients was found to 23% (294 out of 1291 cases). In our study group, the NSP:NSN ratio of TB patients has been found to be reversed (1:2.06*) as compare to national (2.12:1**) data. Offer of CXR to all SN patients helped in identifying 12% more TB cases.

Conclusions and key recommendations: The study found that offer of CXR facility to all smear negative cases can prevent sizeable number of NSN TB cases getting missed. We recommend replicating this on a larger scale to significantly reduce the existing gap of 'missing million' in India.

* Projected figure

** TB India Report, 2016

EP-15-C1 LTBI management: it can be done!

EP-15-235-02 Strategic PEPFAR investment helps scale up isoniazid preventive therapy in Kenya

H Weyenga,[1] A Katana,[1] D Achwoka,[1] [1]US Centers for Disease Control and Prevention, DGHT, Nairobi, Kenya.
e-mail: xmm4@cdc.gov

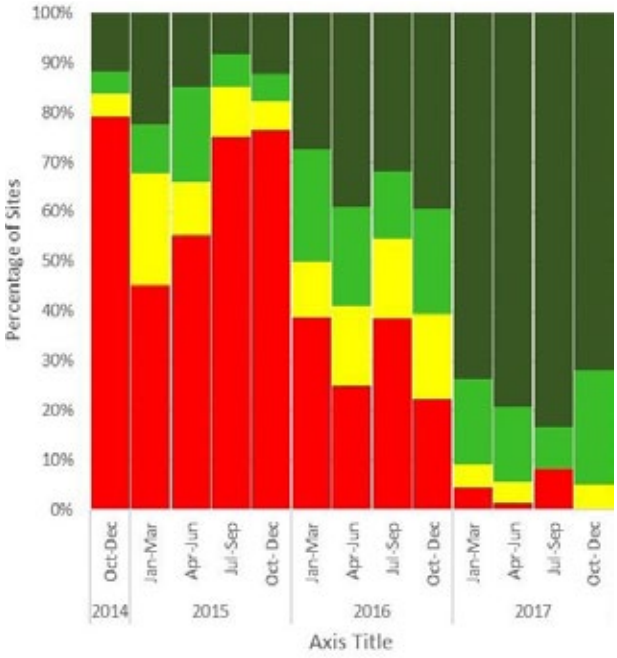
Background and challenges to implementation: Isoniazid preventive therapy (IPT) reduces the risk of tuberculosis and death among people living with HIV (PLHIV). Despite availability of policy guidelines for IPT among PLHIV, many countries have not implemented this intervention. We reviewed the role of the President's Emergency Plan for AIDS Relief (PEPFAR) in IPT scale-up in Kenya to inform potential investments

Intervention or response: We reviewed PEPFAR activities including policy and standard operating procedures (SOP) dissemination, program coordination, capacity building, supply chain management, service delivery and monitoring and evaluation. We analyzed PEPFAR site improvement through monitoring systems (SIMS) data collected from CDC-supported sites and Ministry of Health District Health Information System IPT data (October 2014-December 2017).

Using published PEPFAR SIMS scoring system sites were assigned scores based on IPT uptake: 1-red (< 60% uptake; requires urgent remediation), 2-yellow (60%-79% uptake; needs remediation), 3-light green (80%-100% uptake; meets expectations and requires no remediation), and 4-dark green (80%-100% uptake and SOPs available on-site; surpasses expectation and requires no remediation). Sites requiring remediation were supported to develop corrective action plans. Feedback was provided to stakeholders, and follow-up visits were scheduled for site support.

Results and lessons learnt: The proportion of sites requiring remediation (red and yellow scores) declined from 83.5% (n=56) in October 2014 to 5% (n=2) in December 2017 based on 872 sites supervised over this period (Figure 1). National IPT uptake increased 70 times (9,501 in October 2014 to 667,722 in December 2017). PEPFAR helped disseminate guidelines and SOPs, supported technical working group meetings, developed IPT scale-up plans, trained county and site-level staff, and provided mentorship. Funds were allocated annually for procurement of isoniazid, and systems were supported for recording and reporting service delivery and commodity consumption.

Conclusions and key recommendations: Our findings illustrate PEPFAR's critical role in supporting rapid IPT scale-up in Kenya. Similar investments are recommended for countries planning IPT scale-up.



[Figure 1. Trends in Proportion of sites requiring remediation CDC Kenya, October 2014-December 2017]

EP-15-236-02 Mapping gaps in the latent TB care cascade for persons initiating ART when isoniazid stock was available at HIV-care facilities in Kampala-Wakiso districts, Uganda, 2017

N Kalema,[1] A Semeere,[1] A Cattamanchi,[2] M Armstrong-Hough,[3] [1]Infectious Diseases Institute, College of Health Sciences, Makerere University, Research Department, Kampala, Uganda, [2]University of California, Division of Pulmonary & Critical Care Medicine San Francisco General Hospital, San Francisco, CA, United States of America, [3]Yale School of Public Health, Epidemiology of Microbial Diseases, Yale, CT, United States of America. e-mail: nkalema@idi.co.ug

Background: A third of 34 million people living with HIV (PLWH) globally are co-infected with latent Tuberculosis. The World Health Organization (WHO) recommends latent TB screening and treatment for PLWH. However, isoniazid stock availability continues to limit guideline uptake.We determined the proportion of eligible persons completing each step of the latent TB care cascade at four HIV-care facilities.

Methods: We abstracted routinely collected data from HIV-TB care forms and registers at four ART facilities in urban Kampala (2) and semi-rural Wakiso (2) districts. We conducted a retrospective analysis of latent TB care provided to a proportionate random stratified cohort of patients registering for ART when isoniazid stock was available in 2017 and determined the proportion of eligible patients completing each step of the WHO recommended guidelines, namely; TB-symptom screening, initiation and completion of isoniazid therapy. We performed Kaplan-Meier survival analysis to determine the cumulative incidence of completing the 6-months therapy.

Results: Of the 399 persons enrolling for ART in 2017, 92% were enrolled from the out-patient (226) and eMTCT (136) clinics; 309 (77%) were women; the median age, CD4 count and body mass index were 29 years (IQR: 25-34), 405 cells/uL (IQR: 22-573) and 23 Kg/m^2 (IQR: 21-25) respectively. 390 (98%) of 399 were screened for latent TB infection; 372 (93%) of 390 had no TB symptoms and were eligible for isoniazid preventive therapy; however only 62 (17%) of 372 eligibles were prescribed and initiated therapy and 36 (58%) of 62 completed the six-month treatment. The cumulative incidence of completing therapy in 6-months was 56%, (95% CI: 44-69).

Conclusions: While latent TB screening is practiced almost universally, initiation and completion of 6-months preventive therapy remains a challenge even when isoniazid stock is available. Our findings suggest a need for stakeholder engagement and implementation science approaches to understand why.

EP-15-237-02 Implementation of tuberculosis preventive therapy in an urban HIV clinic in Kampala: effect of an intervention on completion rates

A Arinaitwe Samuel,[1] MR Nabisere,[1] R Muyise,[1] J Asienzo,[1] G Anguzu,[1] N Owarwo,[1] I Lwanga,[1] M Lamorde,[1] C Sekaggya-Wiltshire,[1] E Laker,[1] [1]Infectious Diseases Institute, College of Health Sciences, Makerere University, Prevention Care and Treatment, Kampala, Uganda. e-mail: aarinaitwe@idi.co.ug

Background: Despite the documented benefits of Tuberculosis Preventive Therapy (TPT), high TB burden countries report low treatment completion rates (40-50%). Inconsistent prescribing by health workers is a predictor of low completion rates. The Infectious Diseases Institute (IDI), Kampala, Uganda rolled out TPT in July 2017 and in response to the poor completion rates, purple identifier TPT cards were introduced in April 2018 to enable ease of clinician tracking of patients on TPT by prompting clinicians to prescribe isoniazid at follow-up visits. We assessed the effect of these cards on TPT completion.

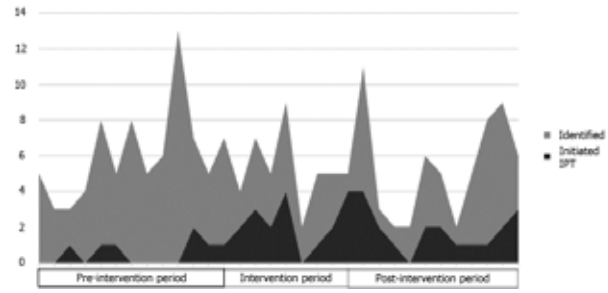
Methods: We conducted a retrospective cohort study using routinely collected clinic data. Data on patients initiated on TPT from July 2017 to October 2018 were extracted from the clinic database. We determined TPT completion (defined as Isoniazid 300mg dispensed for 180 days) among those who received TPT cards and those who did not. Bivariate analysis (with chi square test) was used to determine association between completion of TPT and categorical independent variables.

Results: Of 198 patients initiated on TPT (51% female), 76 (38 %) patients received TPT cards. Median age of the participants was 38 (IQR (31 - 47). The overall completion of all patients was 47%. 53/76 (70%) and 39/ 122 (32%) of patients who did and did not receive the card completed TPT respectively. Patients using a TPT card had greater odds of completing TPT (odds ratio (OR): 4.9, 95% C.I: 2.6-9.1, p< 0.01). Completion were similar in men and women.
Conclusions: Using a TPT tracking card, a simple low-cost intervention, increased TPT completion rates. Wider use of such a strategy should be considered in similar high TB burden countries.

EP-15-238-02 A tailored intervention package was effective in improving INH prophylaxis treatment cascade in primary care setting in Indonesia: evidence from a randomised pragmatic cluster trial

R Ruslami,[1] P Hadisoemarto,[1] P Hill,[2] F Fregonese,[3] O Oxlade,[3] B Alisjahbana,[1] D Menzies,[3] [1]Universitas Padjadjaran, Tuberculosis Working Group, Faculty of Medicine, Bandung, Indonesia, [2]University of Otago, Dunedin School of Medicine, Centre for International Health, Department of Preventive and Social Medicine, Dunedin, New Zealand, [3]McGill University, McGill International TB Center, Montreal, QC, Canada.
e-mail: n.ruslami@gmail.com

Background: Coverage of INH prophylaxis treatment (IPT) among eligible under-five in Indonesia was very low (2018: 8.5%). We report results from a part of an international multi-center study (ACT4 trial) that aimed to evaluate the effectiveness of a tailored intervention package to increase IPT coverage.
Methods: Twenty months of randomized pragmatic cluster trial, followed by a 12-month follow up. We randomized fifteen community health centers in Bandung into control and intervention arms where a standardized assessment was conducted and used to develop a tailored intervention package. The intervention was completely ceased at the end of the 20-month period. Cascade of IPT care was measured for intervention groups before and during the intervention, whereas only the proportion of eligible contacts initiating IPT was recorded in the 12-month follow up period.
Results: Almost no under-five contact was put under IPT prior to the intervention. Based on assessment results, the intervention package consisted of
1) an educational flipchart,
2) a cascade indicator registry,
3) a scheduled in-service training,
4) an SMS-based appointment reminder, and
5) toys to be given as non-monetary incentives to eligible under-five.
Monetary incentive was considered but not implemented due to low likelihood of post-trial sustainability. In the 8-month intervention period, the cumulative percentages of under-five contacts starting initial assessment, completed medical evaluation, and initiated IPT in the intervention arm were 51.6%, 51.6%, and 41.9%, respectively (vs. none throughout in the control arm). Of 31 eligible under-fives identified in the intervention arm, 41.9% initiated IPT (vs. none in the control arm). One year after the intervention was ceased, IPT coverage decreased by 7.6% (34.3% vs. 41.9%).
Conclusions: The intervention package was effective and sustainable to increase IPT coverage up to some extent. Although more effective intervention options were available, their implementation were constrained by the availability of resources to sustain them beyond trial period.



[Figure 1. Number of eligible under-five contacts identified and initiated IPT in the intervention group. No eligible under-five initiated IPT in the control arm. (Pre-intervention period: August 2016 - August 2017; Intervention period: September 2017 - April 2018; Post-intervention period: May 2018 - March 2019)]

EP-15-239-02 Planning for elimination: developing a programmatic engagement with latent tuberculosis

J Denholm,[1] [1]Victorian Tuberculosis Program, Melbourne Health, Melbourne, VIC, Australia.
e-mail: justin.denholm@mh.org.au

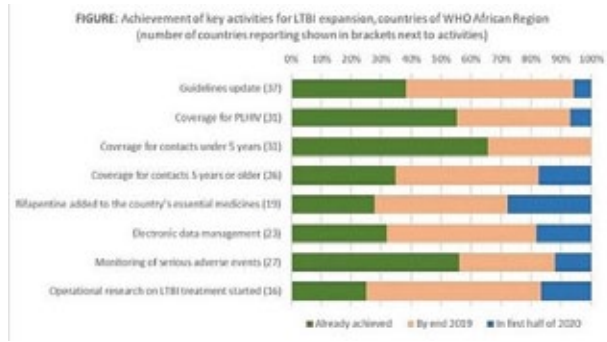
Background and challenges to implementation: In low-incidence settings such as Australia, the considerable majority of tuberculosis (TB) cases arise from reactivation of latent TB infection (LTBI). Most TB programs have expertise and capacity focused on active TB cases and contacts, with less focus on population-based diagnosis and treatment of LTBI. However, such capacity is needed in order to develop sufficiently large-scale programmatic responses towards TB elimination.
Intervention or response: We adopted a multimodal approach to evaluating the burden of LTBI in Victoria, and planning an effective and efficient approach, acceptable in relation to both government and community priorities. This included novel estimation of LTBI prevalence and distribution, risk of reactivation in local context, and evaluation of both health economic implications and community acceptability of strategies towards TB elimination.

Results and lessons learnt: We identified that a high proportion of Victorian residents born overseas had LTBI, and quantified risk to individuals of varying ages and times from arrival. While over 5% of the total population was estimated to have LTBI, 17.9% of overseas-born residents were infected, allowing for the development of a range of more efficient targeted approaches to testing and treatment. Health economic evaluation was then possible using locally calibrated modelling, allowing priority setting for government, public health agencies and affected communities. Optimising health system costs and establishing community priorities are discussed, including the use of community focus groups and ′citizen juries′.
Conclusions and key recommendations: Multimodal evaluation provides valuable insights for TB programs in planning appropriate engagement with LTBI. Such a range of approaches allows quantitative and qualitative engagement with a variety of stakeholders, and is necessary for effective progress towards TB elimination.

EP-15-240-02 Programmatic management of latent TB infection in African countries: current status and short-term plans

AP Wachinou,[1] F Mavhunga,[2] P Gandaho,[1] D Falzon,[3] A Kanchar,[3] K Samson,[3] A Dissou,[1,4] C Merle,[5] [1]West African Regional Network for Tuberculosis Control, (WARN-TB), Cotonou, Benin, [2]World Health Organization, Regional Office for Africa, Brazzaville, Congo, [3]World Health Organization, Global TB Programme, Geneva, Switzerland, [4]Supranational Reference Laboratory for Tuberculosis, (SRL), Cotonou, Benin, [5]Special Programme for Research and Training in Tropical Diseases (TDR), Intervention Research, Geneva, Switzerland.
e-mail: wachinouprudence@yahoo.fr

Background and challenges to implementation: Global scale-up of preventive therapy (TPT) for latent tuberculosis infection (LTBI) will be critical to achieve the WHO End TB Strategy targets by 2035. LTBI prevalence is estimated at around 23% globally but more in high burden settings like Africa. TPT coverage among key risk groups such as people living with HIV (PLHIV) remains low and varies widely from 1% in Eswatini to 53% in South Africa. New tools to identify and treat individuals at risk of progressing to active TB are now recommended by WHO, including rifapentine-based treatment, and may enhance scalability.
Intervention or response: In March 2019 we invited TB programme managers of the 47 countries in WHO African Region to report on short-term plans to scale up LTBI activities. National TB programme staff completed a self-administered electronic questionnaire on timelines to implement key activities for LTBI expansion in line with updated WHO recommendations.
Results and lessons learnt: Between 16 and 37 countries reported interpretable results on one or more of 8 key activities towards nationwide expansion of LTBI (**Figure**). By the end of 2019, of the countries reporting, 86% will have their LTBI guidelines updated; 73%-94% aim to target three key risk groups (PLHIV, contacts < 5 years, contacts >4 years); 68% plan to add rifapentine to their national essential medicines list [26% plan this in 2020]; 78% plan to manage LTBI data electronically; 81% aim to expand drug safety monitoring; and 63% plan to start operational research projects on LTBI.
Conclusions and key recommendations: While the results of this survey need further validation, many African countries report wide acceptance of LTBI recommendations. Ambitious plans will need to be supported with technical and financial assistance on several programmatic components, particularly the introduction of rifapentine, drug-safety monitoring, electronic data management and operational research on barriers to the achievement of coverage targets.



[Figure]

EP-15-241-02 Scaling up isoniazid preventive therapy (IPT) uptake among people living with HIV in resource-limited settings: lessons from East-Central Uganda

N Ruhinda,[1] R Nyinoburyo,[2] B Nsangi,[2] A Muwonge,[1] A Muhwezi,[1] N Tumwesigye,[3] [1]University Research Co., LLC, USAID RHITES EC Project, Health Systems Strengthening, Jinja, Uganda, [2]University Research Co., LLC, USAID RHITES EC Project, TB/HIV, Jinja, Uganda, [3]University Research Co., LLC, USAID RHITES EC Project, Chief of Party, Jinja, Uganda.
e-mail: nruhinda@urc-chs.com

Background and challenges to implementation: Uganda is one of the 30 high TB/HIV burden countries in the world, with 40% of TB patients HIV co-infected. Studies show that IPT reduces the incidence of TB among people living with HIV (PLHIV) by up to 60%. To reduce the burden of TB/HIV, Uganda adopted the WHO recommended IPT guidelines in 2014. However, by June 2017, only 2% of eligible PLHIV were initiated on IPT with low completion rates of 27%. Factors responsible for poor IPT implementation included; insufficient stocks of Isoniazid (INH), limited health worker knowledge on IPT and requirement for monthly follow up visits at the health facilities leading to poor completion rates.

Intervention or response: The USAID's Regional Health Integration to Enhance Services in East-Central Uganda (RHITES-EC) project trained 630 health workers on IPT and thereafter, through Quality Improvement (QI) methods, 126 Health facility teams were mentored by the QI coaches to prioritize clients for IPT and commit the limited available INH stock to only those patients for whom the 6-month course was available. The project designed an appointment tracking system for clients on IPT and synchronized IPT refills with antiretroviral drug refills. IPT uptake among eligible PLHIV was monitored weekly and completion rates were monitored quarterly. We compared IPT uptake for the periods between January- March 2018 and October-December 2018 and completion rates for September 2017 with September 2018.
Results and lessons learnt: The number of PLHIV initiated on IPT increased from 798 in the quarter of January-March 2018 to 2,719 during the quarter October-December 2018, an increment of 240%. Completion rates also improved from 19% in September 2017 to 69% in October 2018.
Conclusions and key recommendations: In resource limited settings, on-job trainings, drug stock quantification and committing of 6-months courses to individual patients, synchronizing ART and IPT visits are essential for a successful IPT program implementation.

EP-15-242-02 "Household contact card" improves tuberculosis screening in contacts of pulmonary tuberculosis patients

V Banurekha,[1] J Lavanya,[2] W Basilea,[3] S Sriram,[3] J Saraswathy,[1] A Dhanalakshmi,[4] D Bella Devaleenal,[5] N Dina,[1] N Pooranagangadevi,[1] S Tripathy,[6] [1]ICMR-National Institute for Research in Tuberculosis, Department of Clinical Research, Chennai, India, [2]Central TB Division, District TB Centre, Chennai, India, [3]ICMR-National Institute for Research in Tuberculosis, Department of Epidemiology, Chennai, India, [4]ICMR-National Institute for Research in Tuberculosis, Department of Socio-Behavioural Research, Chennai, India, [5]ICMR -National Institute for Research in Tuberculosis, Department of Clinical Research, Chennai, India, [6]ICMR-National Institute for Research in Tuberculosis, Director-In-Charge of ICMR-NIRT, Chennai, India.
e-mail: bhannu@gmail.com

Background: Household contacts of tuberculosis (TB) patients are at risk of TB infection and disease. To assess the utility of "Household contact card" for systematic screening of household contacts of pulmonary TB (PTB) patients for TB.
Methods: The "Household contact card" was implemented by the Health Care Workers (HCW) of the TB Control Programme in Chennai District for screening household contacts of Index PTB patients initiated on treatment during June to August, 2018. Contacts were required to be screened within 2 months of treatment initiation in the Index patient. Details collected included age, gender, smoking, alcohol use, immunosuppressive conditions and TB treatment. Symptom screening along with chest radiograph and or sputum examination was attempted. Screening of household contacts was compared pre and post implementation phase. Proportions were computed for the data analysed.
Results: Household contact information could be documented for 93% (1268/1364) of Index PTB patients. The main reasons of non-listing of household contacts in 96 PTB patients were HCW non-avilability or non-co-operation. Of the 2690 contacts identified, 41% were males and median age was 28 years. Smokers, alcohol users and diabetics each constituted 3%. There were 2149 (80%) contacts who were screened for TB symptoms. In addition to symptom screening, chest radiograph was done in 17% and sputum examination in 70%. Lack of time, feeling healthy, stigma, out-station visit were the main reasons for 526 contacts not undergoing TB screening. Anti-TB treatment was initiated in 21 (1%) of contacts diagnosed with TB. Preventive therapy was initiated in 59% (81/138) of contacts aged < 6 years. The screening of household contacts improved from 36% to 80% during the implementation phase (Table).
Conclusions: "Household contact card" improved TB screening in household contacts of PTB patients. Reasons for non-listing and screening have to be addressed to improve screening of household contacts for TB.

Household contact screening	Pre-implementation phase (January to March, 2018)	Post-Implementation phase (June to August, 2018)
Index PTB patients started on treatment (n)	1236	1364
Index PTB patients with documentation of household contacts	1023 (83%)	1268 (93%)
Household contacts identified (n)	2773	2690
Contacts screened	1001 (36%)	2149 (80%)
Contacts diagnosed with TB	40 (4%)	21 (1%)
Contacts started anti-TB treatment	14 (35%)	21 (100%)
Contacts <6 years of smear positive pulmonary TB patients (n)	202	138
Contacts <6 years started on Isoniazid preventive therapy	69 (34%)	81 (59%)

[Comparison of household contact screening for tuberculosis pre and post 'Household contact card' implementation phase]

EP-15-243-02 Impacts of systematic screening and treatment for incident of disease and latent infection of tuberculosis in Taiwan: a model-based analysis

H Fu,[1] N Arinaminpathy,[1] [1]Imperial College London, Infectious Disease Epidemiology, London, United Kingdom. e-mail: h.fu15@imperial.ac.uk

Background: For countries with intermediate tuberculosis (TB) burden, such as Taiwan, reaching the End TB goals may require a combination of active case-finding (ACF) for TB, alongside treatment of latent TB infection (LTBI), in defined risk groups. To guide planning for such efforts, it is necessary to identify which risk groups would be most impactful to target.
Methods: We modelled the potential impact of ACF and preventive therapy in Taiwan, with particular focus on three risk groups bearing a disproportionate burden of TB: those with diabetes, aboriginal populations, and the elderly. Using the model, we projected the impact of regular, sustained screening programmes for TB and LTBI over 2020-2035 in these populations. For ACF, we modelled initial screening by chest radiography, and confirmation using Xpert RIF/MTB. For LTBI, we assumed diagnosis using interferon gamma release assay, followed by preventive therapy with a standard 3-month regimen of isoniazid and rifapentine. To compare with the End TB goals, we evaluated the impacts of different screening programmes on the change in TB incidence rate over 2015-2035.
Results: In the absence of interventions, current declining trends in TB incidence may reverse in future, due to Taiwan's ageing population. Modelling results (see Table) suggest that ACF programmes would show limited impacts in controlling the TB burden. Screening programmes including LTBI testing and preventive therapy revealed large declines within individual risk groups, with the greatest impact when targeting the elderly. A combination of these measures in all the risk groups would achieve a 20.6% reduction in TB incidence rate at the country level.

		Reduction in TB incidence rate by 2035 compared to 2015	
Risk groups	Screening programmes	Within risk groups	At the country level
-	End TB goal	-	90%
-	Baseline	-	2.2%
Aboriginal	ACF + preventive therapy	67.1%	2.6%
Diabetic	ACF + preventive therapy	33.8%	12.0%
Elderly	ACF + preventive therapy	49.9%	18.4%
Aboriginal + Diabetic + Elderly	ACF	-	2.6%
Aboriginal + Diabetic + Elderly	ACF + preventive therapy	-	20.6%

[Table. Impacts of systematic screening and treating for TB and LTBI in selected risk groups]

Conclusions: Systematic LTBI screening and preventive therapy in high-risk populations show potential in reducing TB burden in an intermediate TB burden setting. However, additional control strategies are needed to achieve the End TB goals, especially in the face of headwinds such as population ageing.

EP-16-E2 TB testing amongst at-risk and hard-to-reach populations

EP-16-244-02 Incentivising tuberculosis testing among low income individuals in the Philippines: a randomised controlled trial

S Lee,[1] L Lau,[1] W Dodd,[2] R Pickard,[3] DC Cole,[3] [1]International Care Ministries, Research, Manila, Philippines, [2]University of Waterloo, School of Public Health and Health Systems, Waterloo, ON, Canada, [3]University of Toronto, Dalla Lana School of Public Health, Toronto, ON, Canada. e-mail: siwon.lee@caremin.com

Background: Despite the high prevalence of TB, Filipinos of low income experience a number of barriers to obtain testing for TB. Recognition of these barriers and early case detection within this population is crucial in curbing the country's high TB incidence rate. The objective of this study was to examine if food and financial incentives were effective in promoting TB testing among low income individuals.
Methods: This study was carried out as part of the International Care Ministries (ICM)'s TB active case finding (ACF) program. Communities were randomly allocated to four different groups that received: nothing (control); micronutrient fortified rice packages (rice packages); transportation subsidy; or rice packages and transportation subsidy. Participants were screened for TB symptoms, and symptom positive individuals were referred to the closest health facility for testing.
Incentives were distributed when symptom positive individuals were given a referral. Data was collected by ICM staff, and data analysis was completed using R statistical package.
Results: From May 2018-January 2019, a total of 46,199 participants were screened for TB symptoms across 24 provinces. Overall, 750 were referred to the closest healthcare facility for testing. Of these, 399 were tested for TB, 30 (7.5%) were confirmed positive. Participants who received rice packages and a transportation subsidy were most likely to get tested (75.3%), followed by those that received transportation money (64.7%), rice packages (40.6%), and the control group (23.4%).
Conclusions: In resource limited settings, financial assistance for transportation could change TB testing behaviour among Filipinos of low socioeconomic status. Both food and financial assistance intervention groups

demonstrated significant change in the likelihood of TB testing. From these implementation research results, ICM will redesign its ACF program. Health policymakers should subsidize transportation costs for individuals experiencing low income to access local health centres in the Philippines.

EP-16-245-02 Gender differences in symptoms which influence care seeking among chest symptomatics in tribal populations - a study from India

B Thomas,[1] R S,[1] A S,[2] C Vedachalam,[1] VG Rao,[3] R Yadav,[3] V Paluru,[4] AJ Purty,[5] T Hussain,[6] S Rani,[1] [1]National Institute of Research in Tuberculosis, Social and Behavioural Research, Chennai, India, [2]National Institute of Epidemiology, Social and Behavioural Research, Chennai, India, [3]National Institute of Research in Tribal Health, Communicable Diseases, Jabalpur, India, [4]Regional Medical Research Centre, Health Research, Port Blair, India, [5]Pondicherry Institute of Medical Sciences, Community Medicine, Kalapet, India, [6]Regional Medical Research Centre, Immunology, Bhubaneshwar, India. e-mail: beenaelli09@gmail.com

Background: An understanding of health care seeking behavior patterns is crucial for early diagnosis and initiation of treatment which is an integral part of TB control. While 8% of India's population is tribal little is known about the health care seeking behavior among those who present with symptoms of TB.
Methods: This paper is part of a large project to estimate the burden of TB among the tribal population and understand health seeking behaviour from 6 states of India which included the Andaman and Nicobar, Chhattisgarh, Jharkhand, Madhya Pradesh, Maharashtra, and Odisha. The data was collected from 48 clusters were 41404 were screened.
Results: Among those who were screened, 4% (1485) were chest symptomatic. Of these, 63% (934) were male. Of these chest symptomatic, only 19% (M19% vs F18%) sought care and among them 39 %(M40%vs38%) sought care after one month or more. 52% (M53% vs F51%) accessed a public facility and 46% (M44% vs F48%) a private facility. The significant symptoms which influenced males to seek care were blood in sputum (OR=1.7, 95%C.I: 1.1 - 2.5, p=0.011) shortness of breath (OR=1.5, 95%C.I: 1.0 - 2.1, p= 0.031), fever (OR=1.4, 95%C.I 1.0 - 1.9, p= 0.044) and weight loss (OR=1.4, 95%C.I: 1.0 - 2.0, p=0.027). The chest symptoms associated with care seeking behavior among females were shortness of breath (OR=1.8, 95%C.I: 1.2 - 2.8, p=0.010) and weight loss (OR=1.7, 95%C.I: 1.1 - 2.6, p= 0.016).
Conclusions: The care seeking among chest symptomatic among the tribal population is dismal with more than one-third who seek care after one month or more. There are gender differences in the symptoms which prompt care seeking among the tribal population which call for gender specific TB prevention efforts so that the tribal community is made aware of the all-important symptoms to prompt early care seeking.

EP-16-246-02 Understanding social and behavioural barriers to TB case detection in Nigeria: a qualitative study using a human-centred design approach

J Edor,[1] B Aiyenigba,[1] J Orkis,[2] J DeNormandie,[1] A McCartney-Melstad,[2] A O'Reilly,[3] I Uko,[4] A Lawason,[5] T Odusote.,[6] I Tweedie,[1] [1]John Hopkins University Center for Communication Program, Breakthrough ACTION Nigeria Project, Abuja, Nigeria, [2]John Hopkins University Center for Communication Program, Breakthrough ACTION Global, Washington, WA, United States of America, [3]ThinkPlace, Breakthrough ACTION Global, Washington, WA, United States of America, [4]National Tuberculosis and Leprosy Control Programme, ACSM, Abuja, Nigeria, [5]National Tuberculosis and Leprosy Control Programme, Public Health, Abuja, Nigeria, [6]United States Agency for International Development, Office of HIV/AIDS and Tuberculosis, Abuja, Nigeria. e-mail: joseph@ba-nigeria.org

Background and challenges to implementation: Despite free TB diagnosis and treatment in several public hospitals in Nigeria, TB case detection has remained low. In 2017, only 24% of estimated TB cases were diagnosed nationally. This study sought to understand the social and behavioural determinants of TB case detection in Nigeria using a human-centered design (HCD) approach.
Intervention or response: The National Tuberculosis and Leprosy Control Programme and the USAID-funded Breakthrough ACTION Nigeria project conducted immersive, ethnographic, in-depth interviews in Lagos, Kano, Rivers and Enugu States with 242 patients, treatment supporters, community members/leaders, healthcare providers and TB experts over a 3-week period in August 2018. Researchers took detailed field notes, photo-documented interactions and captured and clustered findings daily
Results and lessons learnt: Data synthesis yielded ten key insights and seven personas and journey maps. Long journeys to diagnosis frequently involve medicine stores and religious institutions as first points of contact due to proximity and low cost. Structural barriers to testing sputum samples, Community TB Workers' beliefs that samples must be collected in the morning, incomplete/incorrect data entry, and a lack of systems or structures to conduct follow-up or carry out contact tracing results in missed cases. Stigma across communities and health providers, widespread myths and misconceptions around transmission, and real and perceived costs in accessing TB diagnosis serve as barriers to health-seeking behavior. There is wide variability in the presence, quality, and types of TB materials available. Those that exist are often fear-based, unclear, and/or in English.

Individual counselling tailored to the needs of the client, particularly at the presumptive stage, is infrequent and incomplete. Some private health facilities offer high quality services but do not want to be associated with TB.

Conclusions and key recommendations: Social and behavioural barriers contribute to low TB case detection. Addressing these barriers and exploring identified opportunities will significantly improve TB case detection in Nigeria.

EP-16-247-02 Upfront GeneXpert for TB screening in prisons of Chhattisgarh, India: a policy in practice

K Khaparde,[1] R Prasanna,[2] M Deshpande,[2] P Shukla,[2] KR Nischith,[3] R Bano,[2] [1]World Health Organization, Country Office for India, New Delhi, India, [2]Government of Chhattisgarh, Health and Family Welfare, Raipur, India, [3]World Health Organisation, Country Office for India, New Delhi, India. e-mail: drkshitij78@yahoo.co.in

Background and challenges to implementation: The prevalence of active TB among prisoners has been reported to be 2 to 84 times higher than the estimates reported for the corresponding general population. Tuberculosis is still one of the major public health problem in the prisons of India and is primarily attributable to the high occupancy rate. As per the Prison Statistics India 2015, prisons in Chhattisgarh state has the occupancy rate of 233.9% which is second highest in the country.

Intervention or response: Joint collaboration of Department of Health and Department of Jail led to designing and implementation of a state policy of annual active screening for TB across all Sub-Jails, District-Jails and Central-Jails. A symptom screening was done and for the diagnosis of TB and the presumptive TB cases were subjected to smear microscopy in the year 2016 and shifted to Xpert MTB/Rif for screening in the year 2018.

Results and lessons learnt: In the year 2018, out of the 19593 jail inmates, 17634 (90%) inmates were screened for symptoms of TB. Among those screened 952 (5%) were identified as presumptive TB case, of which 792 (83%) were tested with Xpert MTB/Rif. With the use of Xpert MTB/Rif as a screening tool, the NNS was 333 as compared to NNS of 1228 in the year 2016 when smear microscopy was used as a screening tool. Three Rifampicin resistant TB cases were also diagnosed with Xpert MTB/Rif test.

Conclusions and key recommendations: The results highlighted the importance of regular active screening for TB among prisoners as a policy decision for the national programme. Upfront use of Xpert MTB/Rif upfront as a screening tool gives a better yield along with additional information on rifampicin resistance which would help administrators take appropriate containment measures for infection control in the prisons.

EP-16-248-02 Increase in tuberculosis incidence rate among prisoners, Brazil

G Tavares Magnabosco,[1] DM Pelissari,[1] G Drummond Marques da Silva,[1] F Dockhorn Costa,[1] P Barholomay,[1] D Arakaki-Sanchez,[1] [1]National Tuberculosis Programme / Ministry of Health, Department of Communicable Disease Surveillance, Brasília, DF, Brazil. e-mail: gabimagnabosco@hotmail.com

Background: In Brazil, in 2017, there was an increase in the tuberculosis (TB) incidence rate in comparison with previous years, which showed a tendency of reduction.

Objective: To describe the increase in the TB incidence rate between 2016 and 2017 in Brazil and the contribution of prison population to the trend.

Methods: A descriptive study of new TB cases in prison and non-prison population with age greater than 18 years notified in the Brazilian Notifiable Disease Information System. The TB incidence rates in these two groups in the years 2016 and 2017 and the difference in observed and expected cases were calculated, projecting their respective incidence rates for 2016 in the total population of 2017.

Results: Comparing years 2017 with 2016, there was an increase of 0.8% in TB incidence rate in non-prison population (37.8 to 38.1 cases/ 100 thousand inhabitants), and of 13.9% in the prison-population (890 to 1,013.4 cases/ 100 thousand prisoners). Regarding the difference between the number of TB cases observed and expected in Brazil in 2017, an excess of 2,050 cases was estimated. Of these, 45.7% (n=937) were in prisoners.

Conclusions: The results show the importance of prisoners in the excess of TB cases not expected in 2017 in Brazil. In the country, there is evidence that prisons may be amplifying TB in the general population and are reservoirs of the disease due to overcrowding, poor ventilation, prolonged contact, confinement of risk groups, and intense turn-over. Therefore, the expansion and consolidation of actions aimed at this public, such as the active search for cases at the door and in campaigns carried out in prisons, should be seen as priority strategies for achieving the goals proposed in the End TB National Plan as a public health problem in Brazil.

EP-16-249-02 Contribution of active household contact screening to TB case notification in Afghanistan,

A Hamim,[1] M Zafari,[2] SM Sayedi,[1] L Manzoor,[2] K Seddiq,[2] GQ Qader,[1] MK Rashidi,[1] PG Suarez,[3]
[1]Management Sciences for Health (MSH), Challenge TB (CTB), Kabul, Afghanistan, [2]Ministry of Public Health (MoPH), NTP, Kabul, Afghanistan, [3]Management Sciences for Health (MSH), Technical Excellence Group, Arlington, VA, United States of America.
e-mail: ahamim@msh.org

Background and challenges to implementation: National TB Programs (NTP) recommended active household contact screening for many years, but the implementation process was poor. During the implementation, some barriers and challenges identified, including lack of appropriate management structure and screening tools, lack of human resources, low community awareness, and poor adherence to Isoniazid Preventive Therapy (IPT).

NTP implemented active contact screening by support of Global Fund (GF) and Challenge TB (CTB) project in Afghanistan in 2018. However, active household contact screening can be time consuming and expensive, and the yield needs to be carefully evaluated to determine when it is most effective.

This study focuses on results of active contact screening in 2018.

Intervention or response: NTP agreed that healthcare workers contacted and permission is requested to visit households of index cases.

Household contacts investigated for TB sign and symptoms, followed by sputum microscopy examination.

The intervention strategies included training health staffs, conducting supervision, collecting data, providing feedback, and contacting a random sample of 20% of TB index case contacts for cross check. All household contacts of index TB cases were visited by health facility members. Household contacts with cough for more than two weeks and sputum were taken to the nearest TB diagnostic center for sputum examination. Children under 5 years of age were entered into the TB contact register and received IPT.

Results and lessons learnt: About 22,197 TB index cases were registered; 125,709 household contacts identified and 14,225 presumptive TB screened. Among them, 2,868 (20.1%) TB cases identified and 23,885 (19%) children under 5 put on IPT (Table 1). Considering the total number of household contact for all notified TB cases, the incidence of TB among household contact is 980/100,000 which is 5 times higher than estimated cases (189/100,000).

Conclusions and key recommendations: TB among household contacts is much higher than WHO estimated incidence cases. We recommend strengthening active contact screening nationwide.

Indicator/ Year	2018
# of index cases registered	22,197
# of household contact registered	125,709
# of presumptive TB among household contact screened	14,225
# of all form TB cases identified among contacts	2,868
# of children under 5 years old received IPT	23,885

[Table 1, Result of active household contact screening in 2018]

EP-16-250-02 Intensifying TB screening among community health workers: experience of project challenge TB, Mozambique

A Abdula,[1] [1]FHI 360, CTB, Maputo, Mozambique.
e-mail: aabdula@fhi360.org

Background: The Mozambique Ministry of Health (MoH) recommends screening all health care workers (HCWs) for tuberculosis (TB) at least twice a year. MoH has instituted provider consultation services in all main health facilities (HFs) to improve service delivery for HCW's and their families. However, there are education campaigns to prevent TB for all but no consultation services for community health workers (CHWs), even though there have been intermittent TB cases identified among CHWs. To address this gap, the Challenge TB (CTB) project conducted screening campaign covering majority of 227 CHWs in three provinces.

Methods: CTB, in close coordination with MoH and Provincial directorate of health (DPS), implemented a campaign to screen CHWs at the district level. In preparation for the campaign, CTB held consultative meetings with high-level provincial and district medical personnel to ensure their support and commitment to the intervention. The campaign objective was to find and treat TB cases, improve infection control (IC) and health of CHWs. Voluntary screening was conducted using questionnaires and physical exams. People with presumptive TB were referred for further testing with GeneXpert and chest x-ray.

Results: Between January to March 2019, CTB supported campaign implementation in three target provinces (Sofala, Zambezia and Nampula), covering 15 districts and 227 CHWs. From a total of 227 registered CHWs, 205 (90%) were screened for TB, and 52 (25%) were identified as presumptive TB cases. All 52 (100%) presumptive cases were referred for further testing and one CHW was found to have MTB Detected Rif negative and initiated treatment. The remaining 51 cases were all evaluated and treated accordingly: 5 had Malaria, 12 had Flu, 7 had pulmonary infection and the remaining 28 doesn't had nothing significant.

Conclusions: It is essential to include CHWs in regular screening campaigns for HCWs to early identify and treat TB cases among this risk group.

EP-16-251-02 Evaluation of a community-based X-ray screening initiative to improve TB detection among older people in Ho Chi Minh City, Viet Nam

NT Nguyen,[1] AJ Codlin,[2] T Dao,[3] RJ Forse,[4] HT Nguyen,[5] HT Nguyen,[6] GC Do,[7] TN Vu,[8] GT Le,[8] LNQ Vo,[3,9] [1]Friends for International TB Relief, M&E, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [3]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [4]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [5]Go Vap District Health Center, Department of Business Planning, Ho Chi Minh City, Viet Nam, [6]Go Vap District Health Center, District TB Program, Ho Chi Minh City, Viet Nam, [7]Pham Ngoc Thach Lung Hospital, Quality Assurance Department, Ho Chi Minh City, Viet Nam, [8]Ho Chi Minh City Public Health Association, Board of Directors, Ho Chi Minh City, Viet Nam, [9]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam.
e-mail: nga.nguyen@tbhelp.org

Background and challenges to implementation: In Viet Nam, older people (aged 55+ years) have high rates of TB and a 20% increased risk of being missed by public-sector TB services, frequently owing to their limited mobility and dependency on family members. By 2030, Viet Nam's older population is projected to grow by +65%, highlighting the need for TB services tailored for this key population.
Intervention or response: As part of the TB REACH-funded SWEEP-TB project, we implemented 36 days of community-based, mobile chest X-ray (CXR) screening in quarter 4 of 2018 across the 16 wards of Go Vap District, Ho Chi Minh City. Older people were targeted, but household contacts of index cases and anyone with TB symptoms were eligible to participate. Participants were first screened for TB symptoms using a mHealth app and then by CXR. A field reader interpreted the CXRs and individuals with abnormal results were tested using the Xpert MTB/RIF assay. After each screening event, Xpert-negative individuals were evaluated for clinical diagnosis.
Results and lessons learnt: 9,659 people were screened by CXR, 60.3% of whom were aged 55+ years. In total, 820 people were tested on Xpert (41.5% of those eligible), resulting in the detection of 40 people with bacteriologically-confirmed (Bac(+)) TB and 29 people with clinically diagnosed TB. The number needed to screen for older participants was 122 compared to 181 for younger participants. These screening activities resulted in an increase of +33.0% for Bac(+) and +24.8% for all form TB notifications over the same quarter in 2017.
Conclusions and key recommendations: This community-based CXR screening initiative resulted in improved TB detection and treatment, particularly for older people. However, it suffered from CXR over-reading, which resulted in higher than expected Xpert cartridge utilization and lower than expected test yields. Future CXR screening events should consider using a computer-assisted reading software to systematically interpret CXR images in a more standardized fashion.

	0-54 years	55+ years	All ages
Verbally screened for TB symptoms	3,892	5,914	9,806
Screened by CXR	3,803 (97.7%)	5,856 (99.0%)	9,659 (98.5%)
CXR abnormal	426 (11.2%)	1,550 (26.5%)	1,976 (20.5%)
Tested by Xpert and/or AFB	157 (36.9%)	663 (42.8%)	820 (41.5%)
Diagnosed with Bac(+) TB	15 (9.6%)	25 (3.8%)	40 (4.9%)
Diagnosed with All Forms TB	21	48	69
Bac(+) TB started on treatment	11 (73.3%)	23 (92.0%)	34 (85.0%)
All Forms of TB started on treatment	17 (80.9%)	46 (95.8%)	63 (91.3%)

[Breakdown of the TB care cascade for cohorts of 55+ years and >55 years]

EP-16-252-02 Community innovations: workplace visits (WV) to screen tuberculosis in men in Senegal

AO Diallo,[1] AN Fall,[1] B Diallo,[1] EM Dioukhane,[2] M Nelson,[3] M Kitane,[1] CT Niang,[1] F Fall,[1] NO Diouf,[4] N Ndiaye,[5] [1]Plan International Senegal, Global Funds Project, Dakar, Senegal, [2]Plan Canada, Global Funds Project, Toronto, ON, Canada, [3]Plan Canada, Global Funds, Toronto, ON, Canada, [4]Plan International Senegal, Global Funds Project, Kaolack, Senegal, [5]Plan International Senegal, Global Funds Project, Saint Louis, Senegal.
e-mail: alpha.diallo@plan-international.org

Background and challenges to implementation: In Senegal, tuberculosis under detection remains a major public health problem with 1/3 of the cases not detected. The disease affects more men than women with a sex ratio of 2.23. Plan International Senegal, a major stakeholder in the fight against tuberculosis, develops a community approach in collaboration with National TB program and Community Based Organizations to find the "missing cases". However, community interventions through home visits seemed to mostly reach women, leaving behind men who due to their professional activities among other reasons are not often home. Therefore, it was necessary to develop an approach targeting men and aiming to improve their access to health information and increase the TB screening rate.
Intervention or response: Since 2018, Plan International Senegal implemented the strategy of " Workplace Visits ". The intervention consists on visiting workplaces mostly frequented by men in populated urban areas. A sixty minutes sensitization followed by screening sessions at the workplace is organized. Workplaces gathering mostly men from the minorities and functioning during day time were prioritized such as construction workers, tailors, miners, drivers etc.
Results and lessons learnt: From July to December 2017, 170 000 men was reached by awareness sessions included in the Home Visit only approach against 163 799 in 2018 by the combined Home visits + Workplace Visits approach. Contrasting with this reduced number of men reached, the TB detection increased for adult men aged 15 years and over from **17.94% in 2017 to 19% in 2018.**

Conclusions and key recommendations: This approach which has resulted in better targeting vulnerable and at-risk men seems to be the reason of an increased TB cases detection among men. Contrasting with community gender blind awareness sessions, focusing on minorities at their workplace could better improve the rate of detection especially among men.

EP-16-253-02 Intensified active case finding (TB screening) intervention among high-risk, poor and vulnerable populations improved TB case notification, and successfully brought patients into care in Odisha, India

G Mallick,[1] PK Hota,[2] MS Munir,[2] S Mishra,[3] B Panda,[2] B Patnaik,[2] R Tarelakar,[4] HS Sahu,[5] S Mohanty,[6] [1]The Union, TB, New Delhi, India, [2]Government of Odisha, TB, Bhubaneswar, India, [3]Government of India, TB, Bhubaneswar, India, [4]World Health Organisation, TB, Bhubaneswar, India, [5]Centre for Health Research and Innovation, TB, Bhubaneswar, India, [6]The Union South East Asia, TB, New Delhi, India. e-mail: gmallick@theunion.org

Background and challenges to implementation: Tuberculosis is-a-major public-health-problem globally where only 6.1 million-cases were diagnosed-and-officially-notified in-2016-17 of-the-estimated 10.4 million-new-cases, leaving a-gap-of 4.3 million-cases. India,Indonesia,Nigeria accounted-for nearly-half-of-this global-gap. While the-routine-TB-services are-essential for-case-management-in-India, it has-been-a-major-challenge to-diagnose these-cases particularly-among the-high-risk-poor and vulnerable-populations where-TB-often-concentrates.

Odisha being-one-among the-high-TB-burden and low-detection-states in-the-country, it was critical-to-making-the strides necessary-to-proactively diagnose-TB-cases by putting-into-practice a-more-appropriate rights-based-approach like A*ctive-Case-Finding(ACF)*. The-state choose-to-be-involved in *the-'National-ACF-Campaign'* that aims-to screen-with-a-target-for *120 million TB-symptoms-populations, to-conduct-sputum-examination-of 6 million-symptomatics, and find-&-treat additional-infectious-0.3-million-TB-patients* among-the "*bottom-of-the-pyramid"* populations.

Intervention or response: Considering TB-screening as a-dynamic-and-innovative-process for-its low-detected-areas, the-state-RNTCP launched the-provider-driven ACF- initiative among-its- high-risk-poor and vulnerable-populations with-the-primary-objectives of screening-to-ensure that active-TB is detected-early to reduce-the-risk-of-poor-disease-outcomes-&-health-sequelae, reduce TB-transmission-&-the-adverse-social and economic-consequences-of-the-disease, and to-achieve the-National "Sweep-Out-TB"/"TB-Mukt-Bharat" target-by-2025.

Intensified case-finding-activities were planned-and-implemented in-all-31-districts during-2018. District-level-micro-planning involving key-officials were-made to map-&-identify vulnerable-areas-&-Key-Affected-Populations. Systematic-active-TB-screening through house-visits among-the-slum,prison-inmates-&-other-penitentiary-institutions,orphanages, school-hostel,tribal-residential-schools,unreached-villages,stone-crusher-units and PLHIVs was-carried-out for 4,235,030 populations by-trained-&-dedicated 214 Medical-Officers, 2,306 health-care-staffs, 37 local-NGOs and around 4,125 community-volunteers. The team reached-out-to-nearly 12 lakh-persons for screening-in-two-phases.

WHO-recommended-algorithms for screening-and-diagnosis(GRAD- tables) were-followed. All possible-ethical-practice was maintained-to-protect their privacy-and-confidentiality while indiscriminate-mass-screening was-avoided. Repeat-test was done-for-around-10% of-the-screened-cases while HIV-counselling-and-testing offered to all-presumptive-TB-cases. People who-were-not-diagnosed with-active-TB were informed-about the importance-of- seeking-medical-care when TB-symptoms-continue,emerge,re-emerge or worsen-later.

Results and lessons learnt: ACF saved the lives of 987 highly vulnerable,poor and key-affected-people. The team reached-out-to nearly 12 lakh-persons for screening-against a target-of-around 42.35 lakh populations. 42,133 presumptive-TB-cases were tested-for-sputum-microscopy out-of-which 902 were diagnosed-as-TB. 37 TB-cases were confirmed-thru CXR against 382.

Few presumptive-TB- cases identified-through-ACF refused care while 48 positive-cases diagnosed from-the-repeat-sputum-test were put-on treatment later. Table:1

Conclusions and key recommendations: Planned intensified-ACF-activities saved 987 lives-of never-to-be-diagnosed/treated key-populations and improved-TB-case-notification. Despite scaling-up and decentralizing-diagnostic and treatment-services, the-challenge-to-close the-case-detection-gap and reduce-the-delays in diagnosis still-remains a challenge.

Although current-studies provide insufficient-evidence to-show that active-screening-for-TB-disease impacts on TB-epidemiology, but this intervention proved-benefitting key-populations and public-health. The effects of a successful-ACF-program to close-the-case-detection-gap and reduce-the-delays-in-diagnosis will-be-sustainable if Passive-Case-Finding is-strengthened-alongside. TB-screening-approach should be-developed and implemented-in-a-way that-optimizes synergies-with the-delivery-of-other-health-services and social-services.

Target population mapped	No. of Persons screened	No. of Presumptive TB tested for sputum smear microscopy	No. of Microbiologically confirmed TB Patients diagnosed	No. of Presumptive TB examined for CXR (other than those diagnosed as Microbiologically confirmed TB)	No. of TB patients diagnosed based on CXR (other than those diagnosed Microbiologically confirmed TB)	No. of TB cases diagnosed after repeat sputum examination
4,235,030	1,196,031	42,133	902	382	37	48

[EP-16-253-02 Table:1 Summary of Active Case Finding Activities conducted in Odisha in 2018:]

EP-16-254-02 A way towards active case finding in key affected populations (KAP) area

D Tigga,[1] N Mulackal,[1] S Robart,[1] M Perumpil,[1]
[1]Catholic Bishops' Conference of India-Coalition for AIDS and Related Diseases (CBCI-CARD), Health, New Delhi, India. e-mail: deepak.tigga87@gmail.com

Background and challenges to implementation: Early case detection and prompt treatment of TB disease are means to cut the chain of transmission and reduce incidence. The most important is to select geographically-socially vulnerable population area of intervention. Correct identification of Key Affected population(KAP) is one of the major challenges to implementation.
Intervention or response: Project Axshya undertook an extensive exercise to mapping the KAP populations. The exercise involved secondary data of TB patients reported in the programme, consultative meetings with programme staff at various levels, district, block, village and in lines of programme reporting structures - district level tuberculosis centers, Tuberculosis units, designated microscopic centers and peripheral health institutions. Following this identified villages were categorized into one of the KAP - slum/migrant, tribal, hard-to-reach, etc. Key interventions - Active Case Finding, Active Community Surveillance and Health camps are conducted in 28 districts of 4 states by CBCI-CARD. Identified PTBPs through the interventions are linked to diagnostic and treatment services under the programme.
Results and lessons learnt: Over a period of one year, team reach a KAP population of **2,142,721** from the interventions mentioned above. A total of **31,776** PTBPs tested among whom **3,100** cases were identified. Out of which **66.45%** cases, **13.81%**, and **10.10%** TB diagnosed through Contacts, Tribal and Hard to Reach KAP respectively. Other 3 KAP having less than 5% TB diagnosed.
Conclusions and key recommendations: Among KAP outlined, "Contacts" of known TB patients are most vulnerable populations and focused interventions are needed to END-TB.

EP-16-255-02 Understanding contexts of TB-affected migrant population in Thailand: civil society perspective

NW Phyo,[1,2] [1]World Vision Foundation of Thailand, Health Department, Bangkok, Thailand, [2]WHO, Global TB Program, Bangkok, Thailand.
e-mail: nyan_win_phyo@wvi.org

Background and challenges to implementation: In 2014, estimated 3.7 millions of migrant were working 3 Ds (Dirty, Difficult and dangerous) job in Thailand and its occupied over 10 percent of total Thai Labour force mainly come from neighboring countries like Myanmar, Cambodia, Laos and Vietnam and all are high TB burden countries. Among them, approximate only half of them were able to access public health insurance and these groups were identified as hard to reach due to legal constraints, language barriers and social discrimination.
Intervention or response: WVFT launched community engagement TB control model funded by Global Fund for screening, diagnostic and treatment adherence in this key affected population which include Reach- Recruit-Test-Treat-Retain and Resilience (4Rs and 2Ts model)
As civil society organization, WVFT engaged 4Rs(Reach- Recruit- Retain and Resilience) and 2Ts(test and treat) were under control of Government health facilities.
Results and lessons learnt: Grant period starting from 1 Jan 2015 to 31 Dec 2017, WVFT recruited 1,262 migrant health volunteers and 48%(605) people are still active after grant. As a result of productivity of migrant volunteers, 99,145 migrant people were screened by Intensified case finding survey and identified 6%(6362) as presumptive TB cases and 593 people were notified as TB. 91% of total TB patients came from Myanmar followed by 6% from Cambodia, 2% from Laos and 1 % from other nationalities . As occupational wise, 30% from factory, 26% from construction sites, 20% from fishery related industry, 19% from fishermen and the rest 5% from other sectors. 76% of TB patients were aged between 25 to 54 and 62 % were male.
Conclusions and key recommendations: By seeing these results, community engagement model was really effective and efficient in ending TB in hard to reach population. Knowing exact demographic data of migrant context could help future TB design, decision makings and precise to hit the key affected population.

POSTER DISCUSSION SESSION (PS)

PS-28-B6 TB-HIV: African-Asian experience

PS-28-799-02 Adherence support groups for patients with drug-resistant TB/ HIV in South Africa: the PRAXIS study intervention

B Seepamore,[1] J Zelnick,[2] G Friedland,[3] R Boodhram,[4] A Daftary,[4,5] N Cele,[4] N Depargo,[4] A Wolf,[6] N Padayatchi,[7] M O'Donnell,[4,8,9] [1]University of KwaZulu-Natal, Social Work, Durban, South Africa, [2]Tuoro College and University System, Social Work, New York, NY, United States of America, [3]Yale School of Medicine, Infectious Diseases, New Haven, CT, United States of America, [4]Caprisa MRC HIV TB, Caprisa Pathogenesis and Treatment Research, Durban, South Africa, [5]McGill University, Epidemiology, Biostatistics & Occupational Health, Montreal, QC, Canada, [6]Columbia University College of Physicians and Surgeons, Division of Pulmonary, Allergy, & Critical Care, New York, NY, United States of America, [7]Caprisa MRC HIV TB, Caprisa, Durban, South Africa, [8]Columbia University College of Physicians and Surgeons, Division of Pulmonary, Allergy, and Critical Care Medicine, & Department of Epidemiology, New York, NY, United States of America, [9]Mailman School of Public Health, Epidemiology, New York, NY, United States of America.
e-mail: boitumelo7@ukzn.ac.za

Background and challenges to implementation: Psychosocial support may improve medication adherence and retention-in-care for multi/extensively drug-resistant TB/HIV patients facing a long treatment course and stigma. We evaluated the feasibility and impact of support groups as one component of a randomized controlled intervention trial aimed to increase adherence in patients initiating Bedaquiline treatment in KwaZulu-Natal, South Africa.
Intervention or response: Participants with MDR-TB/HIV in the intervention group attended monthly adherence support groups (ASG) at the centralised hospital site. Groups were separated by gender and led by trained facilitators. Outpatients were offered transport. Psychoeducational sessions covered the following themes: stigma, traditional and alternative medicines, disclosure and relationships, self-perception, income generation and accommodation. Guest speakers discussed special topics on treatment literacy and alcohol use. Patients were referred out to community-based organisations for ongoing individual support as needed.
Results and lessons learnt: To date 35 participants have participated in 14 ASG sessions with median 2 ASGs attended per participant. Group size varies between 3 -11 members per session. ASG sessions promote self-support, catharsis, treatment literacy, side effect management, and motivation to complete treatment. The feeling of belonging appears to enhance patient self-worth and has made it easy to share issues that would remain hidden from clinicians or family members such as alcohol use and feelings of depression. Community-based groups have been raised as a viable alternative to hospital-based support, to circumvent transport challenges.
Conclusions and key recommendations: Psychosocial support groups are an underutilised social work intervention in M/XDR-TB HIV treatment. The safety of the group allows openness and offers peer-to-peer motivation. This could be a feasible and impactful way to improve social cohesion among patients facing severe treatment challenges. Groups are an important component of patient-centred care and may support adherence in the context of decentralized roll out of new DR-TB treatment regimens.

PS-28-801-02 Tuberculosis in patients co-infected with visceral leishmaniasis and HIV - a new diagnostic and management challenge

S Burza,[1] K Pandey,[2] R Mahajan,[1] S Kazmi,[1] A Harshana,[1] N Alexander,[3] L Moreto,[4] N Verma,[2] VNR Das,[2] P Das,[2] [1]Médecins Sans Frontières, OCBA, New Delhi, India, [2]Rajendra Memorial Research Insitute of Medical Sciences, Tropical Diseases, Patna, India, [3]London School of Hygiene & Tropical Medicine, Statistics, London, United Kingdom, [4]Médecins Sans Frontières, OCBA, Barcelona, Spain.
e-mail: msfe-delhi-epidem@barcelona.msf.org

Background: Between 6-10% of adults with Visceral Leishmaniasis (VL) are co-infected with HIV in Bihar, India. There is minimal evidence on the co-occurrence of tuberculosis (TB) in these patients, and no evidence on how best to diagnose and manage this triad.
Methods: 150 confirmed VL-HIV cases were enrolled in a randomized trial investigating VL treatment with AmBisome therapy vs. combination of AmBisome and Miltefosine. All patients were screened for TB through Chest X-ray, CB-NAAT and abdominal Ultra Sound. Patients were treated initially for VL, then commenced on anti-tubercular treatment (ATT) between day 7-14, followed by antiretroviral therapy 2 weeks after ATT.
Results: 21% of all patients (n=31; 27 pulmonary and 4 extrapulmonary) were found to be infected with TB, with one identified as DRTB. Five patients were on ATT at enrolment; while 21 were diagnosed in the first 29 days.
Total 8 cases develops immune reconstitution inflammatory syndrome (IRIS) associated TB; 5 were unmasking TB. Symptoms predictive of IRIS were refractory pyrexia more than 10 days after VL treatment initiation and enlarged abdominal necrotic lymph nodes on ultrasound. IRIS incidence reduced with increasing the

gap between ATT and ART initiation from two to three weeks, and improved early diagnosis. Case-fatality rate of TB-VL-HIV patients was 16.1% , compared to 0.8% in VL-HIV patients (p< 0.01).
Mean change (95% CI) in CD4 cells/μl from initiation of VL treatment to day 29 was +114 (91,137) and +101 (82,120) in those already on ART (n=68) and those starting on day 14 (n=71) post initiation of VL treatment respectively.
Conclusions: VL-HIV patients should all be screened for TB using CB-NAAT. The results suggest that VL treatment results in IRIS that may require delayed initiation of ART, while severe IRIS associated TB remains a major risk in this cohort of patients.

PS-28-802-02 Paradoxical tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS) in HIV with culture positive rifampicin-sensitive pulmonary TB: risk factors and influence on TB outcome

G Narendran,[1] N Palaniappan,[1] P Chandrashekaran,[1] VA Srinivasalu,[1] T Senguttuvan,[1] M Ayyamperumal,[2] S Lakshmanan,[1] S Swaminathan,[3] BDB Andrade,[4,5] SP Tripathy,[1] [1]ICMR-National Institute for Research in Tuberculosis, Clinical Research, Chennai, India, [2]Madras Medical College, Institute of Thoracic Medicine, Chennai, India, [3]World Health Organization, Research, Geneva, Switzerland, [4]Instituto Goncalo Moniz, Fundacao Oswaldo Cruz, Salvador, RJ, Brazil, [5]Vanderbilt University Medical Center, Medicine, Nashville, TN, United States of America. e-mail: gopalannaren@yahoo.co.in

Background: Paradoxical Tuberculous Immune Reconstitution Inflammatory Syndrome (TB-IRIS) due to dysregulated immunity, frequently complicates concomitant therapy with anti-tuberculosis treatment (ATT) and early anti-retroviral therapy (ART) initiation. This unique report of culture-confirmed rifampicin-sensitive pulmonary TB coupled with confirmed TB-IRIS cases makes evaluation of risk factors for IRIS occurrence and its subsequent influence on TB treatment outcome reliable and valid.
Methods: 292 newly diagnosed pulmonary TB patients with HIV, started on INH, rifampicin, Ethambutol and Pyrazinamide, in a randomised clinical trial (NCT00933790), along with EFZ based ART initiated as per prevailing guidelines, after due consenting and ethics committee approval. Treatment was fully supervised. An independent panel diagnosed TB-IRIS, using standard criteria supplemented with a 0.5 log reduction in viral load and culture being negative for mycobacterium tuberculosis at IRIS event. Risk factors for TB-IRIS occurrence and subsequent sputum culture conversion, TB treatment outcomes (failure and deaths) were studied. Logistic regression analysis for baseline risk factors for TB-IRIS occurrence included TB regimen, CD4 count, Viral load, opportunistic infection, Haemoglobin, extra-pulmonary focus, X-ray lesions >3 zones, sputum culture grade >2 and ATT-ART interval ; level of significance taken as p< 0.05.
Results: 28% (82/292) of patients experienced TB-IRIS, (pulmonary -26 and extra-pulmonary in 56). Table 1. provides the baseline demographic details, improvement over time and TB outcome at 6 months. In multivariate analysis, the significant risk factors for TB-IRIS occurrence were baseline CD4 cell count (0.016), extra-pulmonary focus (0.0000), opportunistic infection (0.004) and ATT-ART interval (0.04). P values for other risk factors were viral load (0.065), culture grade >2+ (0.5), HB (0.36) regimen (0.7), X-ray lesions > 3 zones (0.16).
Conclusions: Baseline CD4 cell count, extra-pulmonary focus, opportunistic infection and ART-ATT interval determined IRIS occurrence. TB-IRIS had no influence on sputum conversion or TB outcome.

Baseline Demographics			**Baseline Immunological Parameters**			**Trends at 2 months**		
Mean ± Standard deviation(SD) or percentage (%)	TB IRIS (82)	No IRIS (210)	Median{Inter Quartile Range(IQR)}or percentage(%)	TB IRIS (82)	No IRIS (210)		TB IRIS (82)	No IRIS (210)
Age in years	37.9 ± 8.2	39.2 ± 8.6	CD4 Cell Count (cells/mm3)	92 (45-175)	159 (90-287)	% Culture Negative for TB bacilli @ 2 months	93 (75 / 80)	92 (176 / 190)
Weight in Kg	24.4 ± 5.2	42.9 ± 7.8	ATT-ART interval (Days)	17 (2-45)	16 (9-33)	Mean increase in Haemoglobin ± SD	2.09 ± 0.2	1.73 ± 0.12
% Males	86 (71 / 82)	73 (154 / 210)	CD4 / CD8 ratio	0.17 (0.08-0.36)	0.24 (0.15-0.41)	Median reduction in log10 viral load @ 2 months (copies/ml) (IQR) (p < 0.001)	2.73 (2.0-3.2)	1.1 (0-2.5)
% Extra Pulmonary Focus	40 (33 / 82)	27 (57 / 210)	Mean log10 Viral Load ± SD	5.2 ± 1.0	4.7 ± 1.27	Median Increase in CD4 cells (IQR) (p < 0.01)	114 (16-189)	75 (8-159)
% Daily Regimen	32 (27 / 82)	33 (71 / 210)	Pre-treatment Bacteriological parameters			TB Outcome at 6 months		
% Chest X-Ray >3 zones	62 (51 / 82)	69 (146 / 210)	% Sputum smear grade AFB >2+	45 (37 / 82)	50 (107 / 210)	Failure	4	7
% Opportunistic Infection	24 (20 / 82)	12 (27 / 210)	% Sputum culture grade M.TB > 2+	42 (35 / 82)	67 (142 / 210)	Deaths	6	12

[PS-28-802-02 Table 1. Characteristics of patients experiencing Paradoxical TB-IRIS (n=82) and No IRIS (n=210)]

PS-28-803-02 High mortality among smear and Xpert-negative presumptive tuberculosis patients who are empirically treated

L Nakiyingi,[1,2] W Ssengooba,[3] D Nakanjako,[1,2] F Mubiru,[1] ML Joloba,[3] H Mayanja-Kizza,[2] YC Manabe,[4] [1]Infectious Diseases Institute, Research, Kampala, Uganda, [2]Makerere University, Medicine, Kampala, Uganda, [3]Makerere University, Medical Microbiology, Kampala, Uganda, [4]Johns Hopkins University, Medicine, Baltimore, MD, United States of America. e-mail: lydiakiyingi@gmail.com

Background: Incomplete sensitivity of Xpert MTB/RIF in HIV co-infected smear-negative presumptive TB patients has resulted in increased reliance on empiric decision-making in many TB-HIV high-burden countries in sub-Saharan Africa. We sought to describe the outcome of HIV-infected presumptive TB patients treated without bacteriological confirmation of TB in Uganda.
Methods: Prospective study among inpatients and outpatients at Mulago Hospital and Kisenyi Health-Centre-IV, Kampala, Uganda. We recruited HIV-positive sputum smear-negative and Xpert-negative presumptive TB adults. Data on empiric treatment decision, TB symptomatology and chest X-ray were collected. Laboratory results included CD4 counts, sputum MGIT culture, and lateral-flow urine TB-LAM. Monthly follow-up for 6-months post-enrolment for symptoms and vital status was performed.
Results: Of the 350 participants screened, 237 HIV co-infected presumptive TB adults with negative smear and Xpert were enrolled; 61%(144/237) were hospitalized, 57%(134/237) females, median age 38 years (IQR 29-46), median CD4 176 (IQR32-474)cells/mm^3, 83%(196/237) on antiretroviral therapy (ART). Compared to outpatients, inpatients had lower median CD4 (77 cells/μL,IQR15-294 vs.373, IQR 151-619, p< 0.001) and 23% (vs 9%) were ART-naive (p=0.004). MTB culture was positive in 6.3%(15/237); 47%(7/15) were also TB-LAM positive. 17(7.2%) were empirically treated for TB (94% inpatients). Of the 220 diagnosed as 'no TB', (67.6%) were empirically treated for bacterial pneumonia. Among participants with complete 6-month follow-up, overall mortality was 23%(44/191), with 35.2%(37/105) of inpatients compared to 8.1%(7/86) of outpatients (Log-rank test, p< 0.001). Nearly 90% (39/44) of deaths occurred within first 3-months post-enrolment. Mortality was higher among participants empirically treated for TB (42%) compared to not treated (21%) (Log-rank test, p< 0.041).
Conclusions: In this high prevalence TB/HIV setting, we found significantly higher mortality (majority within 3-months) among smear- and Xpert-negative, HIV co-infected presumptive TB patients treated empirically. We recommend development of guidelines that include laboratory tests to identify alternative etiology of patients' symptoms to reduce mortality in this patient population.

PS-28-804-02 Addressing TB and HIV comorbidity in humanitarian emergencies: Bangladesh experience

F Khatun,[1] MA Islam,[1] M Siddiqui,[1] S Reza,[1] S Islam,[1] [1]BRAC, Communicable Disease, Dhaka, Bangladesh. e-mail: fatema.kh@brac.net

Background and challenges to implementation: Access to health care is more important than ever in humanitarian emergencies such as refugee crisis. There was an influx of Myanmar nationals in Cox's Bazar district of Bangladesh from September, 2017. As a part of emergency response to Forcibly Displaced Myanmar Nationals (FDMN), BRAC with the support of NTP started TB control services among FDMN population.
Intervention or response: Total population of FDMN is 9, 21,000 residing in 34 camps. BRAC established 15 laboratories covering camp areas for TB and HIV integrated services which include quality microscopy and HIV screening among TB patients. Field workers mobilized community for TB presumptive, identify TB presumptives and refer them to the nearby laboratories for microscopy. Smear positive cases are registered at government facilities and the patients are sent back to the community where DOT is ensured by community health workers for treatment adherence. Smear negative cases are referred for higher facilities for other investigations with the permission of camp authority. HIV screening is also done for all TB patients and other high risk group. If anybody found positive are referred to government certre for confirmation followed by registration and antiretroviral therapy.
Results and lessons learnt: From September, 2017 to March, 2019, total 3,913 TB patients are diagnosed among FDMN. Among them, 3636 were bacteriologically confirmed, 124 clinically diagnosed, 75 extra pulmonary, 78 relapses and 5 DR TB. A total of 3,670 TB patients and 345 high risk group are screened for HIV of which 16 found positive among TB patients and 4 among high risk group. Treatment success rate of bacteriologically confirmed cases were 96% in 4th quarter 2017.
Conclusions and key recommendations: As TB is the world's leading killer among infectious disease, quality controlled TB diagnosis and free treatment services should provide in emergency situation. Integrated TB and HIV programme is essential in such humanitarian crisis areas.

PS-28-805-02 Incidence of rates of tuberculosis among HIV infected patients in Northern Tanzania

E Mollel,[1] W Maokola,[2] J Todd,[3] S Msuya,[4] M Mahande,[4] [1]Kilimanjaro Christian Medical University College, Public Health, Kilimanjaro, Tanzania, United Rep., [2]National AIDS Control Organisation Program, Public Health, Dar es Salaam, Tanzania, United Rep., [3]London School of Hygiene & Tropical Medicine, Department of Population Health, London, Tanzania, United Rep., [4]Kilimanjaro Christian Medical University College, Department of Community Health, Kilimanjaro, Tanzania, United Rep.. e-mail: edsonmollel@hotmail.com

Background: HIV and tuberculosis (TB) are leading infectious diseases, with a high risk of co-infection. The risk of TB in people living with HIV (PLHIV) is high soon after sero-conversion and continues to increase with depletion of CD4 count but decreases after starting antiretroviral therapy (ART).
Methods: We used routinely collected data from Care and Treatment Clinics (CTC) in three regions in northern Tanzania. Poisson regression with frailty models were used to determine incidence rate ratios (IRR) and 95% confidence intervals (95%CI) for predictors of TB incidences among HIV positive patients.
Results: Among 78,748 PLHIV 405 of patients developed TB over 195,296 person-years of follow-up, giving an overall TB incidence rate of 2.08 per 1000 person-years. There was an increased risk of TB incidence, 3.35 per 1000 person-years, in hospitals compared to lower level health facilities. Compared to CD4 counts of less than 350 cells/ul, higher CD4 count was associated with lower TB incidence, 81% lower for CD4 count of 350-500 cells/ul (IRR 0.19, 95%CI 0.04-0.08) and 85% lower for those with CD4 count above 500 cells/ul (IRR 0.15,95%CI 0.04-0.64). Independently, those taking ART had 66% lower TB incidences (IRR 0.34,95% CI0.15-0.79) compared to those not taking ART. Poor nutritional status and CTC enrollment between 2008 and 2012 were associated with higher TB incidences (IRR 9.27, 95% CI 2.15-39.95) and (IRR 2.97, 95% CI 1.05-8.43) respectively.
Conclusions: Among HIV positive patients attending CTC, poor nutritional status, low CD4 counts and not taking ART treatment were associated with higher TB incidence, highlighting the need to get PLHIV on treatment early, and the need for close monitoring of CD4 counts. Data from routinely collected and available health services can be used to provide evidence of epidemiological risk of TB.

PS-28-806-02 Viral load testing coverage and suppression among HIV and TB-HIV patients in Mozambique

I Munyangaju,[1] S Mikusova,[1] T Simone,[2] A Cassamo,[3] A Nhabanga,[3] B Maculuve,[4] E Filipe,[5] L Greenberg,[6] P Kerndt,[7] N Bhatt,[8] [1]Elizabeth Glaser Pediatric AIDS Foundation, Technical, Maputo, Mozambique, [2]Centers for Disease Control and Prevention, Epidemiology, Maputo, Mozambique, [3]Elizabeth Glaser Pediatric AIDS Foundation, Strategic Information, Maputo, Mozambique, [4]Direcção Provincial de Saúde de Gaza, Núcleo Provincial de Pesquisa, Gaza, Mozambique, [5]Ministry of Health, HIV National Program, Maputo, Mozambique, [6]Elizabeth Glaser Pediatric AIDS Foundation, Research, Washington, DC, WA, United States of America, [7]Centers for Disease Control and Prevention, Center for Global Health (CGH), Division of Global HIV and Tuberculosis (DGHT), Maputo, Mozambique, [8]Elizabeth Glaser Pediatric AIDS Foundation, Research, Maputo, Mozambique.
e-mail: imunyangaju@pedaids.org

Background: HIV/TB coinfection is common in Gaza province, Mozambique, where 24.4% of adults are HIV-positive and 58.0% of ART patients have TB. Active TB in HIV patients is associated with high VL. We evaluated changes in VL testing coverage and viral suppression among ART patients with and without TB co-infection.
Methods: Routine HIV/TB program data from 91 health facilities (Gaza) from an electronic patient tracking system (OpenMRS) were collected and assessed to monitor trends over time and compare VL coverage (≥ one VL test/year) and suppression (< 1.000 copies/mL) between HIV mono-infected and HIV/TB co-infected patients on ≥ 6 months ART.
Results: Numbers of patients on ART increased 24% from 88.270 in January 2015 to 109.625 in December 2018. VL coverage increased from 1% to 47% in the same period, with no difference between HIV mono-infected patients and HIV/TB co-infected patients or between age groups (< 15 or ≥15 years old). Overall VL suppression decreased in the period 2015-2018, from 86.3% [95% CI (80.4%-92%)] to 78.2% [95% (76.5%-79.9%)] ($p < 0.01$). A difference in VL suppression between HIV mono-infected and HIV/TB co-infected patients was noted from 2015 to 2018 (Table 1). In 2018 the VL suppression for HIV/TB co-infected patients was 55.3% [95% CI (39.5% - 61.9%)] vs 78.1% [95% CI (75.5% - 80.7%)] for HIV mono-infected patients ($p < 0.001$). In the same year, VL suppression was markedly lower in children < 15 years at 50.9% [95% CI (44.1% - 52.9%)] compared to adults at 80.5% [95% CI (78.5% - 82.5%)] regardless of co-infection status.
Conclusions: Despite major improvements in VL coverage from 2015 to 2018, nearly half of ART patients in Gaza do not have access to VL monitoring, hindering the achievement of 90% viral suppression. VL coverage and suppression in high-risk groups (co-infected patients and youth populations) needs better prioritization.

Year	HIV <15 years	HIV >15 years	HIV/TB <15 years	HIV/TB >15 years
2015	48 (88%)	463 (88%)	4 (100%)	7 (88%)
2016	124 (68%)	1.434 (83%)	3 (60%)	16 (43%)
2017	802 (55%)	13.640 (80%)	11 (31%)	114 (56%)
2018	1.910 (51%)	34.655 (80%)	15 (29%)	187 (60%)

[Number and percent of HIV mono-infected and HIV/TB co-infected patients with suppressed VL (<1.000 cps./mL) by age group in Gaza Province, Mozambique≥]

PS-28-807-02 Sustaining a national tuberculosis preventive treatment (TPT) scale-up among the PLHIV population through targeted technical assistance to high volume ART treatment sites in Nigeria, 2018

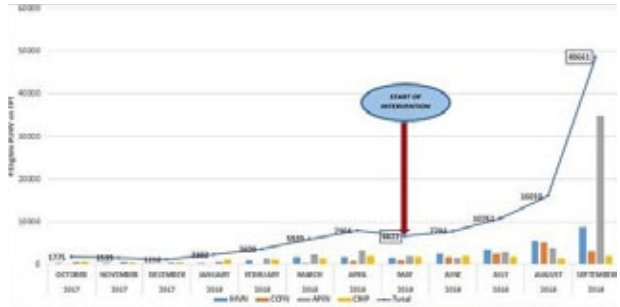
B Odume,[1] A Boyd,[2] K Sidibe,[2] O Ogbanufe,[1] S Odafe,[1] D Onotu,[1] [1]Centers for Disease Control and Prevention, Division of Global HIV/AIDS and TB, Abuja, Nigeria, [2]Centers for Disease Control and Prevention, Division of Global HIV/AIDS and TB, Atlanta, GA, United States of America. e-mail: bodume@cdc.gov

Background and challenges to implementation: Nigeria includes 6-Months 300 mg isoniazid for TPT as a standard of care in its HIV guidelines but implementation and scale-up has been slow. In May 2018, CDC Nigeria initiated a targeted approach to TPT scale-up across selected supported high-volume ART sites. The strategy involved direct staff and implementing partner engagement to identify key limitations to TPT implementation and devise interventions to improve uptake among people living with HIV (PLHIV).

Intervention or response: We targeted 50 CDC-supported ART sites serving the largest numbers of PLHIV to scale up TPT. This represent 4% of all CDC-supported sites nationally but 46% of all PLHIV in care and treatment. We assessed "readiness for scale-up of TPT" at the selected sites and among partners through the use of a standardized tool across five key intervention areas: clinical training/competency, community/patient education, patient management, commodities and logistics, and recording and reporting for TPT. Where gaps were noted, we provided assistance to address them through a quality improvement approach. Implementing partners learned lessons from this approach and applied these lessons to other CDC-supported sites.

Results and lessons learnt: The use of the TPT readiness assessment tool across the 50 sites found that staff showed no resistance to TPT implementation. Some sites experienced recurrent stock outs of isoniazid, and needed support in site-level isoniazid forecasting. Instituting an ongoing continuous quality improvement approach in TPT implementation ensured that gaps were addressed by providers at the sites. Ultimately, the intervention led to the number of PLHIV initiating TPT increasing from 6,622 in May to 48,661 in September 2018, a 635% increase within four months (Fig 1).

Conclusions and key recommendations: Targeting technical assistance within the highest-volume ART sites led to a significant improvement in TPT uptake among PLHIV nationally. This approach is recommended to drive TPT implementation scale-up while ensuring that provisions are adequately made for drug procurement and logistic support.



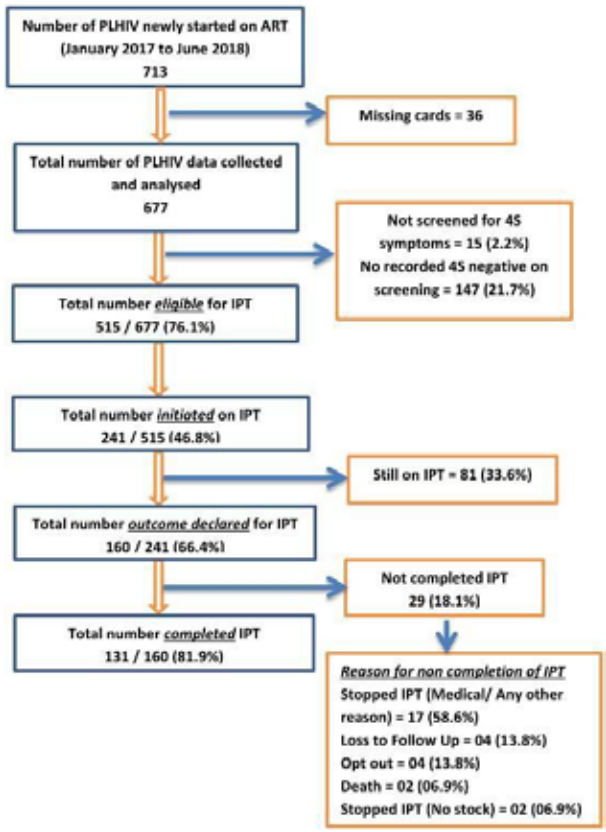
[Fig 1: Trend in TPT uptake in fiscal year 2018 (Oct 2017 to Sept 2018) CDC Nigeria]

PS-28-808-02 Initiation and completion of isoniazid preventive therapy in people living with HIV (PLHIV): a mixed methods study from Kolar district of Karnataka, India

MM Reddy,[1] P Thekkur,[2,3] N Ramya,[1] S Shastri,[4] R Kumar,[5] P Chinnakali,[6] A Nirgude,[7,8] C Rangaraju,[9] N Somashekar,[10] AMV Kumar,[2,3] [1]Sri Devaraj Urs Medical College, Community Medicine, Kolar, India, [2]International Union Against Tuberculosis and Lung Disease (The Union), Centre for Operational Research, Paris, France, [3]The Union South East Asia Office (USEA), Centre for Operational Research, New Delhi, India, [4]Lady Willingdon State Tuberculosis Centre, Department of Health & Family Welfare Services, Bengaluru, India, [5]Karnataka State AIDS Prevention Society (KSAPS), Department of Health & Family Welfare Services, Bengaluru, India, [6]Jawaharlal Institute of Postgraduate Medical Education and Research, Preventive and Social Medicine, Puducherry, India, [7]Yenepoya Medical College, Community Medicine, Mangaluru, India, [8]Yenepoya (Deemed to be University), Centre for Health Professional Education, Mangaluru, India, [9]National Tuberculosis Institute, Epidemiology & Research Division, Bengaluru, India, [10]National Tuberculosis Institute, Office of the Director, Bengaluru, India. e-mail: mahendrabmc@gmail.com

Background: Isoniazid preventive therapy (IPT) is known to reduce the risk of TB among people living with HIV (PLHIV). In India, though the national TB and HIV programmes implemented IPT for PLHIV since 2015, there has been no published literature on extent of IPT implementation and its challenges. In this study, we aim to assess the extent of IPT implementation in Kolar, a district in South India (1.5 million people) and understand the implementation challenges.

Methods: This was an explanatory mixed-methods study with quantitative (cohort study using data routinely collected by national HIV programme) and qualitative (descriptive study) components. All PLHIV newly registered during January 2017 to June 2018 in antiretroviral therapy (ART) centre of Kolar district were included. The demographic, clinical and IPT details of patients were extracted from the 'treatment cards'. Proportion eligible for IPT, IPT initiation and completion rates were summarized as percentages with 95% confidence interval (CI). For qualitative component, the in-depth interviews were conducted among purposively selected patients and healthcare providers.
Results: Of the 713 PLHIV registered, data was available for 677 (95%) patients. The mean (SD) age of participants was 38.9 (12.8) years and 348 (51%) were males. Among 677 patients, 515 (76.1%, 95%CI: 72.8-79.2) were found to be eligible to start IPT. Among 515 eligible, 241 (46.8%, 95%CI: 42.5-51.1) were initiated on IPT. Among 160 PLHIV in whom IPT outcomes were ascertained, 131 (81.9%, 95%CI: 75.3-87.3) had completed IPT (**figure 1**). Issues with supply of IPT, recurrent stock out and adverse effects with IPT were reported as challenges for effective IPT implementation.
Conclusions: IPT implementation was suboptimal with less than half of the eligible PLHIV initiated on IPT. Though, more than three fourths of those started on IPT, completed the regimen. The operational challenges need to be addressed soon for effective implementation.

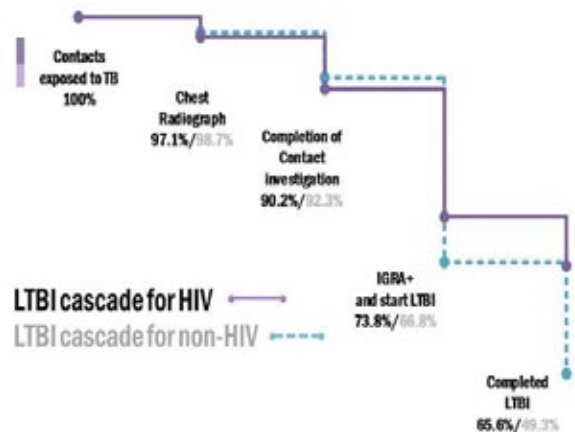


[Figure 1: Flow diagram depicting eligibility, initiation and completion of IPT among PLHIV in Kolar]

PS-28-809-02 The diagnosis and treatment cascade of latent tuberculosis infection among HIV co-infected tuberculosis contacts

P-C Chan,[1,2,3] T-Y Feng,[1] YC Huang,[1] S-B Wu,[1] Y-F Huang,[1] [1]Centers for Disease Control, Division of Chronic Infectious Diseases, Taipei, Taiwan, [2]College of Public Health, Taiwan University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan, [3]National Taiwan University Hospital, National Taiwan University, College of Medicine, Department of Pediatrics, Taipei, Taiwan.
e-mail: pcanita.tw@cdc.gov.tw

Background: Global coverage of latent tuberculosis infection (LTBI) treatment for people living with HIV (PLHIV) has failed to meet WHO expectations. To understand whether HIV infection affects LTBI treatment for Taiwanese TB contacts, we conducted an LTBI cascade analysis stratified by whether contacts were PLHIV or not.
Methods: In April 2016, "the LTBI Treatment for All Contacts Program" was started. A list of 54173 highly infectious index TB patients' contacts aged 5 years and older, from April 2016 to June 2017, including completion rates, diagnostic test results, chest radiographs, and data on the uptake and completion of LTBI treatment (for LTBI positive patients) were linked to the National HIV notification database.
Results: 104 PLHIV comprised of 0.19% of TB contacts. Male and sexually active age HIV co-infected contacts outnumbered were non-HIV co-infected contacts (sex ratio= 12:1 vs. 1:1, p value <0.001 of Chi Square test; age group 15-49= 86% vs. 57%, p value <0.001). For LTBI contacts, rates of treatment commencement and completion were 81.8%, 88% among PLHIV, respectively; rates of 72.4%, 73.8% were observed among non-HIV contacts (p value= 0.480, 0.306) respectively. The LTBI cascade among contacts (Fig) shows similar uptake rates for tests and for both commencement and completion of LTBI treatment for both groups.



[LTBI cascade for HIV and for non-HIV TB contacts]

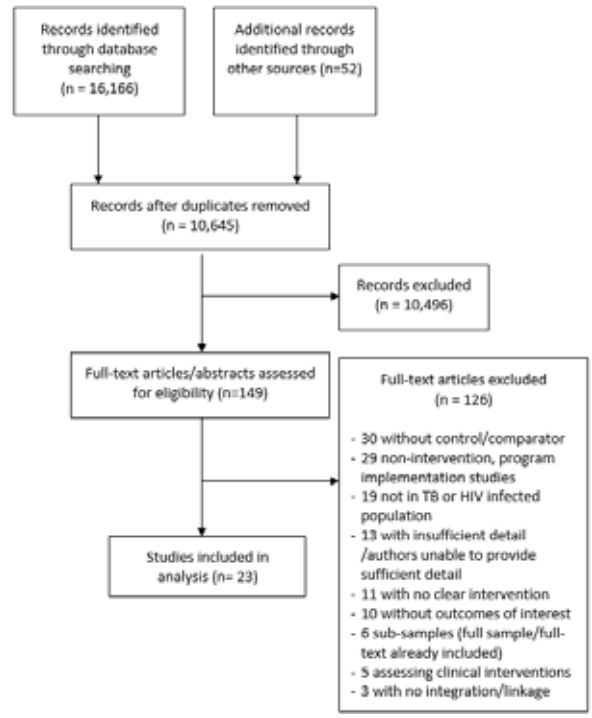
Controlling for age (>=40 year-old and <40 year-old), no significant difference of uptake or completion of LTBI treatment was observed (p=0.120, 0.396 for cochran

mantel haenszel test). Among the 9 PLHIV commencing LTBI treatment, 55% received anti-viral therapy at the time of contact investigation.
Conclusions: Both the overall contact investigation completion rate and LTBI treatment among PLHIV were good, though LTBI treatment gap needs to be improved. HIV infection did not negatively impact on LTBI treatment for contacts.

PS-28-810-02 Interventions to improve linkage gaps along the TB-HIV care cascades in low- and middle-income countries: a systematic review

A Salomon,[1] S Law,[2] A Daftary,[1,3] S Singh,[4] [1]McGill University, McGill International Tuberculosis Centre, Montreal, QC, Canada, [2]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America, [3]Centre for the AIDS Programme of Research in South Africa, CAPRISA, Durban, South Africa, [4]World Health Organization, HIV Department, Geneva, Switzerland.
e-mail: angela.salomon94@gmail.com

Background: We conducted a systematic review of interventions addressing linkage gaps in the TB-HIV care cascades of LMICs, which targeted HIV diagnosis and treatment initiation among people with TB disease (PWTB), and TB diagnosis and treatment initiation among people living with HIV (PLHIV).
Methods: We searched Embase and MEDLINE for original studies (published January 2003 to February 2019) comparing the effect of non-biomedical interventions to local standard of care on: TB case detection among PLHIV; HIV testing among PWTB; and/or ART/TB treatment initiation among co-infected patients. We excluded program evaluations and studies without comparator arms. We performed subgroup analyses by intervention type and pooled effect estimates using the DerSimonian and Laird random-effects method.
Results: We included 23 of 10,645 intervention studies identified through our search that targeted: TB case detection (21.7%); TB treatment initiation (13.0%); HIV testing (47.8%); and ART initiation (78.2%). Interventions were diverse and multi-faceted, with high statistical heterogeneity in subgroup analyses (I^2 ranging 51.4% to 98.1%). Enhanced patient education and support had the broadest impact and improved three of four outcomes: TB case detection [pooled RR 1.6 (95%CI 1.5-1.7, n=2)]; HIV testing [pooled RR 2.5 (95%CI 1.6-3.3), n=3]; and ART initiation among co-infected individuals [pooled RR 1.1 (95%CI 1.07-1.14), n=2]. Integration of TB/HIV services coupled with provider-initiated treatment and counselling (PITC) also increased HIV testing among PWTB [RR 3.48 (95%CI 3.1-3.9)] and ART initiation among co-infected individuals [RR 1.3 (95%CI 1.0-1.5)]. There was limited evidence to support interventions for improving TB treatment initiation among co-infected individuals.
Conclusions: Program-level efforts (service co-location) and patient-level efforts (education and counselling) have a positive impact on the TB-HIV linkages to care. Our review identified potentially effective interventions linking PWTB to HIV testing and ART initiation, but more evidence is needed for interventions to link PLHIV to TB testing and treatment.



[PRISMA Flow Diagram]

PS-28-811-02 Integrating tuberculosis screening services in differentiated care models for HIV to increase detection of TB-HIV coinfection

D Kamerhe,[1] R Mwamba,[1] C Banzakadilo,[1] V Cikobe,[1] I Thior,[2] D Canagasabey,[2] J-C Kiluba,[1] [1]PATH, DRC Country Program, Lubumbashi, Congo (Democratic Rep.), [2]PATH, HIV/TB Programs, Washington, DC, United States of America. e-mail: cbanzakadilo@path.org

Background and challenges to implementation: DRC ranks third among African countries with the highest tuberculosis (TB) burden, with low TB detection (48%). 85% of people living with HIV (PLHIV) are screened for TB, potentially resulting in missed cases of TB/HIV coinfection.
Intervention or response: The USAID-funded Integrated HIV/AIDS Project in Haut Katanga and Lualaba (IHAP-HK/L) introduced three differentiated care models (DCM): antiretroviral treatment (ART) support groups, fast-track circuits at facilities, and community-based points of ART distribution (PoDi+). To increase TB detection among PLHIV, TB screening and preventive therapy were integrated into the standard service package in DCMs.

IHAP-HK/L developed a TB screening tool for use in DCMs and trained peer educators to screen PLHIV for TB at every ART pick-up appointment. PLHIV who screened positive were referred to a facility for TB diagnosis and treatment initiation. PLHIV who screened negative were initiated on isoniazid at the facility and received monthly refills in DCMs.

We used descriptive and inferential statistics to analyze programmatic data from Haut Katanga to evaluate the effect of TB screening integration in DCMs on TB case detection.

Results and lessons learnt: IHAP-HK/L referred 2,388 PLHIV to a DCM by September 2018. The table summarizes TB screening and diagnosis rates by treatment model. High TB screening rates were observed across all DCMs, with the highest proportion at PoDi+ sites. TB screening was more likely to be offered in DCMs than the traditional care model (OR = 3.5 [95% CI: 2.76 - 4.63]). Cumulative TB incidence within our cohort was 0.4%, with no statistically significant difference in cumulative TB incidence among DCMs (0.6%) or between DCMs and the traditional care model (0.7%).

Conclusions and key recommendations: IHAP-HK/L successfully integrated TB screening into DCMs, leading to earlier detection of PLHIV with TB. These results underscore the necessity for continuous adaptation of service models based on patient needs to achieve global targets to end the dual epidemic.

Treatment model type	Number of PLHIV enrolled in treatment (as of September 2018	Number of PLHIV screened for TB (%)	Number of PLHIV with presumptive TB (%)	Number of PLHIV with active TB (%) [95% CI]
Health facility (traditional care model)	20,138	18,291 (90.8%)	184 (1.0%)	142 (0.7%) [0.6% - 0.9%]
PoDi+	1,408	1,402 (99.6%)	10 (0.7%)	3 (0.2%) [0.04% -0.6%]
ART support group	359	349 (97.2%)	80 (22.9%)	3 (0.9%) [0.1% -2.5%]
Fast track circuit	621	571 (91.9%)	114 (19.9%)	8 (1.0%) [0.6% - 2.7%]

[TB screening and diagnosis rates by treatment model, Haut Katanga]

PS-29-A3 TB diagnostics beyond GeneXpert

PS-29-812-02 Analysis of time to positivity by MGIT System to predict culture-negatives for Mycobacterium tuberculosis complex: a consideration for issuing preliminary reports guiding patient management

U Gaikwad,[1] V Kumar,[1] P Das,[1] A Wankhade,[1] A Bhargava,[1] S Negi,[1] [1]All India Institute of Medical Sciences, Microbiology, Raipur, India.
e-mail: ujugaikwad@gmail.com

Background: Despite molecular techniques have accelerated Tuberculosis diagnostics, culture remains the gold standard. The rapid and automated broth based culture systems recommend six weeks of incubation to declare the negative result. While, recommendations can't be altered but the reporting practices of the individual laboratory can be modified. It is hypothesized that, preliminary findings on culture-negativity can be reliably issued earlier than the recommended time frame and final report at the end of standard incubation, to expedite informed decision making by the treating physician.

Methods: A cross sectional study to analyze the retrospective data on time to positivity (TTP) of samples processed (n=3676) by Mycobacterial growth Indicator Tube (MGIT) system was conducted. The time to detection for all Mycobacterial species as well as Mycobacterium tuberculosis complex (MTBC) was analyzed with respect to site of disease, smear status as well as new or treated cases.

Results: Median TTP for all mycobacterial species and MTBC was 14.2 (IQR= 9-24.5) and 12 (IQR = 7-18) days respectively. The median TTP was significantly less ($p>0.05$) for smear positive (5 days; IQR= 7-16) than smear negative MTBC isolates (20.5 days; IQR= 12.9-29). Pulmonary samples had less TTP (10.5 days; IQR=7-18) compared to extrapulmonary samples (21 days; IQR= 13-31). The overall recovery rate was 100%, 96%, 82%, 71% and 48% from sixth to second week of incubation respectively.

Conclusions: Based upon the results it can be predicted that, preliminary reports of culture-negativity for pulmonary samples can be issued at the earliest of 3 weeks for smear positives while at the end of 4th week in case of smear negatives with 100% probability. Exclusion of TB in a suspect case has major implications in terms of appropriate management of patients and rational utilization of public health resources.

PS-29-813-02 Comparison of direct vs. indirect assays to diagnose isoniazid and rifampicin-resistant tuberculosis

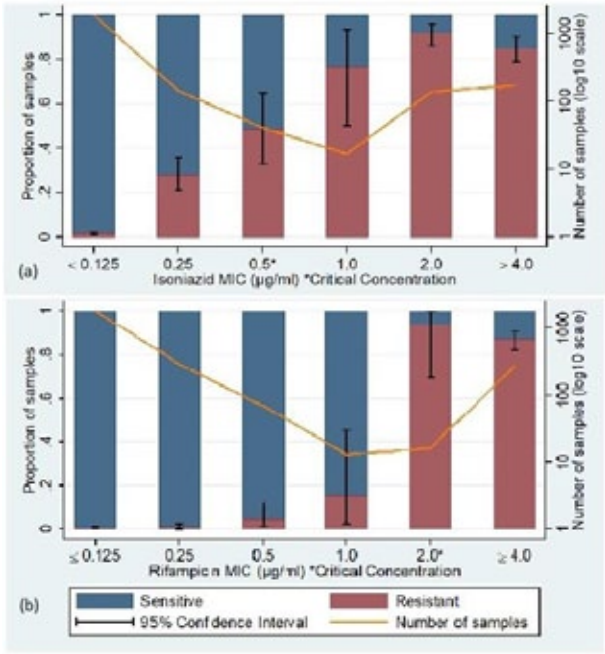
JP Wilson,[1,2] T Valencia,[1,2] R Montoya,[1,2] ES Ramos,[1,2] K Alvarado,[1,2] L Bernaola,[1,2] N Bailon,[1,2] B Herrera,[1,2] S Datta,[1,2,3] CA Evans,[1,2,3] [1]IFHAD - Innovation for Health and Development, Universidad Peruana Cayetano Heredia LID 416, Laboratory for Health and Development, Lima, Peru, [2]IPSYD - Innovación por la Salud y Desarollo, Asociación Benéfica Prisma, Lima, Peru, [3]IFHAD - Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, London, United Kingdom. e-mail: jpwilson123@outlook.com

Background: Globally, only 1/3 of patients with tuberculosis are tested for rifampicin-resistance. Accessible and timely drug susceptibility testing (DST) is urgently needed. The 'MDR/XDR-TB Colour Test' is a non-commercial, thin-layer agar technique combining tuberculosis diagnosis with direct DST for rifampicin, isoniazid and fluoroquinolones. We present DST concordance between the Colour Test and an established, indirect liquid colorimetric assay: the Tetrazolium Microplate Assay (TEMA).

Methods: Sputum samples were collected from symptomatic patients between 2013 and 2018 in a low-income, Peruvian population. Samples were disinfected and directly inoculated onto Colour Test quadrants containing rifampicin (0.4 mg/L), isoniazid (1.0 mg/L), ciprofloxacin (2.0mg/L) and control. Plates were sealed and screened for growth twice-weekly by naked-eye inspection. Growth was confirmed with microscopic identification of typical colony cording. After 6 weeks, colonies from the detection quadrant were sub-cultured for TEMA DST. DST concordance was calculated for TEMA minimum inhibitory concentrations (MICs) > 1 dilution from the critical concentrations.

Results: Of 3,179 samples, interpretable DST readings were available in 78.6% and 81.7% Colour Tests for isoniazid and rifampicin-resistance respectively. Figure 1 shows the proportion of sensitive and resistant Colour Tests by TEMA MIC. Isoniazid: Figure 1(a), Rifampicin: Figure 1(b). Isoniazid and rifampicin-resistant Colour Tests were TEMA concordant for 91.5% (95% confidence interval (CI)=87.7-94.4%) and 96.7% (95% CI=93.5 - 98.5%) of samples, respectively. Isoniazid and rifampicin-sensitive Colour Tests were TEMA concordant for 98.1% (95% CI: 97.3 - 98.6%) and 98.4% (95% CI=97.7- 98.8%), respectively.

Conclusions: In by far the largest study to date reporting Colour Test DST, we demonstrate high concordance with established liquid culture DST. For isoniazid especially, the degree of Colour Test/TEMA concordance decreased across intermediate MICs. With simultaneous diagnosis and DST without need for subculture, and at USD 1$ material costs per plate, the Colour Test is well placed for resource-limited settings with frequent drug resistance.



[Figure 1: Colour Test DST outcomes by TEMA MIC for (a): isoniazid and (b): rifampicin]

PS-29-814-02 The addition of filter paper during the staining of sputum smears for tuberculosis microscopy is an unnecessary step

N Bailon,[1,2] ES Ramos,[1,2] K Alvarado,[1,2] L Bernaola,[1,2] JP Wilson,[1,2] S Talavera,[1,2] R Montoya,[1,2] T Valencia,[1,2] CA Evans,[1,2,3] S Datta,[1,2,3] [1]Universidad Peruana Cayetano Heredia LID 416, IFHAD - Innovation for Health and Development, Lima, Peru, [2]Asociación Benéfica Prisma, IPSYD - Innovacion por la Salud y el Desarollo, Lima, Peru, [3]Wellcome Trust Imperial College Centre for Global Health Research, Infectious Diseases & Immunity, London, United Kingdom. e-mail: nataly.bailon.g@upch.pe

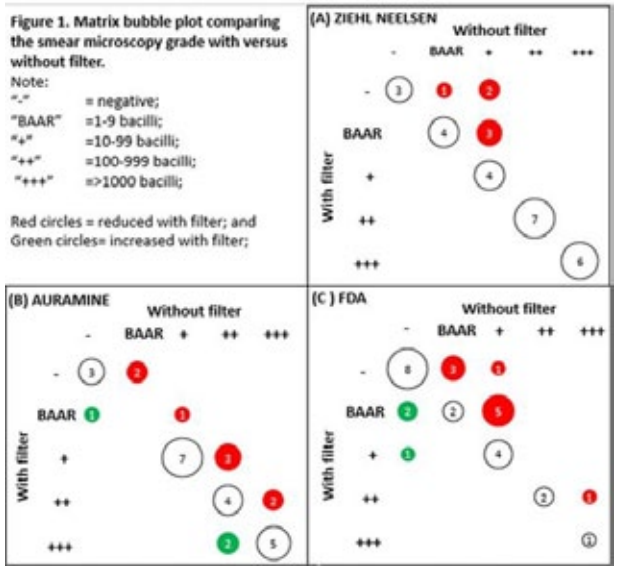
Background: In some tuberculosis (TB) laboratories, filter paper is rested upon sputum smears during staining, potentially to increase staining and reduce precipitates. We studied whether this affected results.

Methods: Sputum samples were collected from 30 patients with GeneXpert confirmed TB and 4 healthy controls. From each sample 6 smears were prepared for staining with Ziehl-Neelsen (ZN), auramine or the viability stain fluorescein diacetate (FDA), with or without filter paper. Whatman grade 3 filter paper was placed over dried smears prior to the application of stain, and removed when the stain was washed off. All slides were read with the Zeiss Primo Star iLED microscope at ×1000-magnification with oil immersion. The number of acid-fast bacilli (AFB)/100 fields was recorded.

Results: In patients' samples, 85% (n=51/60) were positive with ZN, 85% (n=51/60) with auramine, and fewer 62% (n=37/60) with FDA (p< 0.001). Compared with

ZN, smears stained with auramine visualized 1.7-times more AFB (p=0.05) and FDA 0.2-times i.e 80% less AFB (p< 0.001). Filter paper did not significantly affect the percentage of positive patient samples with ZN, auramine nor FDA (all p>0.08). Filter paper reduced the number of AFB seen with auramine an average of 0.60-times (95% confidence interval=0.30-0.80, p=0.03), ie by 40%. In adjusted regression analysis, filter paper tended to decrease the number of AFB visualized 0.66-times, i.e by 34% in all staining techniques (p=0.065, figure). In ZN, using filter paper led to a larger proportion of sputum smear washing away during staining (p=0.03). Addition of filter paper did not affect the number of precipitants visible (all p>0.2).

Conclusions: Auramine visualized more AFB than ZN, and FDA the least. We recommend not using filter paper during staining of sputum smears with ZN, auramine or FDA because it is an unnecessary step that does not improve, and tended to reduce the number of bacilli visualized.



[Figure 1. Matrix bubble plot comparing the smear microscopy grade with versus without filter]

PS-29-815-02 A comparative study of auramine staining using LED fluorescent microscopy with Ziehl-Neelsen staining in the diagnosis of tuberculosis

S Smaoui,[1,2] S Hachicha,[1,2] A Chakroun,[2] C Marouane,[1,2] S Kammoun,[1,2] A Ghorbel,[1,2] D Gamara,[3] L Slim,[2,4] F Messadi Akrout,[1,2] [1]Regional Laboratory of Hygiene Tertiary Health Care Hedi Chaker, Microbiology, Sfax, Tunisia, [2]Faculty of Pharmacy, University of Monastir, Microbiology, Monastir, Tunisia, [3]Direction Management of Basic Health Care, Management of Basic Health Care, Tunis, Tunisia, [4]Laboratory of Microbiology Abderrahmen Mami, Microbiology, Ariana, Tunisia. e-mail: ssalmahch@gmail.com

Background: In developping countries, the diagnosis of tuberculosis (TB) relies primarily on smear microscopy for Acid Fast Bacilli (AFB) but its sensitivity is limited in paucibacillary cases. The aim of our study was to study the efficacity of fluorescent Light Emmitting Diode (LED) microscopy in the diagnosis of TB in comparison to Ziehl Neelsen (ZN) staining.

Methods: This is a retrospective study performed at the regional laboratory of hygiene Sfax Tunisia over the period of 3 years (2013-2016). The study included all specimens stained by auramine and ZN staining. All specimens were also cultured on solid Lowenstein Jensen media and BACTEC MGIT 960 media. The results of the two microscopy methods were compared with the culture results taken as the gold standard.

Results: A total of 4583 specimens were included in our study. More than half (61.1%) were respiratory specimens. Out of 4583 smears, 6.6% and 4.8% were positive by auramine and ZN respectively. Using culture as the reference method, the sensitivity of direct staining was 49.5% (199/399) for auramine and 41.4% (165/399) for ZN. Fluorescent microscopy showed a significantly higher sensitivity (p< 0.005) both in pulmonary TB (< 0.0001) and lymph nodes TB (p=0.003). The specifities of auramine and ZN staining were comparable (97.7% versus 98.6 respectively). Fluorescent microscopy detected 76 paucibacillary samples and 13 multibacillary that were missed on ZN staining.

Conclusions: Compared to ZN staining Fluorescent microscopy showed higher sensitivity with keeping a similar specificity. With the advent of newer inexpensive Light Emitting Diode (LED) based fluorescent microscopes, the use fluorescent microscopy allows us a considerable gain in terms of reading time and sensibility and this at lower cost.

PS-29-816-02 Mutation associated with atpE and R0678 gene resistance among multidrug-resistant tuberculosis patients: a pilot study from a tertiary care centre in India

B Singh,[1] M Soneja,[1] R Sharma,[2] J Chaubey,[1] P Jorwal,[1] S Mase,[3] S Kumar,[4] S Chandra,[3] R Ramachandran,[3] N Wig,[1] [1]All India Institute of Medical Sciences (AIIMS), Medicine, New Delhi, India, [2]National Tuberculosis Institute, Microbiology, Bangalore, India, [3]World Health Organisation, Public Health, New Delhi, India, [4]Moti Nagar Chest Clinic, Public Health, New Delhi, India.
e-mail: binitkumar786@gmail.com

Background: The increasing burden of multi-drug resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) poses a significant challenge to TB control programs. After a long wait, bedaquiline (BDQ) a potent new drug has been approved by WHO for management of these patients. It inhibits the adenosine 5′-triphosphate (ATP) synthase encoded by *atpE* gene with reduction of bacterial ATP synthesis. Mutations in *atpE* gene or transcriptional repressor *Rv0678*, which is associated with up-regulation of efflux pumps may potentially lead to in-vitro resistance to BDQ.
Methods: In 2019, a total of 68 laboratory confirmed pre-XDR-TB [fluoroquinolone mono-resistant (n= 52) and second-line injectables mono-resistant (n=12)] and XDR-TB (n=4) culture specimens were selected. All specimens were evaluated for genetic analysis using predesigned primes of *atpE* and R0678 genes at the Intermediate Reference Laboratory situated in All India Institute of Medical Sciences, New Delhi. Phenotypic drug susceptibility testing (DST) was not performed.
Results: Among the pre-XDR-TB isolates (n=64), there were no mutations found in either *atpE* or RV0678. However, among the XDR-TB isolates (n=4) one specimen (25%) was found to be associated with a mutation in *atpE* gene at position 145 (CTG-145-CCA) resulting in the amino acid leucine replaced by proline (L49P). No mutation was observed with RV0678 gene.
Conclusions: In our study, genetic analysis showed that only 1/4 XDR-TB isolates had a mutation in the in *atpE* gene; there were no other mutations found in either the in *atpE* gene or the RV0678 gene in 75% of XDR-TB isolates and 100% of pre-XDR-TB isolates. The significance of a mutation in either of these gene loci needs to be further studied and correlated with phenotypic DST and clinical outcomes under programmatic setting.

PS-29-817-02 Clofazimine (CFZ) and bedaquiline (BDQ) MIC distribution in isolates from multidrug- resistant tuberculosis (MDR-TB) patients in Maputo, Mozambique

E Ardizzoni,[1] P Graulus,[1] P Rupasinghe,[1] M Bastard,[2] L Molfino,[3] C Mutaquiha,[4] P Zindoga,[4] I Mahinca,[4] A Telnov,[5] L Rigouts,[1] [1]Institute of Tropical Medicine, Biomedical Science, Antwerp, Belgium, [2]Epicentre - MSF Paris, Epicentre, Paris, France, [3]Medecins Sans Frontières, Maputo project, Maputo, Mozambique, [4]Ministry of Health, National TB Programme, Maputo, Mozambique, [5]MSF GENEVA, Medical Department, Geneva, Switzerland.
e-mail: eardizzoni@itg.be

Background: Due to limited drug susceptibility testing (DST) availability, patients are often started on BDQ and CFZ treatment without DST information. As CFZ-BDQ cross-resistance and baseline BDQ increased minimal inhibitory concentrations (MICs) have been reported, use of BDQ in patients previously exposed to CFZ, and starting of treatment without baseline DST are questioned. In this study we describe the relation between BDQ- and CFZ-MICs for MDR-TB patients in Maputo, Mozambique.
Methods: Patients were treated with standard or short MDR-treatment BDQ-free at baseline and including or not CFZ. In ITM samples were cultured then tested for MIC on 7H11 (0.008-2µg/ml for BDQ and 0.006-2µg/ml for CFZ; 0.25µg/ml and 1 mg/ml cut-off respectively).
Results: For 276 isolates retrieved, 185 MICs were defined for 169 baseline (alone or in pairs) and 15 follow-up isolates. At baseline, 94% (n=160) of isolates were CFZ-susceptible (MIC≤1): 14% having an MIC ≤0.25 (n=25), 44% an MIC=0.5µg/ml (n=74) (both groups with median BDQ-MIC=0.03µg/ml) and 36 an MIC=1µg/ml (n=61) (median BDQ-MIC=0.06µg/ml). All but two CFZ-susceptible isolates were BDQ-susceptible, with parallel MICs increase (see Table).

		BDQ MIC (µg/ml)							
		0.008	0.01	0.03	0.06	0.125	0.25	0.5	≥2
CFZ MIC (µg/ml)	0.06 (n=1)		1						
	0.125 (n=6)	1	2	2	1				
	0.25 (n=18)		3	11	4				
	0.5 (n=74)		12	27	28	5	1	1	
	1 (n=61)		2	20	27	12			
	2 (n=9)			2	2		4	1	

[BDQ and CFZ-MICs distribution for baseline isolates]

The two CFZ-susceptible/BDQ-resistant isolates had a CFZ-MIC of 0.5 µg/ml. Among the 9 CFZ-resistant isolates (MIC=2µg/ml), 5 had a BDQ-MIC at 0.25µg/ml cut-off (BDQ-susceptible) while one was resistant (MIC=0.5 µg/ml) with an overall BDQ-MIC range of 0.03-0.5µg/ml.

Of 6 paired isolates from patients treated with CFZ and without BDQ none showed acquired increase of CFZ- or BDQ-MIC above 1-fold dilution.
Conclusions: Overall there was a trend of MIC-BDQ increase when CFZ-MIC augmented in all isolates. At baseline 7.2% of the isolates were CFZ-resistant and 4.3% showed BDQ-MIC at the cut-off or above. Though a clinical relevance of it is yet to establish, these results suggest that baseline resistance for these drugs is low but not neglectable and that CFZ may not be a protecting drug for BDQ.

PS-29-818-02 Identification of the prevalence of isoniazid resistance without concurrent rifampicin resistance in Myanmar using whole-genome sequencing (WGS)

WW Nyunt,[1] GM Cook,[2] HL Aung,[2] ST Aung,[3] [1]National TB Programme, National TB Reference Laboratory, Department of Public Health, Yangon, Myanmar, [2]University of Otago, Department of Microbiology and Immunology, Dunedin, New Zealand, [3]Disease Control Division, Department of Public Health, Naypyitaw, Myanmar. e-mail: wintwintnyunt@gmail.com

Background and challenges to implementation: Acquired drug resistance has negative consequences for public health through the spread of drug-resistant TB, poorer health outcomes for patients, and cost to the healthcare system. In 2016, a patient with previous history of TB treatment in Myanmar diagnosed with Rifampicin-susceptible by Xpert. The patient then received a treatment regimen containing first-line drugs, but failed to achieve smear conversion at the 3-month follow up. WGS and phenotypic drug susceptibility testing (DST) were used to show that the isolate was resistant to isoniazid at the baseline and rifampicin resistance was acquired during therapy. This warrants further studies to identify the prevalence isoniazid resistance without concurrent rifampicin resistance in Myanmar.
Intervention or response: In this study, 170 MTB+ve sputum samples were recruited but rifampicin susceptible by GeneXpert (i.e. MTB+ve, RR -ve) from three government TB clinics in Yangon between January 2017 and January 2018. Sputum specimens were decontaminated and were then inoculated onto Löwenstein-Jensen medium for culturing and phenotypic DST of first- and second-line drugs. DNA was extracted from *Mycobacterium tuberculosis* cultures and subjected to WGS on an illumina MiSeq plaform.
Results and lessons learnt: Of 170, 77 were drug-naïve (new cases) and 93 were relapse/retreatment cases. Of 77 drug-naïve patients, 3 (3.9%) with isoniazid resistance, 3 (3.9) with isoniazid and streptomycin resistance. Of 93 retreatment cases, 12 (13%) with isoniazid resistance and 5 (5.4%) with isoniazid and streptomycin resistance. Isoniazid resistance was caused by the S315T mutation in the *katG* gene (74%) and C-15T mutation in the promoter region of the *inhA* gene (26%). Both mutations can be detected with the WHO recommended the Hain GenoType GenoType MTBDR*plus*.
Conclusions and key recommendations: Given the high prevalence of isoniazid resistance in retreatment cases, Hain GenoType MTBDR*plus* is recommended to be used in addition to routine GeneXpert test for rifampicin-susceptible retreatment patients prior to the initiation of standardized drug-susceptible treatment in Myanmar.

PS-29-819-02 No fluoroquinolone resistance detected in first-line drug-sensitive Mycobacterium tuberculosis in Lima, Peru 2004-2017

A Schwalb,[1] R Cachay,[1] T Cáceres,[1] A Blackman,[2] F Maruri,[2] T Sterling,[2] E Gotuzzo,[1] [1]Instituto de Medicina Tropical Alexander von Humboldt, TB Research Unit, Lima, Peru, [2]Vanderbilt University Medical Center, Vanderbilt Tuberculosis Center, Nashville, TN, United States of America. e-mail: alvaro.schwalb@upch.pe

Background: Fluoroquinolones (FQ) are being evaluated in a phase 3 trial (TBTC Study 31/ACTG A5349) to treat drug-susceptible TB. However, FQ are also one of the most commonly used classes of antibiotics for routine community-acquired infections and are available over-the-counter in Peru. Such FQ exposure may generate FQ-resistant *M. tuberculosis* in persons subsequently diagnosed with TB. Drug susceptibility testing (DST) for FQ is not routinely performed for drug-sensitive TB. We assessed FQ resistance in *M. tuberculosis* at two time-points to assess for an interval change in resistance rates.
Methods: We performed a retrospective study of culture-positive TB outpatients diagnosed with first-line drug-sensitive TB from a high TB burden district in Lima, Peru (San Juan de Lurigancho): 238 isolates from 2004-2005 (cohort 1) and 41 isolates from 2017 (cohort 2). FQ DST for ofloxacin (OFX) was performed at Universidad Peruana Cayetano Heredia on all isolates; moxifloxacin (MOX) and levofloxacin (LVX) was performed for cohort 1 and 2, respectively. Agar proportion method was used for cohort 1 and BACTEC MGIT 960 for cohort 2. A random subset of 60 isolates from cohort 1 underwent OFX and MOX DST by agar proportion at the Vanderbilt University Medical Center TB Research Laboratory.
Results: 279 samples were evaluated from TB patients. Among participants, 96% had not previously been treated for TB and 55% were male. There were 0/238 OFX-resistant isolates in cohort 1 and 0/41 OFX-resistant isolates in cohort 2. No resistance to MOX or LVX was identified. The 60 isolates tested in the two labs had the same DST result: OFX-susceptible.
Conclusions: Despite high rates of FQ exposure in Peru, there was no FQ resistance in first-line drug-sensitive TB patients at two time points 13 years apart. This suggests that FQ remain a viable option for treatment of newly-diagnosed TB in Peru.

PS-29-820-02 Diagnosis of tuberculous meningitis in patients in a national hospital in Lima, Peru

RE Newby,[1] A Chiappe Gonzalez,[2] PL Rondan,[3] C Cucho,[4] LM Huaroto Valdivia,[4,5] ES Ramos,[6] S Datta,[7,8] CA Evans,[7,8,9] J Soria,[2] J Zunt,[10] [1]University of Washington, School of Medicine, Seattle, WA, United States of America, [2]Universidad Nacional Mayor de San Marcos, Department of Medicine, Lima, Peru, [3]Hospital Nacional Dos de Mayo, Servicio de Enfermedades Infecciosas y Tropicales, Lima, Peru, [4]Universidad Nacional Mayor de San Marcos, Laboratory Medicine, Lima, Peru, [5]Hospital Nacional Dos de Mayo, Patología Clínica y Anatomía Patológica, Lima, Peru, [6]IFHAD: Universidad Peruana Cayetano Heredia LID416, Innovation for Health and Development, Lima, Peru, [7]Universidad Peruana Cayetano Heredia, IFHAD: Innovation for Health and Development, Lima, Peru, [8]Wellcome Trust Imperial College Centre for Global Health Research, Infectious Diseases & Immunity, London, United Kingdom, [9]Asociación Benéfica Prismaón Benéfica Prisma, IPSYD: Innovacion Por la Salud Y el Desarollo, Lima, Peru, [10]University of Washington, Global Health, Seattle, WA, United States of America. e-mail: naenewby@gmail.com

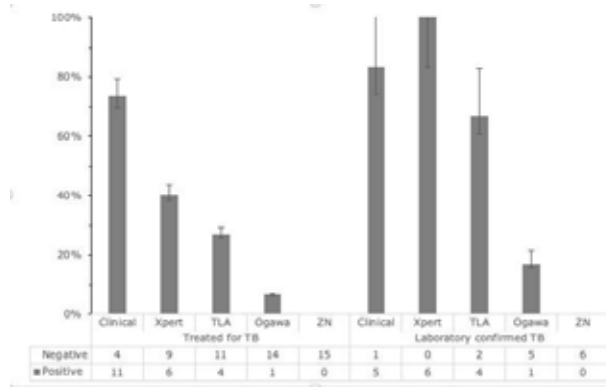
Background: Central nervous system infections with *Mycobacterium tuberculosis* contribute extensively to disability and mortality, especially in resource constrained settings. Delayed diagnosis or inadequate treatment for drug-resistant tuberculosis are associated with poor outcomes.

The objective of this study was to compare the diagnosis yield of various microbiological methods to diagnose TB meningitis (TBM).

Methods: Patients with symptoms suggestive of TBM, admitted to a public hospital in the center of Lima, Peru were recruited to the study (N=45). Cerebrospinal fluid (CSF) was collected by standard aseptic technique and processed for: microscopy with Ziehl-Neelsen and culture using acidified Ogawa media which were the tests offered in the treating hospital; the low-cost thin-layer-agar MDR/XDR Color Test on 1mL of uncentrifuged CSF; and 1mL of non-centrifuged CSF in Cephied´s GeneXpert PCR test. We compared the microbiological method to the diagnosis determined by the treating clinician.

Results: Fifteen patient (33%) were started on treatment for TBM, however, three had their diagnosis rescinded after an alternative diagnosis was found. Of the twelve TBM patients, six (50%) had a positive GeneXpert, four (33%) were Color Test positive, one (8.3%) was positive in Ogawa. None were microscopy positive. The sample positive in Ogawa was also positive in Color Test. Of the twelve patients, eleven had already started treatment due to clinical diagnosis with compatible CSF cytometry. Only one patient was started on treatment due to the microbiological results produced by GeneXpert testing. The Color Test culture caused on patient to be diagnosed with isoniazid-resistant tuberculosis.

Conclusions: Clinical diagnosis with compatible CSF cytochemistry characteristics suggested almost twice as many tuberculous meningitis cases as tuberculosis-specific tests. GeneXpert rarely detected non-clinically diagnosed cases. Thin-Layer-agar Color Test was more sensitive than Ogawa and culture allowed more extensive testing for antibiotic resistance. Microscopy had zero sensitivity for detecting tuberculous meningitis in this study.



[TBM treated or diagnosed patients in the study demonstrating percentage of positives in study tests.]

PS-29-821-02 Handling of human urine samples for the detection of tuberculosis lipoarabinomannan (TB LAM)

A Ball,[1] B Barrios Lopez,[1] B Grant,[1] K Kasavan,[2] V Munsamy,[2] A Pym,[2] A Somoskovi,[3] J Connelly,[1] [1]Intellectual Ventures Laboratory, Global Good, Center for In Vitro Diagnostics, Bellevue, WA, United States of America, [2]African Health Research Institute, Not Applicable, Durban, South Africa, [3]Intellectual Ventures' Global Good Fund, Global Health Technology, Bellevue, WA, United States of America. e-mail: aball@intven.com

Background: Our research focuses on improving point-of-care (POC) diagnostics for tuberculosis (TB). TB lipoarabinomannan (LAM) lateral flow assays (LFAs) have been investigated for this purpose and has been demonstrated to have a mortality benefit for people living with HIV (PLHIV). However, there has not been a large-scale adoption of LAM since its sensitivity and specificity remain still poor. We found that in 10 published studies using human urine samples for the detection of TB LAM, there is a diversity within how urine samples were handled prior to testing, with the largest difference being the use of freshly collected or frozen and thawed samples. We hypothesized that this handling difference might affect the detection of LAM. Our objective was to understand this to aid in the development of a POC TB LAM test.

Methods: In a small pilot study, human urine samples were collected from outpatients at a clinic in KwaZulu-Natal, South Africa, who were confirmed to have TB by

GeneXpert® MTB/RIF. Freshly collected urine samples were tested on the same day of collection by an in-house ELISA. Those determined to contain a detectable concentration of LAM (n=15) were retested after freezing at -70°C in polyethylene terephthalate tubes for at least 1 day.

Results: We found that the mean LAM concentration dropped from 138pg/mL to 76pg/mL while the average percent loss was 50%. In our cohort, all patients were confirmed to have TB by GeneXpert® MTB/RIF and the population was 85.7% PLHIV+ and 14.3% HIV-negative. The mean CD4 count for PLHIV in the cohort was 209 cells/μL.

Conclusions: We concluded that testing of frozen urine samples underestimates the concentration of LAM available for detection in patient samples, especially since the primary use-case for a POC test calls for testing freshly collected urine. Additional studies on a larger cohort is required to confirm these results.

PS-29-822-02 Tuberculosis diagnosis by culture using resuscitation promoting factor

A Dusthackeer VN,[1] R Kumar Mondal,[1] B Mahizhaveni,[1] C Rosaline Nirmal,[1] S Priya,[1] S Kumar,[2] S Prasad Tripathy,[3] G Ramachandaran,[4] H Kumar AK,[4] [1]National Institute for Research in Tuberculosis, Bacteriology, Chennai, India, [2]Rutgers University, Medicine, Belleville, NJ, United States of America, [3]National Institute for Research in Tuberculosis, NIRT, Chennai, India, [4]National Institute for Research in Tuberculosis, Biochemistry, Chennai, India.
e-mail: christy.r@nirt.res.in

Background: Tuberculosis inflicts 8 million individuals per year resulting in 2 million deaths annually according to WHO. Considerable portion of infected individuals remain without showing TB symptoms. The ability of *M. tuberculosis* to enter a phenotypically non-replicating, dormant state is a major impediment in the TB diagnosis since no method is currently available to detect these current methods could catch these non-replicating forms.

Recent studies have shown that the non-culturable forms could be regrown in the presence of resuscitation promoting factor (RPF). Time to detection (TTD) analysis using smear and culture positive specimen showed significant decrease, the mean growth was observed in 6.1 days for RPF exposed cultures whereas it took about 9 days in the presence of 7H9 liquid medium ($P = < 0.001$) (n=48) [previous work].

Methods: Thus, in this work, We were interested to check a. whether the RPF could be used to increase the culture yield in smear and culture negative TB sputum samples (n=268) (7H9 was used as negative control without RPF) and b. potential of crude culture filterate (RPF) versus recombinant cocktail of RPF protein and 7H9 using 98 smear positive and culture negative sputum specimen.

Results: Growth induction was noticed in terms of both the optical density and colonies formed of resuscitable cells (RC) on 7H11 agar plates. Significant (P=0.036) increase in growth was observed between 86 and 77 cultures exposed to RPF and 7H9 respectively. Presence of TB was confirmed by AFB in all these cultures. In second set of experimentation (n=98), RPF from culture filterate induced 4 fold increase in while recombinant RPF showed 2 fold increase in the culture yield.

Conclusions: These data shows that, RPF could increase the culture yield and reduce the time to detection and there by ensures efficient diagnosis that could catch even the non-cultivable forms.

PS-29-823-02 Polymerase chain reaction: a better option for early diagnosis of extrapulmonary tuberculosis

S Baliga,[1,2] L Sharon,[1] D Biranthabail,[1,2] S Shenoy,[1,2] S Nambiar,[1] J Shah,[3] [1]Kasturba Medical College, Manipal Academy of Higher Education, Microbiology, Mangalore, India, [2]Manipal McGill Centre for Infectious Diseases, Manipal Academy of Higher Education, Manipal, India, [3]ID FISH Inc, Pvt., Palo Alto, CA, United States of America.
e-mail: shrikala.baliga@manipal.edu

Background: Diagnosis of ExtraPulmonary Tuberculosis (EPTB) poses a challenge due to low level of clinical suspicion, difficulty in obtaining appropriate and adequate samples. The samples obtained are pauci- bacillary in nature. Molecular based method may help in the early detection of tuberculosis (TB).

Methods: A total of 418 extra pulmonary samples were concentrated by NALC-NaOH method. The concentrated pellet was used for culturing on to LJ medium and smears made were subjected to Auramine O staining. TB PCR (Polymerase Chain Reaction) using IS6110 primer was performed on all the clinical samples. All cultures with growth were biochemically identified as *Mycobacterium tuberculosis* or Non tuberculosis Mycobacteria (NTM). All the biochemically confirmed NTMs were sequenced.

Results: Out of 418 samples, 65 were positive by smear and culture, whereas 143 were positive by smear and PCR. 29 were smear negative and culture positive whereas 38 were smear negative and PCR positive. Significant difference was observed in the sensitivity of PCR test when compared to smear and culture. The sensitivity and specificity of smear , combination of smear + PCR, and PCR alone when compared to culture was 69.14% & 75.61%; 75.2% & 69% and 100% & 63% respectively. Among the 94 cultures, 90 were MTB, one each was *Mycobacterium abscessus*, and *Tsukamurella tyrosinosolvens*. One isolate grown as mixed culture with MTB was unidentified was unidentified due to difficulty in getting the pure culture.

Conclusions: The study highlights the importance of inclusion of molecular method like PCR in the diagnostic algorithm for early and rapid diagnosis of EPTB.

Our study concludes that a combination of Smear and PCR has 100% sensitivity in diagnosing EPTB. Though expensive, rapidity and accuracy of PCR over culture could help in early diagnosis and appropriate treatment.

PS-30-C8 Private engagement across the TB care cascade

PS-30-824-02 Paradigm shift in public-private partnership approach; an innovative model for tuberculosis case detection in Andhra Pradesh, India

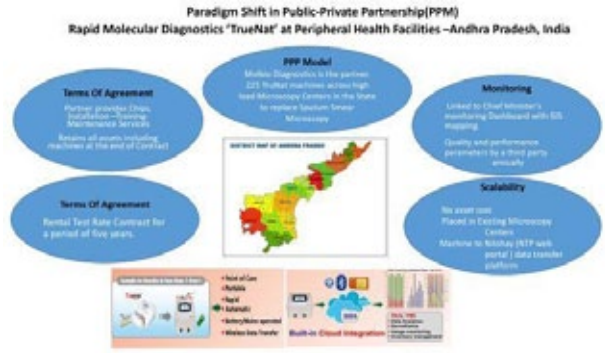
S Achanta,[1] M Gorla,[1] R Tekumalla,[2] J Peravali Carel,[1] K Rade,[1] S Mase,[1] KS Sachdeva,[3] [1]World Health Organization, Country Office, Revised National TB Control Programme, New Delhi, India, [2]Government of Andhra Pradesh, State TB Cell, Department of Health & Family Welfare, Vijayawada, India, [3]Ministry of Health & Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: achantas@rntcp.org

Background: "TrueNat", with sensitivity and specificity comparable to Xpert MTB/RIF (Cepheid, Sunnyvale, CA, United States) has been indigenously developed as a point-of-care molecular tuberculosis(TB) test by MolBio Diagnostics PvtLtd. and recommended for use by the National TB Control Programme after successful feasibility and validation studies. Government of AP collaborated with MolBio Service provider (SP) to deploy two-module TrueNat machines replacing smear microscopy in 225 Peripheral Health Facilities. We describe salient features of the partnership and achievement so far.

Methods: A rate service contract was implemented in which the SP is responsible for providing testing chips, reagents, installation, signage &information material, equipment maintenance and quality assured trainings in TrueNat locations. The SP retains ownership of all machines provided by it at the end of the contract. In the event of machine malfunction, SP provides alternate means of testing until services are restored. An electronic dashboard displays real time tests performed site wise and physicians receive soft copy reports. An innovative strategy was adopted wherein the cost per test is increased (per annum) at the rate of 25% of decline in incidence. This is a first-of-its-kind public procurement norm where the SP has been incentivized to create an increase in access to care and decline in disease.

Results: Between January 2019-March2019, 55353Tests were performed, of which 8131(14.6%) were positive for TB; Of these 265(3.2%) were Rifampicin Resistant and 4428(8%) were invalid. Machine downtime assistance was 85% (2380 out of 2800 samples tested alternatively on Xper MTB/RIFt, 420 by sputum smear microscopy), 90% of module repairs performed within 24hours, 6 Machines replaced and 100% results declared within 24hours.

Conclusions: This is a unique, cost effective partnership that relieves programme of prohibitive machine procurement and maintenance costs. Further implementation will depend on future success of this model. TrueNat has potential as a significant TB intervention globally.



[Figure showing the PPP Model of True Nat deployment]

PS-30-825-02 Lessons from Public Private Interface Agency (PPIA) intervention in TB care: Mumbai, Patna, India

Y Dholakia,[1] S Shah,[1] S Shah,[1] S Kamble,[1] S Rangan,[1] S Rai,[1] N Mistry,[1] [1]The Foundation for Medical Research, TB Department, Mumbai, India. e-mail: fmr@fmrindia.org

Background: PPIA models were developed in Mumbai and Patna (May 2014-June 2016) to reduce diagnosis and treatment delays for pulmonary drug sensitive TB patients (DS-TB). The models engaged private providers, diagnostic facilities and pharmacies into an effective network with provision of free diagnostic tests and treatment.

Methods: A population-based, retrospective study was conducted to assess the models' effectiveness. Care pathways of 86(Mumbai) and 64(Patna) pulmonary DS-TB patients were constructed through in-depth interviews conducted within six months of their diagnosis for identifying types and number of providers accessed, and duration to diagnosis and treatment. The median durations based on providers approached were statistically analyzed.

Results: Compared to non-engaged providers, persons who accessed engaged providers at first point-of-care had shorter pathways [(Mumbai:32days vs 43days) and (Patna:15days vs 40days)]. However the duration for first care-seeking was considerably shorter for patients accessing PPIA in Patna and for both engaged and non-engaged private providers in Mumbai (4 days for both). Whilst PPIA-engaged providers diagnosed more cases than others, the RNTCP in Mumbai provided diagnosis early as compared to the private sector. There was good

retention of patients by PPIA-engaged (1st) providers - 90% post diagnosis in Patna but was affected in Mumbai by the deliberate hub-spoke referral system (13%).
A second diagnosis is a common feature in Mumbai where movement gravitated to PPIA-engaged providers. Spoke-hub model in Mumbai contributed a large proportion of patients showing treatment delay however PPIA-engaged providers were better at retaining patients post treatment initiation 11/25(44%).
Conclusions: The PPIA-engaged provider, accessed at onset can result in marked reduction in care pathway durations. Such initiatives need to engage a critical mass of providers and proximal investigation facilities over defined areas coupled with enhanced disease awareness and literacy efforts amongst the community they serve. Patient movement during care pathway should be minimized for early treatment and retention.

PS-30-826-02 Engaging pharmacists to strengthen TB notification from private sector in Chhattisgarh, India

K Khaparde,[1] R Prasanna,[2] M Deshpande,[2] P Shukla,[2] A Dubey,[2] R Bano,[2] [1]World Health Organization, Country Office for India, New Delhi, India, [2]Government of Chhattisgarh, Health and Family Welfare, Raipur, India. e-mail: drkshitij78@yahoo.co.in

Background and challenges to implementation: In spite of mandatory TB Notification from private health establishments, there are many health establishments not notifying TB cases to the government authority which is leading to inadequate information on actual burden of TB in the state. Also, there is huge problem of uncontrolled unqualified practitioners who are first point of contact of TB patients in rural and tribal areas who also prescribes anti-tuberculosis medicines which are easily available over-the-counter in the pharmacies.
Intervention or response: A state specific decision was taken to gather TB notification information from the chemists. The Food and Drug Administration under the Department of Health and Family Welfare, issued directives to the chemists and druggists to maintain sales register and to retain the physician's prescription copy as a proof of drug sales for tuberculosis. A series of state and district level meetings of chemists and the health authorities were conducted for better partnership. Continued medical educations at the state as well as at district level were also conducted with professional organizations such as Indian Medical Association, Indian Association of Pediatricians, Orthopedic Association to sensitize the private practitioners.
Results and lessons learnt: The intervention yielded TB notification information of 13879 TB patients for the year 2018 and upon validation and removing duplicates 2788 notifications were added against the private practitioners who failed to notify. This intervention along with regular sensitization of private practitioners has led to an increase in private sector TB notification from 30 per lac population in the year 2016 to 43 per lac for the year 2018.
Conclusions and key recommendations: Pharmacist engagement model has proved a way forward to strengthen TB notification information from private practitioners and curb the over-the-counter sales of anti-TB drugs. This model is a zero budget sustainable and replicable model as it utilizes existing resources and requires administrative commitment and regular monitoring.

PS-30-827-02 Leveraging chemist networks to improve access to NTP drugs in the private sector in India: a market approach

RK Gandhi,[1] D Shah,[2] S Vijayan,[3] V Jondhale,[4] [1]PATH, TB Portfolio, Mumbai, India, [2]MCGM, TB Programs, Mumbai, India, [3]PATH, TB Portfolio, Delhi, India, [4]PATH, TB, Mumbai, India. e-mail: cooldrdax@gmail.com

Background and challenges to implementation: India is committed to eliminating tuberculosis (TB) by 2025. Achieving early elimination requires an increased and enhanced focus on private-sector engagement strategies. In this context, the national TB program (NTP) offered free anti-TB fixed-dose combination (FDC) drugs and diagnostics to private providers to treat TB. But often private provider prescribe formulations manufactured by the private pharmaceutical industry and retailed by local chemists.
Representatives from pharmaceutical companies often approach to advocate TB doctors for specific formulations, which affect the uptake of NTP's free drug initiative.
Intervention or response: In Mumbai, private provider engagement is implemented through a Patient Provider Support Agency (PPSA). To promote NTP FDC drugs in the private health sector, PPSA and the Mumbai City TB Office devised an innovative policy. Under this policy, chemists are incentivized for dispensing FDCs (Rs 600/US$9.23 per patient) and logistical management was outsourced through incentivizing (Rs 550/US$8.46 per patient). The barriers and feasibility of free drug implementation was studied through a survey of chest physicians and chemists. A multipronged approach was designed comprising group trainings; deployment of field officers for one-on-one sensitization and messaging, similar to pharmaceutical marketing strategies; dissemination of FDC drugs; and distribution of resource materials and dosing charts.
Results and lessons learnt: With the adoptive strategies, the free FDC distribution increased from 5% of total PPSA notification (June 2017 when the intervention was rolled out) to 55% of total PPSA notification by February 2018.
Conclusions and key recommendations: Effective use of marketing techniques coupled with appropriate communication and strong implementation strategies has

resulted in successful scale-up of anti-TB FDC drug use in the private sector through the PPSA network. The principles have potential for national scale up.

PS-30-828-02 Challenges faced by pharmacies in accelerated TB case finding: findings from the first private sector pharmacy-led referral system in Myanmar

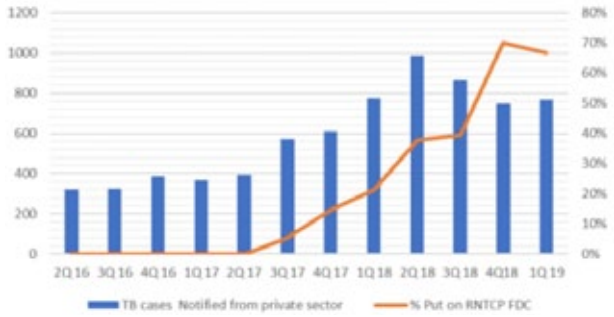
MM Thet,[1] PP Swe,[2] YK Aung,[1] ST Thein,[1] [1]Population Services International/Myanmar, Strategic Information Department, Yangon, Myanmar, [2]Population Services International/Myanmar, Program Management Department, Yangon, Myanmar.
e-mail: mmthet@psimyanmar.org

Background: While currently following the EndTB strategy in Myanmar, Population Services International/Myanmar has initiated the pharmacy-based accelerated TB case finding program since 2012. Pharmacies were trained to screen presumptive TB cases and refer those to respective public health facilities. Since this program is the first private pharmacy-lead referral channel and it has contributed to national TB case notification up to 3% in 2017, there is a need for identifying the barriers faced by those pharmacies for program sustainability in the longer term.
Methods: We conducted a qualitative study with 24 individual in-depth interviews(IDIs). Study participants were 18 trained pharmacies and 6 pharmacy coordinators. ATLAS.ti software version 7.1 was used for coding and organizing the data. Thematic analysis was conducted to generate key findings. This study obtained ethical approval from PSI Research Ethics Board and University of Public Health Myanmar.
Results: Although some pharmacies could make referrals of presumptive TB cases successfully according to the National Tuberculosis guidelines, some failed to do so. Factors such as need for support to pharmacies; fewer monitoring visit by pharmacy coordinators, difficulty in referral form fillings and need for support to TB patients; lack of transportation allowance for diagnosis and treatment and accompanying visits to public health TB clinics when referred were the main challenges discussed in the interviews. Other reported barriers were limited program knowledge of pharmacies, no or low patient loads at pharmacies and having worry of customer or profit loss, patients' time constraint, patients being fear of diagnosed as TB and fear of public hospitals.
Conclusions: The study found that program support played a significant role in referrals of TB cases by pharmacies. This finding is important for sustainability of the program in the long term which again could be considered for future financial and programmatic decision making.

PS-30-829-02 Access to free anti-TB medicines for patients seeking care in private sector: an experience of Nagpur municipal corporation (NMC) Maharashtra

A Kadu,[1] K Tumane,[2] S Dapakekar,[3] P Jogewarr,[4] A Yadav,[5] S Bharaswadkar,[6] S Mase,[7] K Rade,[7] M Parmar,[7] R Ramachandran,[7] [1]WHO Country Office, TB, Nagpur, India, [2]Government of Maharashtra, Nagpur Municipal Corporation, Nagpur, India, [3]Disha Foundation, RNTCP, Nagpur, India, [4]Government of Maharashtra, RNTCP, Pune, India, [5]Government of Maharashtra, Health Services, Mumbai, India, [6]WHO Country Office, TB, Pune, India, [7]WHO Country Office, TB, New Delhi, India.
e-mail: kadua@rntcp.org

Background and challenges to implementation: India is the country with the highest burden of TB and around 50% of the estimated TB patients seek care in the private sector. Ending TB in India may remain elusive unless TB patients in the private sector are provided quality TB management services. There is a need to promote access to quality assured anti-TB treatment available as fixed drug combinations (FDC) under India's revised national TB control programme (RNTCP).
We describe a systematic intervention to provide access of FDCs to patients seeking care in the private sector in Nagpur.
Intervention or response: In April 2017, the RNTCP implemented a Private Public Interface Agency (PPIA) scheme through the Nagpur Municipal Corporation (NMC) NGO. The NGO served as an interface agency between the public and private sector to link private sector patients to public health services.
The objectives were to ensure access to free quality anti-TB drugs with adherence support to private sector TB patients and to establish a TB surveillance system with notification support.
Specific NGO activities include specimen transportation, TB notification, facilitating FDC TB medication distribution through engaged private providers and chemists to patients free of cost, and ensuring that FDC's are pre-fitted with an Information Communication Technology supported adherence tracking mechanism (99DOTS).
Data were collected from April 2017 to March 2019 on the impact of the NGO activities.
Results and lessons learnt: NGO engaged 754 PP's and 164 chemists, notified 5719 private sector TB cases form April 2017 to March 2019. Use of RNTCP FDCs in private sector rose from 0% to 67% (Graph 1).
Conclusions and key recommendations: The public sector needs to engage the private sector in order to meet the goals and targets of the National Strategic Plan 2017-2025. Using this PPIA model for augmenting uptake of RNTCP FDCs in the private sector may be a cost-effective intervention and should be replicated throughout India.



[Graph 1: Uptake of RNTCP supplied free FDC in private sector through PPs/private chemist at NMC,MH]

PS-30-830-02 Periodic performance review with patent medicine vendors, a fulcrum for improving TB case detection in the community: a case study from Nasarawa state, Nigeria

IB Uguge,[1] EN Bassey,[2] D Egbule,[3] M Onuoha,[4] S Useni,[5] A Danjuma,[6] A Oghenetejiro,[7] I-T Adamu,[8] [1]KNCV Nigeria / Challenge TB, Programs, Abuja, Nigeria, [2]KNCV Tuberculosis Foundation, Programs, Abuja, Nigeria, [3]KNCV Nigeria / Challenge TB, Programs, Lafia, Nigeria, [4]KNCV Nigeria / Challenge TB, Monitoring and Evaluation, Abuja, Nigeria, [5]KNCV Nigeria / Challenge TB, Tecnical, Abuja, Nigeria, [6]State TB and Leprosy Control Program, Public Health, Lafia, Nigeria, [7]KNCV Nigeria / Challenge TB, Program, Lafia, Nigeria, [8]KNCV Nigeria / Challenge TB, Teachnical, Lafia, Nigeria. e-mail: basil.uguge@kncvtbc.org

Background: Patent medicine vendors (PMVs) are the first point of care for a large proportion of patients with chronic cough. Though considered as informal health sector, PMVs play a key role in the Nigeria health care delivery especially among the poor. This study demonstrate the effect of periodic performance review with PMVs in increasing TB case finding.
Methods: We identified and trained 120 PMVs across 10 local government areas (LGA) in collaboration with the State TB Program and the National Association Proprietary and Patent Medicine Dealers (NAPPMED). Bi-monthly review meetings coordinated by NAPPMED with technical support from KNCV were held in each LGA to appraise the performance of the PMVs. PMVs were rewarded based on presumptive TB clients successfully referred and TB cases diagnosed. We compared the contribution of PMVs to the overall state report from quarter 1 to quarter 4, 2018.
Results: In Q1 (January-March), PMVs contributed 342 (4%) of the 9540 presumptive and 25 (4%) of the 625 TB cases reported by the state. In Q2 (April-June), PMVs contribution increased to 637 (15%) of the 4194 presumptive and 42 (7%) of total 657 TB cases notified. By Q3 (July-September), contributions from PMVs rose to 956(16%) of the 6010 presumptive and 88(15%) of 606 TB cases notified. By quarter 4 (October-December), PMVs contributed 1155 (19%) of the 6157 presumptive and 107 (16%) of 686 TB cases notified. The TB case yield from presumptives identified by PMVs was 9% while the yield from the total presumptives in the state largely from intra-health facility screening was 11%.
Conclusions: PMVs progressively contributed to overall presumptive and TB cases reported in Nasarawa state in 2018. With Nigeria's low treatment coverage, strategically engaging the informal health sector especially PMVs through NAPPMED presents a unique opportunity for finding and treating missing persons with tuberculosis.

PS-30-831-02 Improving TB case finding through engagement of private health facilities in Nigeria

OO Chijioke-Akaniro,[1] S Onyemaechi,[2] K Joseph,[2] A Lawanson,[1] U Ochuko,[1] E Ubochioma,[2] A Hassan,[3] D Olusoji,[4] H Traore,[5] C Merle,[5] [1]National TB and Leprosy Control Programme, Public Health Department, Abuja, Nigeria, [2]National TB, Leprosy and Buruli Ulcer Control Programme, Public Health Department, Abuja, Nigeria, [3]Association for Reproductive and Family Health, Monitoring and Evaluation, Abuja, Nigeria, [4]Olabisi Onabanjo University, Community Medicine, Sagamu, Nigeria, [5]WHO Geneva, Special Programme for Research and Training in Tropical Diseases (TDR), Geneva, Switzerland. e-mail: ocakaniro@gmail.com

Background and challenges to implementation: Contribution to TB case notification by private health facilities in Nigeria is 14% where more than 60% of Nigerians access medical care from private providers. The private sector offers potential for scaling up TB services. Our study aims to assess the practice of private practitioners on TB treatment services and barriers to TB case detection and notification.
Intervention or response: Between 2017 and 2018, a cross sectional study comprising 316 randomly selected private health facilities (118 in Oyo state, 198 in Federal Capital Territory) was conducted. Data review of TB health facility records were recorded on the electronic data kit (Survey CTO). Key in-depth-interviews of the head or representatives of selected health facilities were done.
Results and lessons learnt: Out of 214 presumptive screened, 75 TB cases (35%) were diagnosed and 56 (75%) referred to public facilities but could not be tracked to notification due to weak referral system. Of the 19 patients managed at the private health facility, 15 were notified by the already aligned NTP-private facilities, 15 (79%) had standardized DS-TB treatment, 2 (10.5%) standardized DR-TB regimen and 2 (10.5%) an un-conventional treatment.
Percentage of treatment success, death and lost-to-follow-up were respectively 21%, 11% and 16% while 53% treatment outcomes could not be evaluated. 316 private practitioners were interviewed. Most reported that they were not trained in the conventional TB DOTS strategy

and could not manage TB patients appropriately hence referring suspected or diagnosed TB patients to public facilities.

Conclusions and key recommendations: Private facilities can significantly increase TB case notification through proper engagement by the National and State TB programmes. Poor case holding in private facilities necessitates the need for trainings, mentoring and supportive supervision of health workers in private facilities.

PS-30-832-02 Contribution of general practitioners and private hospitals in TB patient management and care in selected districts in Sri Lanka

W Jayakody,[1] N Pallewatte,[2] M Jayakody,[3] A Ramachandran,[4] N Galabada Dewage,[5] [1]National Hospital of Sri Lanka, Endocrine and Diabetic Clinic, Colombo, Sri Lanka, [2]Ministry of Health, Nutrition and Indigenous Medicine, Epidemiology Unit, Colombo, Sri Lanka, [3]Regional Director of Health Services Division, Medical Officer of Health, Nugegoda, Colombo, Sri Lanka, [4]National Programme for Tuberculosis Control and Chest Diseases, Central Chest Clinic, Colombo, Sri Lanka, [5]National Programme for Tuberculosis Control and Chest Diseases, Central Unit, Colombo, Sri Lanka. e-mail: mo1nptccdsrilanka@gmail.com

Background and challenges to implementation: Sri Lanka has a well-developed health care system. Although TB diagnosis and treatment is offered at No cost in the Public health sector, significant number of patients with TB symptoms seek care in the private sector as well.

Intervention or response: A descriptive cross sectional study was carried out among general practitioners (GPs) and medical officers (MOs) working in private hospitals in randomly selected nine districts in Sri Lanka, using interviewer administered questionnaires to assess knowledge, attitudes, practises, willingness and needs to provide care to TB patients.

Data was collected by pre trained Public Health Inspectors (PHI). Data was analyzed using the SPSS version 22.0.

Results and lessons learnt: More than 95% of GPs & MOs had good Knowledge on cause, mode of spread and the commonest organ affected by TB. Majority (78%) had encountered with presumptive TB patients. Adequate knowledge on extra pulmonary sites except lymph nodes (< 25%). Diabetes was identified as a risk factor by 85% MOs & 60% GPs. Sputum microscopy (>88% of GPs & MOS) and culture (67% GPs & 44% MOs) were identified as useful diagnostic methods. Majority had good knowledge about treatment of TB (85%), common adverse reactions (80%) and DOT (70%). Majority (95%) knew TB is a notifiable disease. Only 15% GPs & 21% MOs were providing DOT, but only 52% GPs, 31% MOs were willing to provide. Regarding attitudes, only 40% responded TB management as a government responsibility and 17% GPs & 42% MOs didn't expect anti TB drugs to be sold in private pharmacies. Stigma (15%) and lack of space (10%) were reasons and 52% GPs, 37% MOs mentioned DOT provision would affect their practices.

Conclusions and key recommendations: Enhanced collaboration of National TB programme with the private sector is needed. It will improve TB knowledge & practices of private sector to strengthen the TB control activities in Sri Lanka.

PS-30-833-02 Tuberculosis treatment outcomes in public and private hospitals: a comparative study of a public and a private hospital in Lusaka District of Zambia

J Bwembya,[1] V Chalwe,[1] R Kumar,[2] [1]University of Lusaka, Academic, Lusaka, Zambia, [2]Zambart, Eradicate TB Project, Lusaka, Zambia. e-mail: josphat@zambart.org.zm

Background: According to the 2013/14 Zambia tuberculosis (TB) prevalence survey, 4% of all presumptive TB cases seek care from private health facilities. Yet there is limited research investigating TB treatment outcomes for patients managed in private hospitals within Zambia. This study compared TB treatment outcomes for one public hospital and one private hospital in Lusaka District, which is among the districts with the highest TB burden in Zambia and a high concentration of private hospitals.

Methods: This was a retrospective cross-sectional study of patients who initiated TB treatment between January 2015-December 2016 at one public and one private hospital in Lusaka District. We collected routinely recorded TB treatment outcome data (cured, treatment completed, treatment failure, death, lost to follow-up, 'not evaluated' from TB treatment registers. We compared treatment outcomes among the two hospitals using a Chi-square test, at 0.05% level of significance.

Results: 1,313 patients were identified at the two hospitals (n=101 private, n=1,212 public). The proportion of patients cured was lower in the private hospital (11.1%) compared to the public (68.6%) (P-value < 0.001), and loss to follow-up was higher in the private hospital (5.1%) compared to the public (1.2%) (P-value = 0.003). There was no significant difference in the proportion of patients who had treatment success (65.6% vs 62.6%, p-value=0.555), mortality (10.0% vs 10.1%, p-value=0.927), treatment failure (0.2% vs 1.0%, p-value=0.270) and 'not evaluated' (23.0% vs 21.2%, p-value=0.691) for the public and private hospitals.

Conclusions: Although most TB outcomes did not significantly differ for patients managed in the private and public hospitals, the private hospital had less patients cured and more lost to follow up compared to the public hospital. The private hospital can reduce loss to follow-up and increase cure rate by using patient tracking mechanisms like phone calls to patients missing appointments. A more complehensive study is also recommended.

PS-30-834-02 Treatment outcomes of tuberculosis patients treated by private providers in selected districts of West Bengal: a cohort study

V Sharma,[1] P Thekkur,[2] PR Naik,[3] MK Dinda,[4] N Agrawal,[5] P Shanmugam,[4] A Dey,[4] B Saha,[6] B Poojar,[7] N Kanagat,[8] [1]John Snow India, Health, Kolkata, India, [2]International Union Against Tuberculosis and Lung Disease, Centre for Operational Research, Paris, France, [3]Yenepoya Medical College, Yenepoya (Deemed to be University), Department of Community Medicine, Mangalore, Indonesia, [4]WHP India, Tuberculosis Health Action and Learning Initiative (THALI), TB, Kolkata, India, [5]John Snow India, Tuberculosis Health Action and Learning Initiative (THALI), Health, New Delhi, India, [6]State TB Office, Department of Health and Family Welfare, Health and Family Welfare, Kolkata, India, [7]Kasturba Medical College, Pharmacology, Mangalore, India, [8]John Snow India, Tuberculosis Health Action and Learning Initiative (THALI), Health, Boston, NY, United States of America. e-mail: vivek_sharma@in.jsi.com

Background: In India, around 34-57% of the tuberculosis (TB) patients are diagnosed and treated by private health care providers (PHPs). As these patients are not directly monitored by national TB program (NTP), there is limited information on their treatment outcomes. In West Bengal, India, a NGO led Tuberculosis Health Action and Learning Initiative (THALI) project provides support to TB patients and facilitate PHPs in notifying the treatment outcomes.

With this opportunity, we aimed to describe the TB treatment outcomes among patients treated by PHPs and assess factors associated with unsuccessful outcomes.

Methods: A retrospective cohort study using data routinely collected under THALI project was conducted. All TB patients notified during January to April, 2018 by PHPs in the six urban districts of West Bengal were included in the study.

The successful (cured and treatment completed) and unsuccessful (death, loss to follow-up, failure and not evaluated) treatment outcomes were summarized as percentage with 95% CI. We used multivariate generalised linear model to assess the independent association between patient characteristics and unsuccessful treatment outcomes.

Results: Of the 2347 patients included, the mean (SD) age was 39.9 (17.2) and 1436 (61.2%) were males. About 86% of the patients had pulmonary TB, 95% were new cases and 23% were bacteriologically confirmed. Of the total, 444 (19%) received free drugs of NTP under the supervision of PHPs and the rest paid for the drugs.

The successful outcomes were seen in 2020 (86.1%, 95%CI- 84.6%-87.4%) patients and 201 (8.6%) were not evaluated. The older age and using NTP drugs were independently associated with unsuccessful treatment outcomes.

Conclusions: The rate of 'successful outcomes' among TB patients treated by PHPs is promising. The reasons for high rates of 'unsuccessful outcomes' among patients on free NTP drugs has to be explored and corrective actions need to be taken.

PS-30-835-02 Assessment of private healthcare provider capacity for the provision of tuberculosis care and treatment services: case of selected franchised facilities in Kenya

J Limo,[1] [1]Kenya Association for Prevention of Tuberculosis and Lung Diseases, Monitoring and Evaluation, Nairobi, Kenya. e-mail: limojn@gmail.com

Background: Kenya has a large burden of TB and drug resistant TB, a nationwide TB prevalence survey carried out in 2016 suggested that nearly 40% of incident cases are missed yearly. Some of the missed TB may be people who seek and receive care for TB in the private health care sector. Thus private health care provider engagement is a critical intervention in the fight against TB in Kenya.

Methods: A facility-based assessment was undertaken in April 2018 in 51 Tunza and Gold Star Network franchised health facilities using semi- structured questionnaire. Key information sought were; availability of trained Health care workers, knowledge of the health care workers on current TB management and facility's physical infrastructure to support optimized TB care.

Results: Majority of facilities (96%) had a physical environment that was judged to be adequate for the provision of TB services. 47% of facilities had chest radiography on site and 96% were capable of carrying out AFB microscopy.

90% of the health facilities had at least a mix of 3 cadres of health care professionals majority being nurses (47%). Most health care workers were able to correctly identify a presumptive TB case and knew the necessary actions to take upon TB screening in accordance with NTP guidelines; however, 75% of respondents were unsure about appropriate practices for managing drug resistant TB.

Conclusions: Majority of facilities met the basic requirements of TB care and prevention service provision, which provides a good opportunity to develop appropriate interventions to enhance private provider engagement including tailored training.

PS-31-C12 Continuing to interfere: the persistence of the tobacco industry

PS-31-836-02 Institutionalisation of tobacco control programmes is the key to sustained results: a case study from the challenge-ridden state of Bihar in India

DK Mishra,[1] A Pandey,[2] [1]Socio Economic and Educational Development Society (SEEDS), Tobacco Control, New Delhi, India, [2]International Union Against Tuberculosis & Lung Disease, Tobacco Control, New Delhi, India. e-mail: seedsdelhi@gmail.com

Background and challenges to implementation: Bihar is the 3rd highest populated state (99 million) and amongst the poor in health and socio-economic indicators in India. Tobacco use was very high (53.5%) in comparison to national average (34.6 %) as per GATS 2010. A number of initiatives were undertaken over the last five years which resulted in dramatic decrease in tobacco use (25.9%) in GATS 2017 survey, which is not only lesser than national average, but also the largest decrease amongst all states of the country.
Intervention or response: Bihar has started Tobacco control journey since 2010 when National Tobacco Control Program (NTCP) was launched in merely 02 out of 38 districts. In the midst of apathy towards the cause, SEEDS started sensitizing government and other stakeholders in 19 districts for policy developments. Several effective strategic interventions were undertaken. Institutional framework was developed through four pronged strategies i.e. intense advocacy, capacity building & follow up with government officials, effective monitoring at state and district level and consistent media mobilization without losing out to capture even a smaller event related to tobacco control issues. With continuous efforts and series of capacity building programme, tobacco control was institutionalized and State and District Tobacco Control Coordination Committees meets regularly to review the progress of tobacco control.
Results and lessons learnt: Tobacco control is being reviewed periodically by officials at state and district level. 13 out of 19 focused districts have achieved high compliance for Smokefree rules. Two districts have also been declared TAPS-free at point of sale, huge media coverage (more than 1200 clippings) on tobacco control issues.
Conclusions and key recommendations: Sensitization of policy makers, capacity building and regular follow up are instrumental in prioritizing tobacco control in governments' agenda. NGOs and media played very important role and must be considered as key partner for reducing tobacco prevalence in high tobacco burden states.

PS-31-837-02 Declaring educational institutions tobacco free: protecting the young generation to save the nation (multipronged coordinated interventions to declare 3,517 schools tobacco-free in Jharkhand in India)

DK Mishra,[1] A Pandey,[2] [1]Socio Economic and Educational Development Society (SEEDS), Tobacco Control, New Delhi, India, [2]International Union Against Tuberculosis & Lung Disease, Tobacco Control, New Delhi, India. e-mail: seedsdelhi@gmail.com

Background and challenges to implementation: Tobacco Industry (TI) aggressively targets young children and adolescents as new recruits. The early age of initiation for TI assures tobacco usage for longer period. As per GATS 2010, of all ever daily tobacco users (age 20-34), almost 60% initiate tobacco use before age of 17.8. It calls for urgent intervention.
As per GATS 2017, Jharkhand state in India has one of the highest total prevalence rate as 38.9% against national average of 28.6%. This is disturbing.
Government of India enacted its tobacco control law i.e. Cigarette and Other Tobacco Product Act, 2003 (COTPA). It prohibits smoking in all public places including schools (section 4), forbids sale to and by minors (section 6-A) and bans sale of tobacco products within 100 yards of any educational institution (section 6-b).
Intervention or response: 3.5 million students of age 14 to 18 studying in 3517 schools in Jharkhand state were protected through multipronged coordinated interventions adopted by Director of School Education, SEEDS and The UNION, technical support partners to state Government. Massive awareness program was launched. All stake holders including DEOs, teachers, media, school management committee, parents, peer groups were made sensitive and responsible ensuring that
· No sale of tobacco products around 100 Yards of schools.
· No use of tobacco in schools
· Display of two warning signages mandated under section 4 and section 6(b).
Continuous monitoring of implementation process was the key. Strict actions were also taken.
Results and lessons learnt: Visionary Zeal and regular personal monitoring resulted in high compliance of section 4 and section 6(b) ensuring 3517 Schools being declared tobacco-free in two years.
Conclusions and key recommendations: Strategic, collaborative and multipronged coodinated intervention at school level results in reducing students′ exposure and their accessibility to tobacco products significantly. This minimizes chances of picking up this dangerous habit. It protects young generation. And, Protecting Young Generation means saving Nation.

PS-31-838-02 Tobacco industry exploiting religious practices to promote their image: a case study from Sri Lanka

C Perera,[1] S Lakmal,[1,2] H Wijesuriya,[1] I Fernando,[1,2] P Dineshkumar,[1,3] S Kandeepan,[1] M Perera,[1,4] M Rajasuriya,[1,5] [1]Centre for Combating Tobacco (CCT), Faculty of Medicine, University of Colombo, Colombo, Sri Lanka, [2]Alcohol and Drug Information Centre (ADIC) Sri Lanka, Strategic Intervention Program, Colombo, Sri Lanka, [3]Alcohol and Drug Information Centre (ADIC) Sri Lanka, North and East Program, Colombo, Sri Lanka, [4]Faculty of Medicine, University of Kelaniya, Department of Public Health, Ragama, Sri Lanka, [5]Faculty of Medicine, University of Colombo, Department of Psychiatry, Colombo, Sri Lanka. e-mail: chinthi29@yahoo.com

Background: Seventy per cent of Sri Lankans follow Buddhism, a philosophy that dissuades its followers from the use of psychoactive substances.The national tobacco control laws prohibit sponsorships promoting products and direct and indirect image promotion of tobacco products and its manufacturers. Recently, several media agencies reported of Buddhist religious practices that were supported by Ceylon Tobacco Company (CTC),British American Tobacco subsidiary holding monopoly in manufacturing and selling cigarettes in Sri Lanka. We aimed to explore CTC's engagement in religious activities and their potential impact.
Methods: This study is based on TobaccoUnmasked posts developed using investigative research techniques (key informant interviews and content analysis of photographs, media reports, websites and industry reports). Thematic analysis was used to explore the type of activity, CTC investment, potential impact and intensity of media coverage.
Results: CTC utilised both the main annual Buddhist celebration ("Wesak") and the commonest Buddhist ritual ("Bodhi-Pooja"). The main Wesak celebration zone (WCZ) in Colombo, the Gangarama WCZ, was sponsored by proxies of CTC for three years.They sponsored construction of two pilgrims-rests in two popular pilgrimage sites, each ceremoniously and impressively declared open by the President and the Secretary of Defence of Sri Lanka.The direct interference in policymaking was noticeable in the "Bodhi-Pooja" which is said to be organized to empower the tobacco-farmers against the government's plan to eliminate tobacco cultivation by 2020. All these activities received wide positive media coverage in formal, including state television, and informal media.At community level, CTC financially supported numerous religious activities and infrastructure development of temples and worship sites situated in tobacco cultivation areas, generating a positive image amongst the rural farming communities and the community leaders.
Conclusions: Tobacco industry successfully uses religious practices to promote its image among the public and the policy makers at national and grass-root levels.

PS-31-839-02 Perceived effectiveness of pictorial health warnings in Indonesia

N Puspawati,[1] R Fauzi,[2] [1]University of Illinois at Chicago, Health Policy and Administration, Chicago, United States of America, [2]Tobacco Control Support Center-Indonesian Public Health Association (TCSC-IAKMI), Tobacco Control, Central Jakarta, Indonesia.
e-mail: nuradiapuspa@gmail.com

Background: Previous research has shown that pictorial health warnings on tobacco packs were perceived as an effective way to prevent adolescents from smoking, motivate smokers to quit, and convince former smokers to keep quitting smoking. Currently, the pictorial health warnings in Indonesia included graphic pictures at the top 40% of the package. The Minister of Health's Decree No. 40/2013 mandated that the size of pictorial health warnings should be increased to a minimum of 75% during 2015-2018 period. This study aimed to assess perceived effectiveness of the different sizes of pictorial health warnings.
Methods: A cross sectional study was carried out from November to December 2017 in 16 cities/regencies in Indonesia. A total of 5,234 individuals were successfully interviewed using a structured questionnaire. The sample size was determined using Multistage Cluster Sampling method.
Results: Most respondents (78,9%) stated that 90% pictorial health warnings on tobacco packs were highly perceived to be effective scare people. A total of 76,4% of smokers stated that graphic warnings were very effective to motivate them to quit smoking. Besides, 75% of pictorial health warnings effectively convinced 94% of adolescents not to start smoking, and prevented 90% of ex-smokers from smoking again. The most effective size perceived by majority of the respondents was 90% pictorial health warnings.
Conclusions: Most respondents, including smokers, support the larger size of pictorial health warnings. Therefore, Indonesian Government, especially the Ministry of Health should overcome the political barriers to implement a larger size of pictorial health warnings as mentioned in the roadmap of tobacco control in Indonesia.

PS-31-840-02 Bangladesh Tobacco Industry Interference Index 2018: report on implementation of FCTC article 5.3

MD Amin,[1] MM Hasan,[1] [1]PROGGA, Tobacco Control Program, Dhaka, Bangladesh.
e-mail: mahiac2010@gmail.com

Background and challenges to implementation: In 2008, Bangladesh adopted the FCTC Article 5.3 Guidelines which provides specific measures to protect the government from tobacco industry interference. As the Guidelines are still legally non-existent in Bangladesh, the government efforts to implement measures to reduce both

demand for and supply of tobacco are being undermined by tobacco industry. This study attempts to measure the level of tobacco industry influence the country is suffering from and produces a number of recommendations.
Intervention or response: A study has been conducted using Tobacco Industry Inteference Index tools, developed by SEATCA, based on incidences of interference in 2016 and 2017. The main objective was to measure country-level implementation of Article 5.3. The study assesses how government has responded to interference from tobacco industry and what action the government has in place to protect itself. The lower the score, the better the compliance of Article 5.3 Guidelines.
Results and lessons learnt: Overall, the government has performed poorly in implementing Article 5.3 Guidelines. Bangladesh scores 78 out of 100. As this is the first report of its kind for Bangladesh, it is the baseline from which improvements must be made.
Conclusions and key recommendations: The government must fully implement Article 5.3 guidelines. Immediately, following measures should be undertaken including undertakes awareness raising of non-health sectors, disclose all interactions with tobacco industry, halt all participation in award ceremonies involving tobacco industry, ban tobacco-related CSR activities, terminate government officials′ positions in tobacco companies, remove all incentives provided to tobacco industry and adopt a code of conduct for all officials dealing with the industry.

PS-31-841-02 The importance of independent estimates of illicit cigarette trade: evidence from Mexico

B Saenz de Miera,[1] LM Reynales,[2] [1]Universidad Autonoma de Baja California Sur, Economics, La Paz, Mexico, [2]Instituto Nacional de Salud Publica, Tobacco Control, Cuernavaca, Mexico.
e-mail: belensaenzdem@yahoo.com.mx

Background: Illicit trade in cigarettes not only negatively affects public finance but also public health. In particular, illicit cigarettes are normally sold at prices well below the price of legal products and fail to comply with packaging regulations, which stimulates consumption. For this reason, article 15 of the WHO FCTC recognizes that combating illicit trade in tobacco products is a key component of tobacco control. Furthermore, the Protocol to Eliminate Illicit Trade in Tobacco Products specifically aims at eliminating illicit trade. Reliable measures of the extent of the problem are scarce, however. Most available figures come from the tobacco industry, which has incentives to overestimate the problem. The objective of this study is to provide a robust estimate of illicit cigarette trade in Mexico.
Methods: Data were collected from smokers and discarded packs. Both face-to-face interviews in households and the collection of discarded packs were implemented in eight cities distributed throughout the country. The survey sample comprised 2,396 smokers, while the discarded packs sample comprised 8,204 packs. Self-reported brand information at last purchase and compliance of packs with current regulations were employed to determine illicit cigarette consumption.
Results: According to the survey, the average prevalence of smokers who buy illicit cigarettes is 5.0%, while the consumption of illicit cigarettes is 7.6%. The analysis of discarded pack yields similar results, as illicit cigarette consumption is estimated at 8.8%. Both methods also indicate that there is wide variation across cities, very likely associated to corruption and weak governance.
Conclusions: The tobacco industry has strong incentives to overestimate illicit cigarette consumption. Therefore, independent, robust measures are essential to understand the magnitude of the problem and facilitate the implementation of the FCTC and the Protocol. In Mexico, the prevalence of illicit cigarette consumption is between 7.6 and 8.8%, which is half the estimates of the tobacco industry.

PS-31-844-02 How the tobacco industry interferes in Sri Lanka to undermine tobacco control polices

S De Seram,[1] [1]ADIC Sri Lanka, Human Development, Colombo, Sri Lanka. e-mail: sampathde@yahoo.com

Background: Sri Lanka ratified the WHO FCTC in 2003 and established the National Authority on Tobacco and tobacco in 2006 (NATA). Ceylon Tobacco Company (CTC) holds the monopoly of the cigarette business and it's a subsidiary of the BAT. Sri Lanka is planning to introduce plan packaging and ban selling single sticks.
Methods: The study involves discussions with individuals and a desk review of secondary data sources including newspapers, CTC annual reports, government gazettes, websites, social and electronic media etc.
Results: In the 2019 budget period the Chairman of the Internal Finances Committee (MP) requested information from the Ministry of Finance on how the cigarette price is being calculated.He received the answer to his question from the Ceylon Tobacco Company and not the Ministry of Finance.
Study revealed that 9 tobacco industry representatives have been appointed in the higher positions in government organisations. Within the study period the executive presidents, prime ministers, finance ministers and agriculture ministers are the biggest target of the tobacco company. There were 3 executive presidents out of 3, one president has taken part for the CTC activities and 2 prime ministers out 4 have engaged for CTC activities. Four agricultural ministers also participated for the CTC activities. Findings revealed that finance ministers were highly lobbied in NATA Act was introduced, during the pictorial warning period and tobacco tax increased period consequently, The. Most of the argu-

ments made by finance ministers and tobacco industry arguments were same.Front group has been created by the tobacco industry to delaying the effective policies and litigation activities. New Legislation violates human rights and decrease the government levies are the common arguments of them.

Conclusions: The tobacco industry interference could be seen even through very subtle means. Strengthening the civil societies is very useful to expose and challenge the interference of the tobacco industry.


Tobacco Company Panicked After Parliamentary Committee Inquire on Cigarette Prices!

In response to a query raised by the parliamentary finance committee on cigarette price control in Sri Lanka, the Chairman of the Committee MP. Sumanthiran has received a letter from Tobacco Company.

Sumanthiran says that he has received a written request with the same idea, which he has received over the phone by a person calling him as a lawyer. It is surprising that a private company has responded to an order issued to the officers at the finance ministry. He said that he asked the caller how he knows the information discussed in the state finance committee.

[Interference]

PS-31-846-02 Exposing tobacco industry tactics in implementation of 85% GHWs through media advocacy

B Mathew,[1] [1]Voluntary Health Association of India (VHAI), Tobacco Control, Delhi, India.
e-mail: binoymathew84@gmail.com

Background and challenges to implementation: Graphic health warnings (GHWs) are an effective measure to warn tobacco users of the harm of tobacco use. GHWs on packaging of tobacco products is legally mandated as per India's national tobacco control legislation Cigarettes & Other Tobacco Products Act 2003. GHWs were notified on 15th October, 2014 & effective from 1st April, 2015 - pictorial warning to cover 85% area on both sides of tobacco packs. However the notification was kept in abeyance in March 2015, due to tobacco industry pressure.

Intervention or response: Using earned media to expose tobacco industry tactics towards delaying the implementation of 85 percent graphic health warnings. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, VHAI decided to increase consumer awareness about the issue of pictorial warnings in the news through a sustained strategy of media engagement.

We increased our interactions with the media, both on a one-to-one basis and through press meets during the year 2014 - 2016. Brief yet accurate press releases were also issued to the print media for stories.

Results and lessons learnt: This strategy of media advocacy resulted in nearly over 1200 earned media stories on 85 graphic health warnings. More than 100 hours' time on news channels. These stories created pressure and become a national debate. After a two-year battle, India implemented 85 percent graphic health warnings on tobacco products package from 1st April, 2016.

Conclusions and key recommendations: The media was sensitized and in the process, a personal rapport began was developed with journalists. VHAI's state level network, tobacco control partners and linkages with vernacular media helped to make the GHW issue a Pan India campaign.

PS-31-847-02 Over reporting of smuggled cigarettes by tobacco industry to influence policy makers against tax increases on cigarettes: a case study in Sri Lanka

PR Vithanage,[1] NS Gamage,[1] S De Seram,[2] [1]Alcohol and Drug Information Center, Research and Evaluation Programme, Colombo, Sri Lanka, [2]Alcohol and Drug Information Center, Human Development and Administration, Colombo, Sri Lanka.
e-mail: mail2nalaka@gmail.com

Background: Illicit cigarette trade is well organized global network. Tobacco industries themselves were speculated to be behind illicit trade and British American Tobacco (BAT) involvement in tobacco smuggling in Africa and Lebanon had been documented[1]. In Sri Lanka (SL) the tobacco industry is a monopoly of Ceylon Tobacco Company (CTC) which is subsidiary of BAT. Historically, issue of smuggled cigarettes has been used by the industry against raising taxes on cigarettes. Since the increase of excise taxes in 2016, CTC has continuously mentioned about increase of smuggled cigarettes and their annual reports have stated extraordinary figures. As per them illicit cigarette market in SL is 14% of total cigarette market. This study is aimed to explore the validity of their claims.

Methods: SL Customs is the main authorized law enforcement agency which detect illicit cigarettes in SL. They keep records on cases of illicit cigarette ceased by Bandaranayake International Airport, Revenue Task Force Mobile Unit and Central Investigation Bureau. This study analyzed Customs data from 2014 January - 2018 May.

Results: According Customs records, 18,892,980 illicit cigarettes was captured from 2014 to 2018 May. And 14,941,140 illicit cigarettes were seized in 2017. CTC

reported in their annual report, total number of illicit cigarettes as 510 million in 2017. This is 34 times higher than Customs data. CTC has given vague details about information sources and have multiplied ceased cigarettes by 10. Then total illicit cigarettes should be 51 million which is still 3.4 times more than the Customs data.
Conclusions: CTC have apparently over reported illicit cigarette availability in Sri Lanka. This could be a strategy used by them to influence policy makers against raising taxes since same figures has been quoted by pro-industry front groups/studies and newspapers. Therefore the government need to establish proper mechanism to monitor and report illicit cigarettes.

PS-31-848-02 Advertisement-free point-of-sale (PoS) at tobacco vendors: a self-compliant and sustainable model from Indian state of Bihar

DK Mishra,[1] A Pandey,[2] SK Choudhary,[1] [1]Socio Economic and Educational Development Society (SEEDS), Tobacco Control, New Delhi, India, [2]International Union Against Tuberculosis & Lung Disease, Tobacco Control, New Delhi, India. e-mail: seedsdelhi@gmail.com

Background and challenges to implementation: India's tobacco control legislation mandates ban on direct or indirect advertisement, promotion and sponsorship of tobacco products. However as per Global Adult Tobacco Survey-2017, 25.9% adults use tobacco in the state of Bihar. 2.1% adults noticed any advertisement or promotion of Cigarette, 1.8% of Bidis, and 2.0% of smokeless tobacco products at point of sale.
Intervention or response: Through planned institutionalization process mechanisms were established followed by structured law enforcers' capacity buildings, and periodic enforcement drives. In addition following action were also taken to make it self-complaint and sustainable:
- Strong directions to all District for enforcement by State Government
- Joint meeting of Tobacco traders / vendors with Patna District administration to inform them about TAPS ban, and stringent provisions of penalties / punishment against the defaulters.
- Strategic engagement of civil societies and media to build an enabling environment.
- Huge earned media coverage

Results and lessons learnt: Effective Media coverage has generated a wave of awareness on TAPS ban in the state; which was visibly marked through the hassle free removal of advertisements at Point of Sale in Patna and adjoining districts. State government's multi-prong strategy and the lead taken by District Administration on enforcement resulted into removal of 100% PoS advertisements from tobacco vend in Patna district within one week without any enforcement drives.
Conclusions and key recommendations: Strategic planning, sensitising tobacco vendor effective, Government-NGO partnership and engagement with Media leads to the smooth compliance of TAPS provisions at POS and so recommended for a sustainable model for preventing TAPS.

PS-32-C2 Losses and gains across the continuum of TB care

PS-32-850-02 Under reporting among tuberculosis (TB) patients diagnosed in hospital - highlighting a gap in the South African TB Care cascade

S-A Meehan,[1] A Boulle,[2,3] A von Delft,[2,3] A Hesseling,[1] P Hendricks,[1] A Swartz,[4] M Osman,[1] [1]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Cape Town, South Africa, [2]University of Cape Town, School of Public Health and Family Medicine, Faculty of Health Sciences, Cape Town, South Africa, [3]Western Cape Government: Health, Health Impact Assessment Directorate, Strategy and Health Support, Cape Town, South Africa, [4]Western Cape Government Health, TB Program, Cape Town, South Africa. e-mail: sueannm@sun.ac.za

Background: South Africa has a high tuberculosis (TB) burden with an estimated incidence of 322,000 cases (567/100,000 population) in 2017. Case notification was 227,000 (70%). Patients diagnosed with TB , but not entered into a TB treatment register (defined as initial loss to follow up [ILTFU]) contribute to the low case notification. Currently there is little evidence to show how patients diagnosed in hospital contribute to ILTFU. The aim of this study is to describe ILTFU among hospital-diagnosed TB patients in Cape Town, South Africa.
Methods: This retrospective descriptive study identified ILTFU among TB patients diagnosed in 2 hospitals (1 tertiary and 1 district hospital) in 2 sub-districts of the Western Cape Province, South Africa.
The study analyzed the routine health services data (January to March 2018) from the Provincial Health Data Centre (PHDC). The PHDC amalgamates a variety of data sources to identify laboratory and clinically diagnosed TB patients, to ensure a single record with linked data for each patient.
Results: Overall 2,371 TB patients were diagnosed in both sub-districts, of which 551 (23%) were ILTFU. In the 2 hospitals, 451 TB patients were diagnosed, of which 223 (49%) were ILTFU. ILTFU was 60% among children 0-14 years, 45% among HIV-infected patients and 44% among those with a previous TB episode compared to 52% among new TB patients. 35/223 (16%)

ILTFU patients died within 1 month of their TB diagnosis.

Conclusions: In Cape Town, South Africa ILTFU among TB patients diagnosed in hospital is high with a very high mortality. Addressing the high ILTFU rates at hospital level will be important for reducing overall ILTFU and for finding the 'missing TB patients'. On-site registration of TB patients diagnosed in hospital may reduce ILTFU. Operational research could determine the impact of such a health system strengthening initiative.

	Diagnosed in hospital (n=451)	In TB register (n=228)	%	ILTFU (n=223)	%
Gender male	222	108	49	114	51
female	228	120	53	108	47
Age (yrs) <15	84	34	40	50	60
≥15	367	194	53	173	47
HIV status +ve	234	129	55	105	45
-ve	179	78	44	101	56
Previous TB yes	128	72	56	56	44
no	323	156	48	167	52

[Table 1: Initial loss to follow up among TB patients diagnosed in two hospitals in Cape Town, South Africa]

PS-32-851-02 Working with local community leaders to reduce TB pre-treatment loss to follow-up: a case of Kamuli General Hospital, Uganda

AK Muwonge,[1] R Nyinoburyo,[2] N Ruhinda,[1] B Kintu Nsangi,[2] N Tumwesigye,[3] J Isabirye,[4] A Muhwezi,[1] [1]University Research Co., LLC, USAID RHITES EC Project, Health Systems Strengthening, Jinja, Uganda, [2]University Research Co., LLC, USAID RHITES EC Project, Clinical Services, Jinja, Uganda, [3]University Research Co., LLC, USAID RHITES EC Project, Chief of Party, Jinja, Uganda, [4]Kamuli General Hospital, TB Unit, Kamuli, Uganda. e-mail: amuwonge@urc-chs.com

Background and challenges to implementation: Rapid TB case identification and treatment initiation are key in Tuberculosis control. Pre-treatment loss to follow-up (PLTFU) is identified as a failure in the provision of care for TB patients and an enabler for continued transmission associated with case fatality ranging from 0 to 82%. Previous studies have shown poor tracing rates of PLTFU patients ranging from 0 to 77%. Review of East-Central region October 2017-September 2018 program data showed that 2,738 of 2,836 (96.5%) TB clients registered in the TB laboratory register had initiated treatment, translating into 3.5% PLTFU , with Kamuli hospital registering the highest PLTFU rate of 11% (21/193).

Intervention or response: The USAID Regional Health Integration to Enhance Services in East-Central Uganda (RHITES-EC) project supported with hospital staff to employ quality improvement approaches in tracing PLTFU patients. A line list of the PLTFU clients was made, and a root cause analysis showed inadequate contact information captured, with 86% (18/21) of the PLTFU clients having no record of a phone contact as per national guidelines.

The team worked with village leaders to trace the patients. A list of phone contacts for village leaders was obtained from the district authorities.They were called, informed about the PLTFU patients in their respective villages and the risk of community transmission. The leaders then encouraged the PLTFUs to return to the health facility for treatment.Outcomes of traced patients were recorded as traced and treatment initiated, dead, self-transferred or not traced.

Results and lessons learnt: Of the 21 PLTFUs, 18 (85.7%) were traced and treatment initiated, 2 (9.5%) had died and one not traceable. Case notification in the January - March 2019 period increased from 46 the previous quarter to 60.

Conclusions and key recommendations: Engagement of local leaders is an effective strategy in tracing PLTFU patients which contributes to improved case notification. This can be adopted by TB programs in low resource settings.

PS-32-852-02 Finding the missing tuberculosis cases in Ghana: where are the gaps in the pathway to diagnosis?

J Der,[1,2] D Grint,[1] C Narh,[2,3] F Bonsu,[4] A Grant,[1] [1]London School of Hygiene and Tropical Medicine, TB Centre, London, United Kingdom, [2]University of Health and Allied Sciences, School of Public Health, Epidemiology and Biostatistics, Hohoe, Ghana, [3]University Medical Centre Mainz, Institute of Medical Biostatistics, Epidemiology and Informatics, Mainz, Germany, [4]National TB Control Program, Disease Control and Prevention, Ghana Health Service, Accra, Ghana. e-mail: joyce.der@lshtm.ac.uk

Background: Ghana's national survey showed higher than expected TB prevalence, indicating that many people with TB are not identified and treated. The objective of this study was to identify gaps in the cascade of TB care prior to starting treatment.

Methods: A prospective cohort study conducted in south-east Ghana in one urban and four rural health facilities. Consecutive patients identified by a health-worker as needing a TB test completed demographic and health histories using a standardized questionnaire and were followed up two-weekly for two months to find out if sputum was submitted and/or treatment started. The causal effect of health facility location on submitting sputum was assessed before risk factors were investigated in logistic regression.

Results: 428 persons (mean age 48 years, 67.3% female) were recruited, 289 (67.5%) from urban and 139 (32.5%) from rural facilities. Symptoms reported included cough

among 421 (98.4%), fever 319 (74.5%), night sweats 94 (22%) and weight loss 101 (23.6%). Of 410 (96%) individuals followed up, 290 (70.7%) submitted sputum, among which 26 (13.5%) had a positive result and started treatment.

Among those who visited an urban facility, 247/271 (91.1%) submitted sputum, compared to 43/139 (31%) who visited a rural facility. Participants recruited at the urban facility were far more likely to submit a sputum sample (OR: 23.0, CI: 13.2-39.9). After adjusting for confounding (type of residence and cough duration), the odds of submitting sputum were 18-fold higher in an urban facility (aOR: 17.8, CI: 8.0-39.6). In analysis restricted to the urban facility, individuals with cough duration >=14 days (aOR: 0.20, CI: 0.1-0.7) were less likely to submit sputum.

Conclusions: Many presumed TB patients did not submit sputum for testing, particularly if they attended a rural health facility. To improve TB case finding, sputum submission facilities should be more accessible to patients.

PS-32-853-02 Investigating losses in the paediatric TB care cascade from point of entry to TB notification: a case study of Ndola District, Zambia

S Miti,[1] C Munyinya,[2] A Sondashi,[2] W Mwanza,[2] C Kasapo,[3] J Bwembya,[4] A Schaap,[5] J Simbaya,[6] R Kumar,[4] A Mwinga,[4] [1]Arthur Davison Children's Hospital/Tropical Diseases Research Center/Ndola District Health Office, Pediatrics, Ndola, Zambia, [2]Ministry of Health, Ndola District Health Office, Ndola, Zambia, [3]Ministry of Health, National TB Control Program, Lusaka, Zambia, [4]Zambart, Eradicate TB Zambia, Lusaka, Zambia, [5]Zambart, London School of Hygiene and Tropical Medicine, Data/Statistics Unit, Department of Infectious Disease Epidemiology, Lusaka, Zambia, [6]University of Zambia, Institute of Economic and Social Research, Lusaka, Zambia. e-mail: drsammiti@gmail.com

Background: Although the World Health Organization estimates 10% of all tuberculosis (TB) cases occur in children, in Zambia, only 2% of smear-positive TB patients notified between 2004 and 2011 were children. We investigated the losses that occur throughout the TB diagnostic and treatment cascade for children with TB symptoms at 3 high-patient-volume health facilities in Ndola District.

Methods: We conducted a retrospective, cross-sectional study of patients <15 years who presented with symptoms suggestive of TB at 3 health facilities from January to December 2017. We reviewed medical records for any patients in the inpatient or outpatient department diagnosed with respiratory tract infection, pneumonia, or TB. Any patient with 1 or more recorded TB-suggestive symptoms (cough, fever, night sweats, weight loss) was followed in the presumptive TB, laboratory, and TB treatment registers. We recorded the number lost at each stage of the pediatric-TB care cascade.

Results: The study reviewed records of 3,892 patients. Of these, 2,822 (72.5%) had at least 1 TB suggestive symptom; of these, 95 (3.4%) were captured in the TB presumptive register (96.6% loss). Of patients recorded in the presumptive register, 63 (66.3%) appeared in laboratory registers (33.7% loss), 30 of whom were diagnosed with TB (9 bacteriologically confirmed 21 clinically diagnosed). All 30 patients were commenced on treatment and recorded in treatment registers.

Conclusions: The majority of TB-symptomatic pediatric patients presenting to health facilities are not screened and recorded as presumptive TB patients. The low index of TB suspicion for pediatric patients may be responsible for the low paediatric TB notifications in Ndola. The district health office should develop health worker capacity to screen for pediatric-TB by orienting them to the new TB guidelines, providing job aids, intensifing pediatric-TB case finding and strengthening pediatric-TB diagnostics to minimise loss of patients in the pediatric-TB care cascade.

PS-32-855-02 Transfer out to clinic-based TB treatment following hospital TB diagnosis in South Africa

C Hanrahan,[1] L Lebina,[2] L Mmolawa,[2] BAS Nonyane,[3] N West,[3] T Siwelana,[2] N Martinson,[2] D Dowdy,[1] [1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, MD, United States of America, [2]Perinatal HIV Research Unit, Epidemiology, Johannesburg, South Africa, [3]Johns Hopkins Bloomberg School of Public Health, International Health, Baltimore, MD, United States of America. e-mail: chanrah1@jhu.edu

Background: Tuberculosis (TB) treatment indicators include a category for those transferred to another facility. "Transfers" are not well described or tracked, though almost 40% of all TB patients are first diagnosed in hospital in South Africa. The aim of this study was to describe referral to primary clinic-based TB care for those initially diagnosed in hospital either as in- or outpatients.

Methods: We conducted a record review on adults (≥18 years) diagnosed with TB at 11 hospitals in rural Limpopo, South Africa, who were subsequently transferred to their local clinic to continue treatment. We tracked records at primary care clinics to which participants were referred by the hospital. We telephonically interviewed or conducted a household visit to ascertain the outcome of individuals whose records were not located. We used Cox proportional hazards regression to examine predictors of successful transfer of care.

Results: We enrolled 735 individuals diagnosed with TB at hospital from August 2017-April 2018, who were transferred out to local clinics at discharge. Median age was 40 years (IQR:32-50), 72% were HIV positive and 70% were inpatients.

Overall, 80% (n=591) linked to TB care, 6% (n=41)

died, 1% (n=7) chose not to seek treatment, and 12% (n=96) records were not found in clinics. The median time from hospital discharge to presentation at clinic was 8 days (IQR:1-21). An additional 4% (n=33) died after presenting for care. After controlling for sex, HIV status and district, patients less likely to successfully transfer to clinic-based treatment included those >=50 years old (adjusted hazard ratio 0.78, 95% CI 0.65-0.95), hospital inpatients (0.72, 0.60-0.86), and those not reporting cough at diagnosis (0.69, 0.51-0.85).

Conclusions: A high proportion of patients diagnosed in hospitals successfully transferred to TB care in clinics. Targeted interventions could further improve care transfer, especially among older patients, inpatients, and those with symptoms other than cough.

Characteristic	Hazard Ratio	p-value	Adjusted Hazard Ratio	p-gvalue
Age category				
18-29 years	REF		REF	
30-49 years	0.91 (0.73-1.13)	0.380	0.93 (0.75-1.14)	0.506
50+ years	0.75 (0.58-0.96)	0.023	0.78 (0.65-0.95)	0.012
HIV status				
Negative	REF		REF	
Positive	1.07 (0.87-1.3)	0.532	0.94 (0.72-1.24)	0.683
Inpatient at hospital	0.68 (0.58-0.80)	<0.001	0.72 (0.060-0.86)	<0.001
Cough at diagnosis	1.30 (1.16-1.47)	<0.001	1.31 (1.15-1.49)	<0.001

[Univariable and mutlivariable predictors of successful transfer of care between hospital and primary care clinic]

PS-32-857-02 Patient cascade analysis in Tajikistan: following patients using data matching

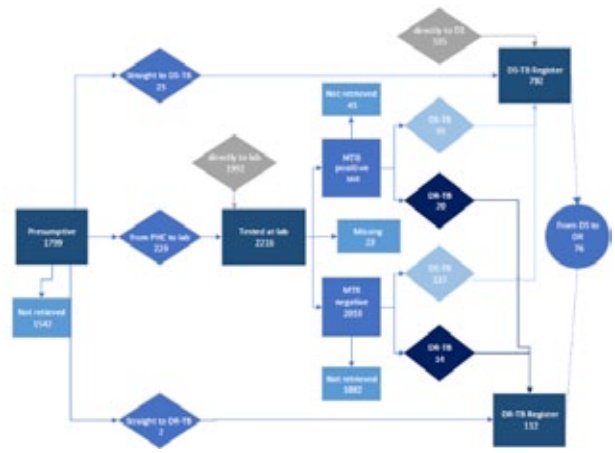
A Soliev,[1] PT Pelzer,[2] S Azamova,[1] B Sharipov,[3] A Rajabzoda,[3] J Maltha,[2] M Makhmudova,[1] E Tiemersma,[2] [1]KNCV Tuberculosis Foundation, Branch Office, Dushanbe, Tajikistan, [2]KNCV Tuberculosis Foundation, Technical Division, The Hague, Netherlands, [3]Ministry of Health, National TB Control Programme, Dushanbe, Tajikistan. e-mail: puck.pelzer@kncvtbc.org

Background: Tajikistan is a high MDR-TB burden country. To halt MDR-TB transmission in Tajikistan, finding the missing patients and placing (plus retaining) them on appropriate treatment is essential.

The goal of this study was to identify the numbers of TB patient losses along the patient cascade from the moment of accessing initial point of care until the end of appropriate treatment, ultimately aiming to inform the national TB program on areas for intervention.

Methods: We reconstructed the patient cascade in four districts and one sub-district: Gafurov, Rudaki, Turzunsade, Vose and Dushanbe, starting from the central public health centers (PHC) that provide diagnostic services to presumptive TB patients. Data from 2015 were extracted from registers in the central PHCs, laboratories, and TB treatment centers. Definitive and fuzzy matching was used to link the different databases. Linkage was done using STATA's "reclink" command.

Results: Among 4,320 unique patients, there were minor linkages between PHC and laboratory; PHC, laboratory and TB registers; and laboratory and TB registers. Of the 1,799 presumptive TB patients registered at the PHC, 229 were retrieved in the lab (Figure 1).



[Reconstruction Patient cascade Tajikistan, 2015]

At the lab, 1,992 new TB patients were registered from outside the PHC, bringing the total patients tested to 2,216. Of the 160 patients with a positive test result, 115 were enrolled on treatment (95 DS-, 20 DR-TB). Only two patients were found in all points of the full cascade.

Conclusions: Using several statistical software packages and linking methods, the analysis found minimal matches between the TB registers. Efforts are needed to improve the registration of patients and follow them through the cascade.

We advise repeating the present analysis for 2018 to investigate reasons for the losses. Individual digital case registers in which patients are followed from presumptive case status until end of treatment could benefit the patient cascade in Tajikistan.

PS-32-858-02 Impact of tuberculosis patient counselling and phone reminders on reducing pre-treatment loss to follow-up: a before-and-after study in Cameroon

E Onyoh,[1,2] C-Y Wu,[1] H-H Lin,[1] [1]National Taiwan University, Institute of Epidemiology and Preventive Medicine, College of Public Health, Taipei, Taiwan, [2]Cameroon Baptist Convention Health Services, AIDS Care and Prevention Program, Bamenda, Cameroon.
e-mail: jenny1004wu@gmail.com

Background: The attrition of tuberculosis (TB) patients after diagnosis (pre-treatment loss to follow-up, PLTFU) can undermine TB control efforts. Effective measures to prevent the occurrence of PLTFU remain to be discovered.
Methods: We conducted a retrospective and prospective cohort study in 39 TB diagnosis and treatment units (DTUs) in two regions of Cameroon, including 2160 bacteriologically confirmed pulmonary tuberculosis (PTB) cases. In the retrospective cohort study (Jul 2016 - Dec 2016), the TB laboratory and treatment registries were cross-matched to ascertain the time from TB diagnosis to treatment initiation.
In the prospective study (Feb 2017-Aug 2017), presumptive TB patients were counseled by DTU staff on the importance of returning for treatment, and laboratory-confirmed TB patients were contacted by phone reminders if they did not return within 3-7 days of diagnosis.
A post hoc analysis was conducted to evaluate whether the proportion of PLTFU (defined by not initiating treatment within 7 days) was significantly different in the retrospective and prospective cohorts.
Results: Among the 2160 PTB cases, 57.8% were males with mean age of 39.2 years. Control group (retrospective cohort) had a PLTFU of 17.5% (95% CI: 15.3-19.8) while the intervention group's PLTFU was 10.6% (95% CI: 8.9-12.6). The intervention group was associated with reduced PLTFU both in the univariable (crude odds ratio: 0.56, 95% CI: 0.44-0.72) and multivariable analysis (adjusted odds ratio [aOR]: 0.61, 95% CI: 0.47-0.79).
Other predictors of PLTFU included diagnosis by Xpert (aOR: 1.79, 95% CI: 1.22-2.63), travel time >30 min (aOR: 1.81, 95% CI: 1.38-2.38), and travel distance >30km (aOR: 1.81, 95% CI: 1.37-2.38).
Conclusions: Implementation of counseling of TB patients and phone call reminders as interventions may have a positive impact on the incidence of PLTFU in Cameroon.

PS-32-859-02 Factors delaying the diagnosis of pulmonary tuberculosis in a rural district of Punjab, India

R Singla,[1,2] J Goyal,[3,4] [1]Civil Surgeon Office, Dept of Health and Family Welfare, Rupnagar, India, [2]Baba Farid University of Health sciences, TB and Respiratory Diseases, Patiala, India, [3]District Hospital, Dept of Health and Family Welfare, Rupnagar, India, [4]PGIMER, Dept of Health and Family Welfare, Chandigarh, India.
e-mail: drromisingla@gmail.com

Background: The key determinant in quality of service in any TB control program is early diagnosis and adequate treatment. Delay in the same results in increased infectivity period, more extensive disease, complications and higher risk of mortality. Hence we analyse the factors delaying the diagnosis of pulmonary tuberculosis (PTB).
Methods: A cross sectional study was conducted in four Tuberculosis Units (TUs) in a district of Punjab in India between 2016 and 2017. Data collection was done by interviewing 200 patients of PTB using a structured questionnaire at the time of initiation of TB treatment. Total treatment delay was defined as the time interval between the onset of first symptom to the initiation of anti-TB treatment, and divided into patient level and healthcare level delay. The data cross tabulated, statistically analyzed using Pearson chi-square test to establish relationship between the studied variables and the type of delay.
Results: The mean total, patient level, healthcare level delays were 67.98 days, 49.68 days, 18.12 days respectively. The median patient level and healthcare delay was 30 days and 8 days respectively. Factors significantly related to patient level delay were low suspicion of TB by patients, substance abuse, smoking and chronic obstructive pulmonary disease (copd). Factors significantly related to healthcare level delay were improper treatment by informal healthcare sector at the onset of symptoms, low suspicion of TB by general physician upon patient´s first visit, inter-physician variability in chest x-ray interpretation, dependence on bronchoscopy, mantoux and sputum culture for diagnosis and lab error.
Conclusions: Targeted interventions in copd patients, drug addicts and smokers, awareness among public and private practitioners about free diagnostics and treatment of TB under national TB control program, sensitization of private practitioners to maintain high degree of suspicion of TB and following the World Health Organisation´s recommended investigations for diagnosis should reduce the delay.

PS-32-860-02 Delays and pathways to diagnosis and treatment among pulmonary TB patients in universal health coverage era in Bandung, Indonesia

BW Lestari,[1] S McAllister,[2] PF Hadisoemarto,[1] N Afifah,[3] PC Hill,[2] B Alisjahbana,[4] [1]Faculty of Medicine Universitas Padjadjaran, Public Health, Bandung, Indonesia, [2]University of Otago, Department of Preventive and Social Medicine, Dunedin, New Zealand, [3]Faculty of Medicine Universitas Padjadjaran, TB Working Group, Bandung, Indonesia, [4]Hasan Sadikin Hospital, Internal Medicine, Bandung, Indonesia. e-mail: bony.wiem@gmail.com

Background: The health seeking pathway of tuberculosis (TB) patients is usually characterized by an initial visit in the private sector then followed by multiple visits to different healthcare providers (HCPs), introducing delays in diagnostic and treatment initiation. The roll-out of universal health coverage (UHC) in Indonesia offers better access to TB services. We investigated risk factors associated with delays to diagnosis and treatment in the UHC era.

Methods: We consecutively recruited adults diagnosed with pulmonary TB in 30 randomly selected Community Health Centers (CHCs), five hospitals, and 320 Private Practitioners (PPs). Odds Ratio (OR) of factors associated with delays were calculated using multivariable logistic regression models.

Results: A total of 448 TB patients completed the interview: 138 (30.8%) in CHCs, 210 (46.9%) in hospitals, and 100 (22.3%) in PPs. Median age was 35 years (IQR 24-49); 56.7% were males. The median number of visits to HCPs before TB diagnosis was 4 (IQR 3-6). The odds of having a diagnostic delay was increased among patients 1) with less education (OR 5.4, 95%CI 1.3-22.8); 2) coughing more than a month (OR 7.3, 95%CI 4.6-12.0); 3) visited multiple HCPs (OR 3.4, 95%CI 2.0-5.6). Total delay was associated with no insurance and consulting private providers in the initial visit with OR of 1.7 (95%CI 1-2.8) and 2.1 (CI 1.1-4.2), respectively. The median times from the onset of first symptom to: 1) visiting a formal HCP was 30 days (IQR 14-61), 2) TB diagnosis was 63 days (IQR 35-113), and 3) starting TB treatment was 67 days (IQR 37-119). Almost half (49.8%) of patients experienced total delay.

Conclusions: Most TB patients suffer from diagnostic and treatment delays, increasing the risk for more severe disease and transmission. Improving PPs capacity to diagnose and treat TB, as well as health insurance coverage may reduce these delays.

PS-32-861-02 Implementing a standardised patient study to evaluate the quality of TB care in KwaZulu-Natal, South Africa

T Mkhombo,[1] J Boffa,[2,3] S Moyo,[1] J Chikovore,[4] A Salomon,[2] A Kwan,[5] B Daniels,[6] S Wu,[2] M Pai,[2,7] A Daftary,[2,8] [1]Human Sciences Research Council, HIV, AIDS, STIs, & TB Unit, Cape Town, South Africa, [2]McGill University, McGill International Tuberculosis Centre, Montreal, QC, Canada, [3]University of KwaZulu-Natal, Centre for Rural Health, Durban, South Africa, [4]Human Sciences Research Council, HIV, AIDS, STIs, & TB Unit, Durban, South Africa, [5]University of California, Health Policy, Berkeley, CA, United States of America, [6]World Bank, Development Research Group, Washington, DC, United States of America, [7]Manipal Academy of Higher Education, Manipal McGill Centre for Infectious Diseases, Udupi, India, [8]Centre for the AIDS Programme of Research in South Africa (CAPRISA), CAPRISA, Durban, South Africa. e-mail: tsatsawanimkhombo@gmail.com

Background and challenges to implementation: Studies utilising Standardised Patients (SPs) to evaluate quality of tuberculosis care have become increasingly common in high burden countries; however, few have been run in South Africa. SPs are trained to portray a scripted medical condition to healthcare providers in real-life settings. Given South Africa's high burden of tuberculosis and the high rate of HIV coinfection, we aimed to describe the implementation of a tuberculosis-related SP study in this setting.

Intervention or response: In preparation of study implementation,we consulted with teams that had run SP studies in India, China, Kenya and South Africa, and local physicians serving communities affected by TB.

Results and lessons learnt: Consultations identified unique challenges - SP recruitment and retention and physician consenting - which we addressed as follows.

We engaged the training programme at the local medical school as part of SP recruitment and introduced a two-day assessment of 23 applicants before commencing training with 12.

Eight SPs were selected based on their acting and recall skills. All were retained to project completion. Several SPs had personal experiences of tuberculosis, which strengthened project buy-in.

Consenting physicians for study participation required long waits and multiple visits, but provided the opportunity to understand and allay concerns, including how South African data would be interpreted by international collaborators. Buy-in from local Independent Practice Associations held more weight with consenting providers than support from national bodies.

Overall 54% of providers approached consented to participate (n=100/186). No adverse events reported regarding SP or provider safety, and only one of 65 providers surveyed correctly detected SP visits.

Conclusions and key recommendations: Engaging with training programmes in medical schools, pre-assessing applicants, and selecting SPs with lived experience of

tuberculosis helped in retaining highly trained SPs. Although time-consuming, the consent process helped to build understanding of the local context and trust with provider participants.

PS-33-C8 Can we find "missing persons" with TB through better quality services?

PS-33-862-02 Assessing the preparedness of health facilities for ambulatory DR-TB care in Zhytomyr, Ukraine

C Laxmeshwar,[1] M Duka,[1] LM Kolomiyets,[2] OV Siomak,[2] K Malakyan,[1] Y Terleeva,[3] N Lytvynenko,[4] VS Didik,[2] D Donchuk,[5] P Isaakidis,[5]
[1]Médecins Sans Frontières, Operational Centre Brussels, Zhytomyr, Ukraine, [2]Zhytomyr Regional TB Dispensary, Pulmonology, Zhytomyr, Ukraine, [3]Public Health Centre of the Ministry of Health of Ukraine, Department of TB programme Coordination, Kyiv, Ukraine, [4]National Institute of Phthisiology and Pulmonology Named after F. G. Yanovsky of National Academy of Medical Sciences of Ukraine, DR-TB Department, Kyiv, Ukraine, [5]Medecins Sans Frontieres, Southern Africa Medical Unit, Cape Town, South Africa. e-mail: dr.n.lytvynenko@gmail.com

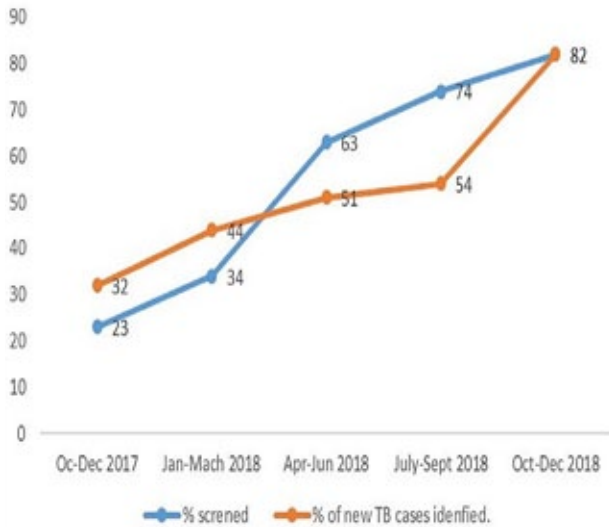
Background: Ukraine has a high burden of drug-resistant tuberculosis. As part of health reform, the country is moving from inpatient-care to ambulatory-care for TB. Médecins Sans Frontières (MSF), since May-2018 has been providing support for early ambulatory care in Zhytomyr Oblast. This study describes the preparedness of ambulatory care facilities in Zhytomyr oblast, Ukraine to provide good quality ambulatory care.
Methods: This is a retrospective analysis of routinely collected program data. Before discharge of every patient from the hospital, MSF teams assess the facilities available at the primary healthcare level using a checklist. The assessment includes human-resources (number, training and attitude), drug supply, comorbidities treatment, psychosocial support, infection control, services available and health-system factors.
Results: Between June-Dec 2018, we assessed 14 TB-units, 8 ambulatory points, 1 sanatorium and 12 health-posts. TB-units were run by TB-doctor. All facilities had at least one nurse. However, staff reported no backup available in case of holidays. Training opportunities were limited and staff were not updated about recent guidelines. Supply and storage of TB drugs was satisfactory at all facilities. However, non-TB drugs were not available anywhere and patients had to buy them. Treatment of comorbidities was managed by respective vertical programs and patients had to visit multiple facilities to access these. Availability of psychosocial support was inconsistent. Infection control was limited to use of respirators. Ventilation, especially during winter, was unsatisfactory. All facilities reported providing DOT. However, weekend DOT was available only in six facilities. Basic laboratory services were available at all TB-units, ECG in five (of 14), while audiometry was unavailable.
Conclusions: Ambulatory points in the study area had basic services available. However, they were insufficient for providing comprehensive care. Capacity of all facilities need to be strengthened, with HR, trainings, infrastructure and funds to ensure that ambulatory care is of good quality.

PS-33-863-02 Finding the missing TB cases in public health facilities using quality improvement (QI) approaches: lessons from Wakiso District, Uganda, East Africa

S Ntudhu,[1] A Burua,[2] S Zawede,[2] E Mwambazi,[3] K Mutesasira,[2] T Nsubuga,[2] N Kirirabwa,[2] A Nkolo,[2]
[1]University Research Company(URC), USAID Defeat TB Project, Technical, Kampala, Uganda, [2]University Research Co. LLC- USAID Defeat TB Project, Technical, Kampala, Uganda, [3]Wakiso District Local Government, Health, Kampala, Uganda. e-mail: syrusntudhu@gmail.com

Background and challenges to implementation: According to national tuberculosis (TB) prevalence survey 2015, about 40% of incident TB cases are "missed" annually in Uganda. Only 32% of the expected 1,366 TB cases were notified in Wakiso district between October and December 2017. Only 23% of the patients at outpatient departments (OPD) were screened for signs and symptoms of TB. The capacity of health workers to suspect, diagnose, initiate patients on TB treatment and document in HMIS tools was very low.
Intervention or response: In January 2018, USAID Defeat TB project supported Wakiso district to implement QI interventions in 25 health facilities which notify 80% of TB cases in Wakiso. Using data, gaps in quality of TB care processes were identified. A team of QI mentors with a clinician, Laboratory technician and community -Facility linkages expert visited targeted facilities monthly, formed work improvement teams and conducted on-site mentorships. Each health provider was mentored individually on how to use intensified case finding (ICF) guide, algorithms, and record in HMIS tools. ICF was used during health education and displayed at waiting areas. Presumptive TB patients were assigned unique codes, escorted for laboratory testing and results returned by laboratory staff. TB focal person was assigned to coordinate the team. Team met weekly to review performance and developed new actions to improve.
Results and lessons learnt: The proportion of patients at OPD screened for TB increased from 23% in Oct-Dec 2017 to 82% Oct-Dec 2018. As a result, 50% additional TB cases were identified, about three times higher as shown in the figure below. Suspicion index and capacity of health workers to use TB care guidelines increased.

Conclusions and key recommendations: Applying QI approaches, increased capacity of health providers to use TB guidelines to screen for TB, reporting thus a threefold increase in case finding within public health facilities. Scaling up this intervention will accelerate efforts to identify missed TB cases.



[Graph showing percentage of patients screened and TB cases identified in Wakiso district by quarter]

PS-33-864-02 Taking capacity building to the workplace increases TB programme efficiency and outcomes in West Coast District, Western Cape, South Africa

I Cillie,[1] P Ziki,[2] G Jagwer,[2] [1]University Research Company, West Coast, Western Cape, Koekenaap, South Africa, [2]University Research Co., LLC - South Africa, National Office, Pretoria, South Africa. e-mail: inac@urc-sa.com

Background and challenges to implementation: Building capacity in Department of Health facilities remains challenging in West Coast, South Africa. Staff numbers are low, making it impossible to take staff out of facilities for capacity building . Identifying gaps is easy but finding ways to build capacity to address challenges remains problematic. West Coast district implemented the low-dose, high frequency model of capacity building.
Intervention or response: The LDHF model comprises in-service training and mentoring. Facilities are visited monthly for evaluations of the TB program and identification of gaps and challenges. In-service training sessions last 30 to 90 minutes and address specific challenges identified. Staff in TB rooms are trained using latest guidelines and treatment regimens while they are working with patients. Staff practically exercise what they have been trained on, and facilitators are available for questions. Mentoring is done monthly to ensure that healthcare workers implement what they were trained on in previous visits.

Results and lessons learnt: Baseline audits of the TB program were done in nine facilities in early 2018. Five out of nine facilities show an average score of lower than 60%, with the lowest one at 34%. In total, 66 LDHF sessions were conducted in nine facilities. The LDHF model was used to capacitate 29 staff members, of which 11 participated in more than four sessions each. After nine months, audits were repeated.
All nine facilities scored higher than 60%, with the highest score being 84%. Four of five facilities showed improvements between 22% and 34% as indicated in the table below:

Name of Facility	First Audit Score	Second Audit score
Malmesbury CDC	58%	82%
Piketberg Clinic	68%	73%
Citrusdal Clinic	58%	69%
Clanwilliam Clinic	40%	74%
Lambertsbay Clinic	56%	84%
Klawer Clinic	59%	65%
Vredendal Central Clinic	34%	61%
Vredendal North Clinic	74%	80%
Lutzville Clinic	65%	67%

[Facility Audit Outcomes]

Conclusions and key recommendations: The LDHF model address the "know-do gap" at intermittent intervals and it is sustainable. Implementation of this capacity building model has positive impacts on TB service delivery. Staff do not need to leave facilities, and services can proceed as normal. The model will be rolled out to all facilities in West Coast.

PS-33-865-02 Patient pathway analysis of presumptive pulmonary tuberculosis patients consulting a tertiary teaching hospital in Karnataka, India

A Kibballi Madhukeshwar,[1] R Raghavendra,[1] [1]Yenepoya Medical College, Yenepoya (Deemed to be University), Community Medicine, Mangalore, India. e-mail: docakshay@gmail.com

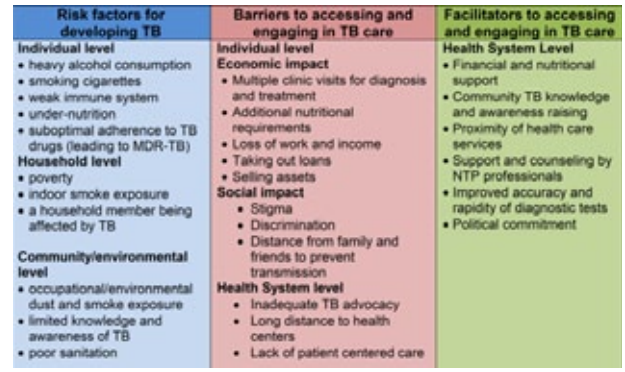
Background: Patient Pathway Analysis (PPA) describes the steps taken by patients with tuberculosis (TB) take from initial care visit to cure. This study was conducted to identify the pathways of care and examine the alignment of care seeking with service availability using the PPA approach among the presumptive pulmonary TB (PPTB) patients consulting a tertiary care hospital.
Methods: Cross sectional study was conducted among 227 PPTB patients consulting or admitted in Medicine and Chest Medicine departments in a tertiary teaching hospital in Mangaluru, Karnataka, India during August and September 2018. Patient interviews were conducted using a pre-tested, semi-structured questionnaire. The health facilities accessed by the PPTB patients were cat-

egorized using standardized naming convention used in PPA approach. Data was analyzed using IBM SPSS Inc, Chicago, USA; Version 23.0.
Results: About half of the study participants had consulted atleast two health care providers (range 1-7) before reaching tertiary care hospital. More than half of the study subjects (53.7%) had first consulted a private hospital for their symptoms. A total of 31 pathways were identified (figure) including consultation with 4-5 providers and also the same type of provider more than once. Easy access and proximity to home was cited by the patients to contact a public healthcare provider ($p< 0.05$). Private providers were preferred because of service availability and belief in the provider. Availability of sputum testing facility in Level 1 facilities was negligible. About one third of the level 2 facilities had sputum testing and X-ray facilities.
Conclusions: This study revealed some highly tortuous pathways of care in PPA. Sub- optimal availability of diagnostics at the first and second level of health care system could effect the care of the PPTB patients. National TB program needs to plug these gaps to achieve universal access to TB care.

PS-33-866-02 Barriers and facilitators to accessing and engaging in tuberculosis care: a qualitative study from Nepal

K Dixit,[1] B Rai,[1] SC Gurung,[1] R Dhital,[1] MK Sah,[1] TP Aryal,[1] RN Pandit,[1] G Majhi,[1] M Caws,[1,2] T Wingfield,[2,3,4] [1]Birat Nepal Medical Trust, Public Health, Kathmandu, Nepal, [2]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom, [3]Karolinska Institutet, Social Medicine, Infectious Diseases, and Migration (SIM) Group, Department of Public Health Sciences, Stockholm, Sweden, [4]Royal Liverpool and Broadgreen University Hospitals NHS Trust, Tropical and Infectious Diseases Unit, Liverpool, United Kingdom.
e-mail: kritika.dixit07@gmail.com

Background: People affected by TB (PATB) face multiple barriers along the pathway of illness, diagnosis, and treatment. As part of a larger project to design a locally-appropriate socioeconomic support intervention for TB-affected households, this study examined the perceptions of patients and key stakeholders on the main barriers and facilitators to accessing and engaging in TB care in Nepal.
Methods: This qualitative study in four districts of Nepal consisted of six focus group discussions (FGDs) with 46 purposively selected participants including: people currently under treatment or who had recently completed treatment for TB at the Nepal National TB Program (NTP) health facilities (PATB, n=21), seven of whom were female, and seven of whom had multi-drug resistant TB) and key stakeholders currently unaffected by TB including community leaders (n=7), civil society organizations (n=6), and NTP TB healthcare professionals (n=12). FGDs used semi-structured questions, were audio recorded, transcribed into Nepali, and translated into English. Major FGD themes and sub-themes relating to risk factors for developing TB disease, and barriers and facilitators to TB care, were identified and analysed using NVivo-12.
Results: Risk factors for developing TB identified across all FGDs included those at an individual level, household level and community and/or environmental level (Figure). Common barriers to access and engagement in TB care identified across all FGDs were mainly social and/or economic barriers at an individual or health system level (Figure). Facilitators to accessing and engaging in care identified across all FGDs included predominantly financial, nutritional and counselling support, and improvements in access to rapid diagnostics and quality care at a health system level (Figure).
Conclusions: People affected by TB face social and economic hardship throughout their illness and during treatment in Nepal. This could be alleviated by locally-appropriate socioeconomic support integrated into NTP activities.



[Risk factors for having TB, barriers and facilitators to accessing and engaging in TB care in Nepal]

PS-33-867-02 Why don't presumptive TB patients reach the microscopy centre? Findings from Tamil Nadu, a southern Indian state

R Poovalingam,[1] R Thiagesan,[1] R Ananthakrishnan,[1] N Krishnan,[1] S Mohanty,[2] S Pandurangan,[3] [1]REACH (Resource Group for Education and Advocacy for Community Health), Program Management Unit, Chennai, India, [2]The Union, Project Coordination, Delhi, India, [3]The Union, M&E, Delhi, India.
e-mail: ramyardr.reach@gmail.com

Background: One of the cornerstone for achieving the END TB goals outlined in the National Strategic Plan is active case finding among vulnerable and marginalized populations. There were several challenges in passive case finding strategy including limited access to TB care services, delayed diagnosis etc. As part of Project Axshya (Global Fund project) implemented in India, door to door screening of all individuals at the house-

hold level is being carried out among the key affected communities in a district. One of the key challenge in the implementation of active case finding is that there is a drop out of people with TB symptoms along the diagnostic cascade.

Methods: A cross sectional study was undertaken in selected areas in 5 districts of Tamil Nadu to determine the reasons presumptive TB patients detected through Project Axshya did not undergo diagnosis. All those who were identified as presumptive TB and referred to the nearest TB diagnostic center but did not go to the centers were followed up.

Results: Among the 231 respondents, 56% were males and 65% resided in rural area. 33% of the respondents had a monthly income of 100-150 USD. While 43% of the respondents said they are not interested or unwilling for further testing, 28% of the respondents said they accessed a private practitioner and 29% said they have no symptoms.

Conclusions: Targeted outreach though active case finding efforts to key affected communities is critical to ensure equitable, affordable and improved access to TB diagnostic services. To maximize case finding through this strategy and for program efficiency, it is important to understand the community level challenges as outlined in the study.

Stigma	25%
No Time	52%
No Family Support	35%
Repeated Visits to DMC	20%
Time Delays at DMC	9%
Unfriendly Staffs at DMC	12%

[Table 1: Reasons for Not Willing to Undergo further testing (Multiple Choice) given in Percentage]

PS-33-868-02 Scaling up of specimen transport mechanism: a continuous effort to ensure greater access to quality TB diagnosis

J Sugiharto,[1] A Juan,[1] W Wahyuningsih,[1] K Andriani,[1] F Damanik,[1] N Sulaiman,[2] [1]Yayasan KNCV Indonesia, Technical Division, Jakarta, Indonesia, [2]National Tuberculosis Program of the Ministry of Health Republic of Indonesia, PMU, Jakarta, Indonesia.
e-mail: jhon.sugiharto@kncvindonesia.org

Background and challenges to implementation: In Indonesia, the current diagnostic algorithm suggests Xpert as the main TB diagnostic tool whenever access to the machine is available. In 2017, The National TB Program had installed 515 Xpert machines in 324 districts in Indonesia. Despite the rapid expansion, access to the Xpert test were limited reflected in low utilization of the machines. A robust specimen transport mechanism needs to be in place. Yayasan KNCV Indonesia has supported the MOH in developing SITRUST, a mobile-based application to aid specimen transport in collaboration with the national post service as the courier provider. Upon successful implementation, the mechanism needs to be expanded beyond the pilot area, especially area with difficult terrain and limited internet connection as well as among private healthcare providers.

Intervention or response: In 2017, the mechanism was piloted in 50 districts. We used SITRUST's dashboard to monitor all specimen transport activities. Expansion kit comprising manuals and training materials were provided to support expansion to other areas. SMS-based version were also developed to support implementation in areas where internet connection remains a challenge.

Results and lessons learnt: Within 1.5 year since its roll-out, SITRUST has been expanded to 156 districts covering 30% of total districts in Indonesia. Expansion in 75 districts were initiated and self-funded by the local governments. Besides central funding from the NTP, SITRUST expansion were also supported by different donors and private entities interested in the success of the mechanism. In Q1 2019, a total of 4,378 facilities (including private healthcare providers) have been trained, contributing a total of 144,681 specimens sent via SITRUST.

Conclusions and key recommendations: SITRUST is an easy-to-scale specimen transport mechanism that can support the national effort to rapidly expand access to Xpert. Its flexible and user friendly interfaces, real-time monitoring system and new SMS-based version will ensure better access to quality TB lab.

[Map of SITRUST Implementation]

PS-33-869-02 Finding the missing TB cases through identification of presumptive TB patients in health facilities: the case of Kapiri Mposhi, Zambia, July-Dec 2017

C Chongo,[1] M Makasa,[2] E Mwangala,[1] M Mwangala,[3] V Mfungwe,[4] T Gachie,[5] J Bwembya,[6] R Kumar,[7]
[1]Kapiri Mposhi District Health Office, TB Department, Lusaka, Zambia, [2]University of Zambia School of Public Health, Community and Family Medicine, Lusaka, Zambia, [3]Kapiri Mposhi District Health Office, Health Information Systems, Lusaka, Zambia, [4]Kapiri Mposhi District Health Office, Path Eradicate TB, Lusaka, Zambia, [5]Zambia Aids Related TB Projects (ZAMBART), University of Zambia, Research, Lusaka, Zambia, [6]PATH Eradicate TB Zambia, TB Department, Lusaka, Zambia, [7]Zambia Aids Related TB Projects (ZAMBART), University of Zambia, TB Department, Lusaka, Zambia. e-mail: chongochama1@yahoo.com

Background: In 2017, Zambia failed to notify a third of incident cases. According to the National TB Prevalence survey (2013-2014) the prevalence of bacteriologically confirmed tuberculosis in Central Province was 200 - 900/100,000. In 2017, Kapiri Mposhi, a district in Central Province, notified 145/100,000 cases and it is unclear whether this reflects the true prevalence or indicates under-reporting. This study ascertained the level of under-reporting in the TB diagnostic cascade in 4 TB diagnostic health facilities of Kapiri Mposhi from July - December 2017.
Methods: We reviewed paper medical records for all adult patients (>15yrs) who were recorded in the outpatient or inpatient department registers with a diagnosis of respiratory tract infections or pneumonia. We reviewed the medical records for symptoms suggestive of TB: cough of any duration, fever, night sweats, weight loss, and chest pain. We calculated the proportion of cases with at least 1 symptom suggestive of TB who were recorded in the facility's TB presumptive, laboratory, and treatment registers.
Results: Of 1,166 records reviewed from the inpatient and outpatient registers, 1,158 (99.3%) patients had at least 1 symptom suggestive of TB. Of these, only 24 (2.1%) were recorded in the presumptive registers, and 18(1.6%) were recorded in the laboratory registers. Of patients recorded in the laboratory register, 2 were bacteriologically confirmed and both were recorded in the treatment registers. An additional 3 patients, whose medical records we reviewed, were recorded in the treatment registers, but were not recorded in either the presumptive or laboratory registers.
Conclusions: The majority of patients with symptoms suggestive of TB were missed at the screening point of entry in the TB care cascade in all 4 facilities. Staff should be re-trained to screen patients presenting to any department for TB disease, and how to correctly record these patients in all TB-related registers.

PS-33-870-02 Determinants of delay on seeking care for TB in Bambey Health District, Senegal in 2017

AN Fall,[1] EHM Dioukhane,[2] AO Diallo,[1] M Nelson,[3] B Diallo,[1] JSN Kally,[4] A Dione,[5] [1]Plan International Senegal, Global Fund Project, Dakar, Senegal, [2]Plan Canada, Global Fund Project, Toronto, ON, Canada, [3]Plan International Senegal, Global Fund Project, Toronto, ON, Canada, [4]Heath District of Bambey, Ministry of Health, Bambey, Senegal, [5]Heath District of Bambey, Health, Bambeye, Senegal.
e-mail: kalystandeurnabi@yahoo.fr

Background and challenges to implementation: In Senegal, the diagnosis of tuberculosis faces two main problems that help keep the disease spread: under-screening and delayed diagnosis.
The overall goal of this study was to identify the determinants of delayed diagnosis of TB in the Bambey Health District in 2018.
Intervention or response: A comprehensive, cross-sectional, descriptive and analytical study of patients with pulmonary tuberculosis was conducted in the Bambey Health District from 3 to 7 September 2017. The data were collected at the Bambey Treatment Center with the help of a semi-structured questionnaire in an individual interview after informed consent. The capture and analysis were done using EPI INFO software version 3.5.3 with a 95% (p=0.05) confidence interval.
Results and lessons learnt: A total of 229 patients were enrolled including 81.6% of TPM +. The average age was 35.1 years; sex ratio 2.7. The median consultation time was 30 days. This delay was statistically related to educational attainment (OR= 2.8), the usage of traditional medicine (OR = 3.9), self-medication (OR = 2.7), 95.2% of patients banalized the major TB sign (coughing), 84.8% of patient are unaware of the existence of treatment and 70,1 don't know the treatment is free.
Conclusions and key recommendations: Early diagnosis of tuberculosis requires public awareness of the disease, training of health care providers and collaboration between traditional healers and health care providers.

PS-33-871-02 Quality improvement approach to increasing paediatric TB case detection in urban settings of Uganda

H Kyokutamba,[1] K Mutesasira,[1] A Ocwero,[1] A Nkolo,[1]
[1]University Research Co., LLC (URC), Technical, Kampala, Uganda. e-mail: kyokutambahellen@yahoo.com

Background and challenges to implementation: In Uganda, Childhood Tuberculosis(TB) is a major cause of morbidity and mortality yet over half of the cases are not diagnosed/notified. In 2014, the pediatric TB case detection was 7.5% in Uganda compared to the expected 15%. Similarly, in Ugandan urban districts of Kampala, Mukono and Wakiso, the pediatric TB case detection was low at 8% (Oct-Dec 2017). The USAID Defeat

TB project has been supporting the urban Districts to improve pediatric TB case detection using Quality Improvement (QI) methods.

Intervention or response: A QI collaborative of 10 health facilities was set up in January 2018 to demonstrate interventions for improving pediatric TB case detection. Onsite training and mentorship was done followed by setting QI teams and projects to improve screening and clinical evaluation for pediatric TB. Monthly QI meetings and mentorship on pediatric TB were held to brainstorm on challenges and interventions to strengthen the cascades of care. The main gap identified was limited capacity and confidence to make a pediatric TB clinical diagnosis. The QI changes implemented included formation of clinical evaluation teams, phone call and WhatsApp learning network. These interventions have been scaled up to 20 more health facilities.

Results and lessons learnt: The screening for pediatric TB at the 10 collaborative sites improved from 4% to 88%, cases notified from 45 to 82 and 8 to 29 at scale up sites (Jan 2018-Feb 2019). The pediatric TB case detection in the urban districts of Kampala, Mukono and Wakiso has almost doubled from 8% in Oct-Dec 2017 to 15% Jan-Mar 2019.

Conclusions and key recommendations: QI approach to improve capacity for pediatric TB diagnosis and strengthen pediatric TB cascades of care improves pediatric TB case detection in addition to training on diagnosis and management of paediatric TB.

PS-33-872-02 Is joint effort for elimination of TB (JEET) project making any difference in urban project districts? Comparative crude analysis from five Indian provinces

V Ghule,[1] D Parija,[1] A Kalra,[1] A Lone,[1] T Showket,[1] S Sarin,[1] S Chadha,[1] [1]Foundation for Innovative & New Diagnostics, TB and Communicable Diseases, New Delhi, India. e-mail: drvaibhavghule@gmail.com

Background and challenges to implementation: Despite being declared as notifiable disease since 2012, quantum & quality of TB patient notification from private healthcare sector is still negligible in India. Due to the diversity of health care sector across nation, challenges and local solutions to enable notification practices also defer regionally. Government of India with support from multiple sources has been implementing various private sector engagement interventions subnationally.

Intervention or response: Joint Effort for Elemination of TB (JEET) is one such Global Fund supported project at national level being implemented by varius non governmental organizations during Jan2018-Mar2021. JEET project has two engagement models called as patient provider support agency (PPSA) for urban cities and PPSA lite model for semi-urban cities. We compared TB Notification details of 21 reporting districts for Apr-Sep and Oct-Mar periods for analysis.

Results and lessons learnt:

1. There's significant increase in TB patients notified from private health sector (rise by 62%) during initial project phase (Apr'18toSep'18) and six months after implementation (Oct'18toMar'19) as compared to last year.
2. Number of private health facilities registered on Nikshay who did notify TB patient has increased by >75% over Apr'18toMar'19 as compared to last year.
3. Intervention closure phase of similar projects encouraging private sector TB notifications in these districts during Oct'18toDec'18 might have adversely affected TB notifications.

Conclusions and key recommendations: Strategic resource investments in terms of any project interventions are known to have positive impact on overall TB patient notifications as well as quantum of private sector engagement at large, while negative impact is observed during transition phases especially when these transitions are not taken up well by existing public health systems. Though the exact incremental yield may not be directly & entirely attributable to project interventions, absence of such efforts does clearly impact the overall notifications. Pre-post analysis of geographies with project transition holds further scope of qualitative research.

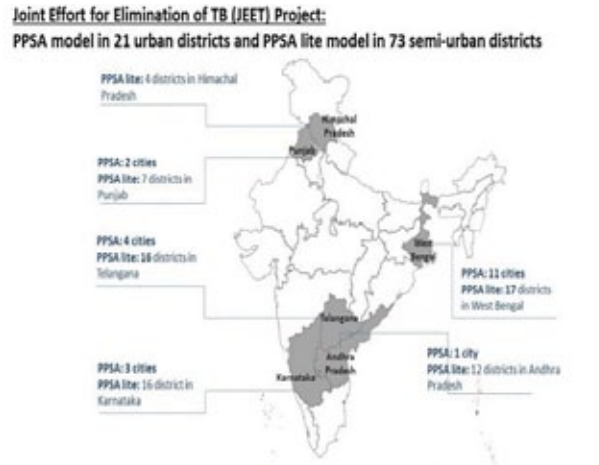


Table1: Comparative analysis of TB patient notifications from private health sector in 21 urban districts across five provinces covered under JEET project, India

Indicator? / Period ?	Apr'2017 to Sep'2017	Apr'2018 to Sep'2018	Oct'2017 to Mar'2018	Oct'2018 to Mar'2019
TB patient Notifications (Pvt)	7,255	11,808	6,093	11,897
TB patient Notifications (Pvt) – Range	1 to 273	1 to 769	1 to 352	1 to 363
Number of Pvt health facilities notifying at least 1 patient	618	1,164	665	1,171

[Comparative analysis of TB patient notifications from private health sector in 21 urban districts ac]

PS-33-873-02 Reducing pre-treatment costs incurred by tuberculosis patients through community-based active case finding in Ho Chi Minh City, Viet Nam

RJ Forse,[1] LNQ Vo,[2,3] AJ Codlin,[4] LMT Hoang,[5] NV Nguyen,[6] HB Nguyen,[6] K Lonnroth,[7] SB Squire,[8] M Caws,[9,10] N Teixeira De Siqueira-Filha,[9] [1]Friends for International TB Relief, Operations, Ho Chi Minh City, Viet Nam, [2]Friends for International TB Relief, Board of Directors, Hanoi, Viet Nam, [3]Interactive Research and Development, Viet Nam Country Office, Hanoi, Viet Nam, [4]Friends for International TB Relief, Research and M&E, Ho Chi Minh City, Viet Nam, [5]Ho Chi Minh City Public Health Association, Operations, Ho Chi Minh City, Viet Nam, [6]Vietnam National Lung Hospital, Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [7]Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden, [8]Liverpool School of Tropical Medicine, Clinical Tropical Medicine, Liverpool, United Kingdom, [9]Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, United Kingdom, [10]Birat Nepal Medical Trust, Operations, Kathmandu, Nepal. e-mail: rachel.forse@tbhelp.org

Background: Tuberculosis (TB) can have an impoverishing impact on patients and their households. In response, the WHO included a target of 0% of TB-affected families facing catastrophic costs (spending >20% of annual household income) in the End TB Strategy. More evidence is needed on how best to achieve this target and the role that active case finding (ACF) can play.

Methods: The study was conducted in six districts of Ho Chi Minh City, Viet Nam. Patients diagnosed through ACF (household & close contact investigations and systematic screening of vulnerable populations) and passive case finding (PCF) were included. 102 patients (52 ACF and 50 PCF) were consecutively recruited for the cost survey. WHO's patient costing questionnaire was applied during the intensive phase of treatment to collect pre-treatment costs (direct medical, non-medical and indirect costs). Median and mean costs were calculated and compared between the ACF and PCF patients using the Mann-Whitney U-test and Student's T-test. We fitted a generalized linear model to measure the association between pre-treatment costs and case finding model, as well as other patient covariates.

Results: Median pre-treatment costs were lower in the ACF cohort compared with PCF (USD30.70 vs USD161.40, p< 0.001). Median direct costs (USD16.40 vs USD76.60, p< 0.001) and indirect costs (USD5.70 vs USD47.50, p< 0.001) were also lower for ACF patients. Adjusted for age, sex and secondary parameters, patients from the PCF cohort incurred on average USD239.26 (USD83.00-USD395.53; p=0.003) higher costs during the pre-treatment period.

Conclusions: This study suggests that ACF interventions resulted in 81% lower pre-treatment costs and can contribute to the elimination of catastrophic cost incurrence in TB-affected households. While our parallel study on health system cost requirements for ACF scale-up suggested the need for extensive investment, programs should nevertheless consider expanding ACF to provide person-centered TB care and to meet the End TB Strategy targets.

Cost items	ACF cohort (n=52)		PCF cohort (n=50)		P-value[1]
	Mean (95% CI)	Median (IQR)	Mean (95% CI)	Median (IQR)	
Direct medical	44.2 (23-65)	14 (4-45)	204.5 (106-303)	74.1 (31-227)	<0.001
Direct non-medical	5.3 (2-8)	2.1 (1-5)	13.7 (5-22)	51. (2-12)	0.008
Total direct	49.5 (28-71)	16.6 (6-56)	215.9 (114-318)	76.6 (33-233)	<0.001
Total indirect	43.0 (22-64)	5.7 (3-39)	102.0 (67-137)	47.5 (10-148)	<0.001
Total pre-treatment costs	**92.5 (59-127)**	**30.7 (13-133)**	**317. (201-434)**	**161.4 (58-435)**	**<0.001**

[1] Mann-Whitney U test

[Mean and median pre-treatment costs by case finding model]

PS-34-B2 Curing TB: self-cure, surgery, new medications

PS-34-874-02 Transmission pattern of Mycobacterium tuberculosis based on whole genome sequence analysis

L Fu,[1] Y Wang,[1] W Wang,[1] [1]Fudan University, Department of Epidemiology, Shanghai, China. e-mail: 2860293625@qq.com

Background: Rural residents in China are at a higher risk of tuberculosis transmission and infection than urban residents. We aimed to combine genomic, spatial and epidemiological data to describe the dynamics of tuberculosis in a rural setting with relatively stable residents.

Methods: We did a community-based study of bacteriologically-confirmed Mycobacterium tuberculosis isolates in Changshan and Jiangshan County, Zhejiang, China. Social-demographic data, medical records and geographical data were collected through questionnaire survey. Whole-genome sequencing was carried out by second-generation sequencing. SNPs were called and the differences of SNPs between every two strains were analyzed. The multi- variate Logistic regression analysis was used to analyze the risk of clustering. Finally, we used genomic, spatial, and epidemiological data to clarify the epidemiological links and analyze the pattern of tuberculosis transmission among rural residents.

Results: Between July, 2015, and June, 2018, 622 cases of bacteriologically-confirmed tuberculosis were recruited. 55.3% were elderly and 73.5% were farmers. A total of 35061 SNPs was called by WGS of 390 strains, and the difference of 50 SNPs was used as the threshold for judging the clustering of strains, forming 21 clusters. 18 patients were from the same town and shared geographical epidemiological link. The median geographical distance between paired patients with ≤50 SNPs was 11.98 km.

Logistic regression analysis showed the exposure history to tuberculosis was significantly associated with recent transmission. Among the total 21 clusters, 8 were identified with confirmed-epidemiological links of sharing the same residential communities, workplace, classroom or game rooms.
Conclusions: The transmission pattern of tuberculosis in rural areas is mainly endogenous reaction of long-term infection. Patients with exposure history to tuberculosis showed higher risk of clustering. Recent transmission occurred in a relatively small geographical range within close contacts, suggesting prevention and treatment for close contacts of tuberculosis patients should be conducted.

PS-34-875-02 Self-cure of Mtb infection: implications for a population at-risk and lifetime risk of reactivation of the disease

JC Emery,[1] AS Richards,[1] KD Dale,[2,3] CF McQuaid,[1] RG White,[1] JT Denholm,[2] RMGJ Houben,[1] [1]London School of Hygiene & Tropical Medicine, TB Modelling Group, TB Centre and Centre for the Mathematical Modelling of Infectious Diseases, Department of Infectious Disease Epidemiology, London, United Kingdom, [2]Melbourne Health, Victorian Tuberculosis Program, Melbourne, VIC, Australia, [3]The University of Melbourne, Department of Microbiology and Immunology, Melbourne, VIC, Australia. e-mail: jon.emery@lshtm.ac.uk

Background: It is generally assumed that individuals with a latent tuberculosis infection (LTBI) remain at lifelong risk of active disease via distal reactivation. However, there is substantial evidence that spontaneous self-cure of LTBI can occur, implying a smaller population at risk of developing active disease. In this work we explore the quantitative implications of such self-cure on tuberculosis (TB) epidemiology.
Methods: We developed a cohort model describing the natural history of recently infected individuals. Ranges for self-cure parameters were inferred from various data sources, such as the proportion of individuals with evidence of previous infection in whom viable bacilli could not be identified post-mortem. We then estimated the population at-risk and their lifetime risk of active disease, comparing to a standard scenario of no self-cure. Finally, we used annual risk of infection data to re-examine the at-risk populations in India, China and Japan.
Results: We estimate that 3-10% of individuals self-cure LTBI within 2 years of infection, and 21-52% within 10 years. In this scenario, the cumulative risk of active disease in the first two years following infection amongst individuals that retain a viable infection is 7.8-8.0%, and 4.5-9.5% thereafter, compared to 7.8% and 3.2% in the standard scenario. Our estimates for the current populations at risk of developing active disease in India, China and Japan are then 45-90% lower than under the assumption of no self-cure.
Conclusions: Our model demonstrates how the population with viable LTBI may be markedly smaller than is generally assumed, with individuals retaining a viable infection at correspondingly greater risk of active disease. The ability to discern such individuals, particularly within established high-risk groups, could dramatically improve the targeting of preventive programmes. It is therefore critical that we better understand the natural history of LTBI to bring TB elimination within reach of feasibility.

PS-34-877-02 Transmission of Beijing genotype/ST1 among multidrug-resistant tuberculosis isolates in extra-pulmonary tuberculosis cases

AK Maurya,[1] S Kant,[2] VL Nag,[3] K Srivastava,[2] TN Dhole,[4] [1]All India Institute of Medical Sciences (AIIMS), Microbiology, Bhopal, India, [2]King George Medical University, Respiratory Medicine, Lucknow, India, [3]All India Institute of Medical Sciences (AIIMS), Microbiology, Jodhpur, India, [4]Sanjay Ghandi Post Graduate Institute Medical Sciences, Microbiology, Bhopal, India. e-mail: anand.microbiology@aiimsbhopal.edu.in

Background: The emergence and spread of multidrug-resistant tuberculosis (MDR-TB) is a major public health problem. Beijing genotype is a major cause of tuberculosis in this high incidence region of Asia. Beijing genotype of Mycobacterium tuberculosis is contributing to the epidemic through its widespread presence and associated with treatment failure and relapse. A very limited data is available on MDR-TB among Extrapulmonary tuberculosis (EPTB) cases. The aim of this study to analyze the transmission of MDR-TB strains from extra pulmonary tuberculosis cases at tertiary care centre.
Methods: This study was prospective manner; seven hundred fifty six specimens were collected from suspected cases of EPTB cases in two tertiary care hospitals in Northern India. Specimens were processed for Ziehl-Neelson (ZN) staining, culture & first line drug susceptibility test (DST) using BacT/ALERT 3D system. *M. tuberculosis* DNA was extracted using a recommended method for spoligotyping and profiles were compared to databases.
Results: Of these 164 *M. tuberculosis* complex isolates, 100(60.9%) strains were fully susceptible and 64(39.1%) strains were resistance. We noted prevalence of MDR-TB among EPTB was 22 (13.4%). Spoligotyping showed that the majority of MDR strains belonged to the ST1/Beijing type.
Conclusions: The prevalence of MDR-TB among EPTB was 13.4% and rising trend of MDR-TB has been reached an alarming level. Beijing type (ST1) was most predominant genotype from MDRTB among EPTB cases and it showed strongly associated with drug resistance strains. Circulation of MDR *M. tuberculosis* isolates of the ST1/Beijing type continues to critically influence the current situation with the MDR-TB control in this region.

PS-34-878-02 First results from six months of using conventional regimens with bedaquiline for pre-XDR-TB patients in Ukraine

N Lytvynenko,[1] M Pogrebna,[1] J Senko,[1] O Chobotar,[1] N Grankina,[2] [1]National Institute of TB and Lung Diseases, MDR-TB Research Department, Kyiv, Ukraine, [2]Regional TB Dispensary, MDR-TB Department, Dnipro, Ukraine. e-mail: dr.n.lytvynenko@gmail.com

Background: Treatment efficacy for MDR-TB patients are not high in Ukraine: only 51% of them were cured (WHO report). Since July 2017 National Institute of Phthisiology and Pulmonology (supporting Challenge TB project (PATH) financing USAID) is implementing innovative treatment including Bedaquiline for pre-/XDR-TB patients.

The objective of this study is to describe first results at the 6-th months after start of treatment with Bedaquiline for pre-/XDR-TB patients in Ukraine.

Methods: This is a retrospective analysis of the 192 patients with pre/XDR-TB who were started treatment between July 2017 to December 2018. 146 (76.0%) of patients had results at the 6th month after start of treatment, other patients continue treatment for less than 6 months at the moment of analysis. The step-by-step principals of the prescribing not less 4 effective ATDs in conventional treatment regimens were used. Treatment regimens included bedaquiline, linezolid, clofazimine - for all patients, cycloserine - in 62,3 %, thioamide - in 42,9 %, carbapenems - in 29,9 %, Pas - in 62,3 %, injectable ATDs - in 29,9 % patients, respectively.

Results: At the end of 6 month of treatment was received: culture conversion - in 135 (92,5%), LTFU - in 7 (4,8%), died - in 3 (2,1%) of patients.

Most results of the culture conversion were determined at the 1st or 2nd month after start of treatment - in 64 (45,4%) and 43 (30,5%) patients, and at the 3th, 4th, 5th and 6th months - only in 17 (12,1%), 12 (8,5%), 3 (2,1%) and 2 (1,4%) patients, respectively.

Conclusions: First results of the using conventional regimens with Bedaquiline for pre-/XDR-TB patients are very high in Ukraine. At the 6-th months after start of treatment culture conversion were determined in 92,5% of patients without the result of "failure" among patients of the studied cohort.

PS-34-879-02 Short 12-month regimen with intravenous linezolid for MDR-TB: treatment outcomes and 24-month follow up results

N Lytvynenko,[1] M Pogrebna,[1] J Senko,[1] O Chobotar,[1] N Grankina,[2] [1]National institute of Phthisiology and Pulmonology Named after F.G. Yanovsky NAMS of Ukraine, MDR-TB Research Department, Kyiv, Ukraine, [2]Regional TB Dispensary, MDR-TB Department, Dnipro, Ukraine. e-mail: dr.n.lytvynenko@gmail.com

Background: The treatment outcomes among MDR-TB patients are poor (successful treatment was only in 55% patients in 2016 cohort in the world and 51 % - in Ukraine). Short MDR-TB regimens recommended by WHO in 2016 are not applicable for Ukraine due to high-level of resistance to second line ATDs in Ukraine among new MDR-TB cases. The aim: improve the treatment outcomes and 24 month follow up results among MDR- TB patients using the short 12-month regimen.

Methods: In the prospective observational "case-control" study were included 86 patients with new MDR-TB cases and with susceptibility to second line ADTs. Patients of the first group (n=43) received following short 12-month MDR-TB regimen: during intensive phase (20 weeks): linezolid (0.6 g), levofloxacin (1.0 g), kanamycine (1.0 g) and pyrazinamide, prothionamide, cycloserine; continuation phase (28 weeks) - without kanamycine. The patients of the second group (n=43) received conventional 20-month regimen (without linezolid). Linesolid and levofloxacin were prescribed as a step-by-step therapy: intravenous until the smear conversion after that - oral in ambulatory treatment.

Results: Among patients, who were treated by short MDR-TB regimen, comparing to the conventional treatment regimen the success rate increased from 30 (69,7%) to 41 (95,4 %)). The adverse events registration wasn`t significantly higher -in 69,8 % vs. 58,2 %, respectively. Among success rate patients, relapses during 24 month follow up period were only in 5 (11,6 %) patients after end of conventional 20-month regimen. So, failure of treatment (included relapses) had 24,7 % of patients with conventional 20-month regimen, in comparison 2,3 % patients with 12-month short regimen with linezolid.

Conclusions: Administration of short 12-month regimen for MDR - TB patients improved the successful treatment outcomes in patients with MDR-TB to 95.4% in comparison with the use of conventional regimen. Relapses were only in 5 (11,6 %) patients after conventional 20-month regimen.

PS-34-881-02 Treatment outcome of isoniazid-resistant (rifampicin-susceptible) tuberculosis patients under programmatic conditions in India

P Agarwal,[1] S Kumari,[2] J Kular,[3] [1]World Health Organization, Revised National Tuberculosis Control Programme, Chandigarh, India, [2]TB Hospital, Pulmonary Medicine, Patiala, India, [3]State TB Cell, Health and Family Welfare, Chandigarh, India. e-mail: agarwalp@rntcp.org

Background: Isoniazid (INH) is an essential drug for tuberculosis (TB) treatment. INH resistance (Hr) may contribute to negative treatment outcomes. A standard regimen to treat Hr TB among R susceptible TB patients (DST to other drugs not known), was introduced in India in 2016 in line with the WHO guidelines.
Methods: We retrospectively analyzed the treatment outcome of Hr TB patients who were enrolled in Punjab state under the Revised National TB Control Programme (RNTCP) in 2017-18. The patients received the treatment as per WHO guidelines with (3-6) Lfx Km R E Z + (6) Lfx R E Z.
Results: A total of 415 patients were started on the Hr treatment during the study period and treatment outcome were available for 337/415(81%) patients, remaining 78(19%) patients are still on treatment. At the end of treatment, 222/337 patients (65.8%) experienced cure or treatment completion and defined as treatment success. Deaths reported in 47/337 (13.9%) while loss to follow up and failure reported in 44/337(13%) and 12/337(3.5%) patients, respectively. The treatment was changed in 4/337 (1.1%) patients due to drug resistance and adverse events. The treatment outcome 8(2.2%) who were transferred out, was not evaluated.
Conclusions: A total of 415 patients were started on the Hr treatment during the study period and treatment outcome were available for 337/415(81%) patients, remaining 78(19%) patients are still on treatment. At the end of treatment, 222/337 patients (65.8%) experienced cure or treatment completion and defined as treatment success. Deaths reported in 47/337 (13.9%) while loss to follow up and failure reported in 44/337(13%) and 12/337(3.5%) patients, respectively. The treatment was changed in 4/337 (1.1%) patients due to drug resistance and adverse events. The treatment outcome 8(2.2%) who were transferred out, was not evaluated.

PS-34-882-02 Treatment outcomes in drug-resistant tuberculosis patients who were offered treatment with shorter multidrug-resistant tuberculosis regimen in Delhi, India

A Khanna,[1] S Chandra,[2] KK Chopra,[3] N Sharma,[4] A Bhatnagar,[5] N Singla,[6] M Hanif,[7] S Matta,[3] N Babbar,[1] TJ Padmini,[1] [1]Government of NCT of Delhi, State TB Control Office, New Delhi, India, [2]Office of World Health Organization India, Tuberculosis Division, New Delhi, India, [3]New Delhi TB Centre, State TB Training and Demonstration Centre, New Delhi, India, [4]Maulana Azad Medical College, Department of Community Medicine, New Delhi, India, [5]Municipal Corporation of Delhi, Rajan Babu Institute of Pulmonary Medicine and TB, New Delhi, India, [6]National Institute of TB & Respiratory Diseases, Nodal DRTB Centre, New Delhi, India, [7]New Delhi TB Centre, Intermediate Reference Laboratory Delhi, New Delhi, India. e-mail: stdcdl@rntcp.org

Background and challenges to implementation: Standardized shorter Multi Drug Resistance Tuberculosis (MDR-TB) regimen with seven drugs and a treatment duration of 9-11 months has been rolled out under programmatic conditions in Delhi from April 2018. Framework for laboratory and treatment centre scale up was deployed to achieve the fastest expansion of shorter MDR-TB regime uptake in the country. Our aim is to assess the treatment outcomes of the first cohort of patients who were enrolled for shorter MDR-TB regimen between April 2018-June 2018 in Delhi.
Intervention or response: Facilities for second line drug sensitivity test though Line Probe Assay (SL-LPA) was scaled up in the city across the three Culture Drug Sensitivity laboratories. The Integrated Algorithm for DRTB under the Revised National Tuberculosis Control Program was followed and District TB Centres were upgraded for decentralised management of shorter MDR-TB regimen. All patients with first line DRTB resistance were evaluated for uptake of shorter MDR-TB regimen. Based on SL-LPA results, the treatment regimen was either individualized or continued on shorter MDR-TB treatment in accordance with program guidelines.
Results and lessons learnt: With the introduction of SL-LPA for Rifampicin resistance (RR) TB cases, 87% out of the 487 RR TB diagnosed had their results available, based on which they were enrolled for shorter MDR-TB regimen or individualised treatment regimes. In the study period, 234 DR TB patients were started on shorter MDR-TB regimen. Among them, there were 184 culture conversions (79%) in the first four months of therapy. Statistically significant improvement ($p< 0.01$) in culture conversions and treatment outcomes was observed for DR TB patients started on shorter MDR-TB regime (when compared with previous year on longer treatment protocol).
Conclusions and key recommendations: Standardized shorter MDR-TB regimen engenders successful treatment outcomes among DR TB patients. This emphasiz-

es the need to fast track the implementation guidelines for shorter MDR-TB regimen within program framework across high burden settings.

PS-34-883-02 Good final treatment outcomes amongst patients receiving bedaquiline and delamanid with highly resistant MDR-TB in Georgia

N Danielyan,[1] M Bastard,[2] T Kotrikadze,[1] N Cumburidze,[3] N Kiria,[4] Z Avaliani,[4] N Melikyan,[5] H Huerga,[5] C Hewison,[6] F Varaine,[6] [1]Médecins Sans Frontières, Medical, Tbilisi, Georgia, [2]Epicentre, Scientific Research, Geneva, Switzerland, [3]Médecins Sans Frontières, Research, Tbilisi, Georgia, [4]National Center for Tuberculosis and Lung Diseases, Tuberculosis and Lung Diseases, Tbilisi, Georgia, [5]Epicentre, Scientific Research, Paris, France, [6]Médecins Sans Frontières, Medical, Paris, France. e-mail: mathieu.bastard@geneva.msf.org

Background: From 2015, Georgia implemented MDRTB regimens containing bedaquiline and delamanid according to WHO interim recommendations, as part of the endTB observational study. The regimens used for this cohort of patients, most with challenging to treat forms of MDRTB, were often similar to those WHO recommended in 2018. We present the final treatment outcomes and reasons for non-successful treatment outcomes.
Methods: Consented patients, prescribed bedaquiline or delamanid between April 2015 and June 2017 are included. Treatments outcomes were assigned by clinicians as defined by WHO. Non-successful outcomes were failure, death and lost to follow-up (LTFU).
Results: The majority of the 297 persons included, were males (81.1%,) with difficult to treat forms of tuberculosis: 60.0% had extensive disease, 71.4% MDRTB with resistance to fluoroquinolones, 69.7% previously treated for MDRTB and 36.7% experienced previous treatment failure. A quarter (24.2%) had hepatitis C.
End of treatment outcomes were: 204 (68.7%) cured, 25 (8.4%) treatment complete, (success rate 77.1%), 11 (3.7%) death, 24 (8.1%) treatment failure and 29 (9.8%) LTFU. Median time to death and treatment failure were: 2.9 months [IQR 1.4-8.3] and 12.3 months [IQR 8.0-14.8], respectively. Causes of death were: 4/11 TB contributed to or caused death, 4/11 causes other than TB (illicit drug overdose, malignancy, kidney and liver failure), 1/11 related to treatment and unknown in 2/11. Most treatment failures were due to bacteriological failure (71.4%). Most common reasons for LTFU were patient decision (44.8%) and emigration (20%).
Conclusions: In Georgia, treatment with new and repurposed drugs achieved very good outcomes in persons with challenging to treat forms of MDRTB. Additional analysis of deaths and failures are needed to improve further these results. Shorter regimens and patient centred treatment could contribute to a reduction in LTFU. These results support new WHO recommendations for a wider use of new and repurposed drugs.

PS-34-884-02 End of treatment outcomes of an Armenian cohort of patients on bedaquiline and delamanid containing regimens for MDR-TB

N Melikyan,[1] H Atchemyan,[2] C Hewison,[3] M Bastard,[4] N Khachatryan,[5] N Avagyan,[1] L Yegiazaryan,[6] L Kocharyan,[6] L Hovhannisyan,[7] H Huerga,[1] [1]Epicentre, Scientific Research, Paris, France, [2]Médecins Sans Frontières, Research, Yerevan, Armenia, [3]Médecins Sans Frontières, Medical, Paris, France, [4]Epicentre, Scientific Research, Geneva, Switzerland, [5]Médecins Sans Frontières, Medical, Yerevan, Armenia, [6]Ministry of Health of the Republic of Armenia, National Tuberculosis Control Centre MDRTB Unit, Yerevan, Armenia, [7]Médecins Sans Frontières, Data Manager, Yerevan, Armenia.
e-mail: cathy.hewison@paris.msf.org

Background: Bedaquiline and delamanid programmatic use was implemented by the Armenia National Tuberculosis Control Centre with the support of Médecins Sans Frontières and the endTB project. We assessed end of treatment outcomes and reasons for non-successful outcomes for patients started on bedaquiline or delamanid.
Methods: We conducted a prospective and retrospective observational study. Patients started on bedaquiline or delamanid between April 2015 and March 2017 were included. End of treatment outcomes were clinician assigned as per the WHO 2013 definitions. Non-successful outcomes included failure, death and lost to follow-up (LTFU).
Results: The majority of the cohort of 107 patients were men (82.2%), with a median age of 43 [IQR 32-52]. Hepatitis C comorbidity was common (24.3%). Resistant profiles include XDR (25.2%), MDR with fluoroquinolone (22.4%) or injectable resistance (23.4%). Most were previously treated for TB (85.1%), including 81 (90%) for MDRTB, with previous treatment outcomes of 59.3% treatment failure and 14.8% LTFU. Most had extensive disease (92.5%).
End of treatment results were: 38 (36.5%) cured, 9 (8.7%) treatment completed, 47 (45.2%) success), 11 (10.6%) died, 11 (10.6%) treatment failed and 35 (33.6%) LTFU. Median time to LTFU was 6.2 months [IQR 4.2-13.0]. Reasons given for LTFU were: 61.1% left region/country, 30.6% patient decision, 8.3% social problems.
More than half of deaths were caused or contributed to by TB (54.5%). The majority of treatment failures were bacteriological failure (66.7%).
Conclusions: Amongst this cohort of patients with difficult to treat forms of MDRTB, treatment outcomes were disappointing due to extremely high rates of lost to follow-up, mostly due to emigration. Therefore as well as effective drugs and shorter treatment, considerable additional social support and innovation such as salary replacement is necessary to encourage treatment completion, requiring further studies on possible models and their cost effectiveness for these strategies.

PS-34-885-02 Building a case for introduction and scale-up of a new TPT regimen, three months weekly rifapentine and isoniazid (3HP), in the South African public sector

Y Pillay,[1] S Bryer,[2] L Mvusi,[3] L Agrawal,[4] D Goldberg,[5] P Madhav,[5] P Chituku,[5] [1]National Department of Health South Africa, HIV & AIDS, TB and Maternal, Child and Women's Health (MCWH), Pretoria, South Africa, [2]Clinton Health Access Initiative, Drug Access, Pretoria, South Africa, [3]National Department of Health South Africa, Drug-Sensitive Tuberculosis Control and Management, Pretoria, South Africa, [4]Clinton Health Access Initiative, Global TB Drug Access, Pretoria, South Africa, [5]Clinton Health Access Initiative, TB Drug Access, Pretoria, South Africa. e-mail: sbryer@clintonhealthaccess.org

Background and challenges to implementation: Given recent evidence about the clinical effectiveness of 3HP, an investment case was prepared for the National Department of Health (NDoH) to assess whether 3HP was a viable and cost-effective alternative standard of care to IPT for the national health system. The case considered the potential reduction in drug-sensitive TB (DS-TB) burden as well as in TPT patient adverse events.
Intervention or response: A mathematical model was developed to quantify and compare the cost and public health impact of delivery of 3HP against IPT. The first step was forecasting several scenarios ranging from conservative to ambitious volume estimates for target patient cohorts, namely PLHIV newly initiating on ART and household contacts (HHC) between 2 and 5 years old. Estimates were based on historical programmatic data and adjusted using assumptions to exclude ineligible sub-populations i.e. those who might have active TB. Scenarios compared the use of 3HP to IPT at varying speeds of scale-up (over 1 year vs. 3 years) and adherence rates, presenting detailed costs and impact.
Results and lessons learnt: On commodities costs alone 3HP (~$45) is more expensive than IPT (~$18). In 2018, SA treated a cohort of ~462,000 with IPT, recording average completion rates of 65%. Studies present higher completion rates for 3HP at ~87%. Using these inputs, the model demonstrated that treating the same cohort with 3HP potentially averts ~6,500 more TB cases and ~9,000 adverse events, resulting in potential savings depending on the introduction price of 3HP.
The model provided a clear view of the financial investment required and public health impact, and has informed national decision-making around 3HP scale up.
Conclusions and key recommendations: Underpinned by a comprehensive eligible cohort selection exercise, considering additional value-add through parallel scale up with novel ART in SA in 2019, the model demonstrated a positive public health impact and potential cost savings depending on the introduction price of 3HP.

PS-35-D1 Extra-pulmonary TB: clinical and diagnostic considerations

PS-35-886-02 Retrospective real-world study of linezolid for the treatment of tuberculous meningitis

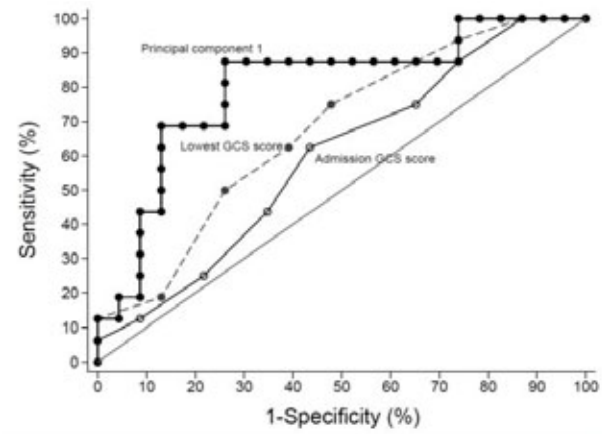
X Zhou,[1] F Sun,[1] T Wang,[1] Q Ruan,[1] Y Li,[1] W-H Zhang,[1] [1]Huashan Hospital, Fudan University, Department of Infectious Diseases, Shanghai, China. e-mail: zhouxian-13@163.com

Background and challenges to implementation: Tuberculous meningitis (TBM) causes mortality and disability in >50% of the patients. Current standard treatment for TBM is based on regimen for pulmonary tuberculosis, which neglects the different ability of anti-tuberculosis drugs to penetrate the brain. With both good central nervous system (CNS) penetrance and anti-tuberculosis efficacy, the purpose of this study is to evaluate the effectiveness of linezolid in the treatment of TBM.
Intervention or response: The cohort study involved patients diagnosed as CNS tuberculosis who were treated with without linezolid throughout the treatment course (Background group, n=68), with linezolid added in the middle of the treatment course but not in the initial treatment regimen (BG-LZD group, n=58), and linezolid in initial treatment regimen (linezolid-initial group, n=41) between January 1, 2010, and December 31, 2017, using data from the electronic medical records of Huashan Hospital, Shanghai, China. The primary outcome was survival in 5 years. The secondary outcome was rates of participants with Medical Research Council (MRC) grade deterioration and rates of participants with new neurological complications.
Results and lessons learnt: Among the cohort of 161, 106 (65.8%) patients were MRC II or III. The overall 5-year survival of the cohort was 92.8%, no statistical significance among groups. Old age (p=0.039, 95%CI 1.003-1.129) and MRC deterioration after anti-TB treatment (p=0.004, 95%CI 113.879-2813.438) were independent risk factors for death. Linezolid-initial group had significantly fewer patients with MRC deterioration (4/41, p=0.046) compared to combined other 2 groups (30/120). Linezolid-initial group also had significantly fewer patients with new neurological complications (8/41, p=0.0343) compared to other 2 groups (45/75). We separately analyzed the second group of MRC deterioration and new complications before and after the addition of linezolid. We found that after the addition of linezolid, there was fewer MRC deterioration (p=0.0042) and fewer new complications (p< 0.0001).
Conclusions and key recommendations: Linezolid can be used for the initial or salvage treatment of TBM.

PS-35-887-02 Cerebrospinal fluid biomarkers of astroglial and neuroaxonal injury and treatment outcome in tuberculous meningitis

T Kadhiravan,[1] A Thoibisana,[1] G Saranya,[1] R Soundravally,[2] N Joseph,[3] [1]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Medicine, Puducherry, India, [2]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Biochemistry, Puducherry, India, [3]Jawaharlal Institute of Postgraduate Medical Education and Research, Department of Microbiology, Puducherry, India. e-mail: kadhir@jipmer.edu.in

Background: We aimed to study the association of cerebrospinal fluid (CSF) biomarkers of astroglial and neuroaxonal injury with Glasgow coma scale (GCS) score and treatment outcome in patients with tuberculous meningitis (TBM).
Methods: We studied serial GCS scores, baseline CSF concentration of biomarkers (glial fibrillary acidic protein [GFAP], S100B, neuron-specific enolase [NSE], total tau, phosphorylated neurofilament-heavy [pNF-H]), and treatment outcome in a consecutive sample of HIV-negative adults with TBM. We performed Pearson correlation, receiver-operating characteristic (ROC) and principal component (PC) analyses.
Results: We enrolled 39 patients with TBM; 21(54%) were male, and mean age was 38±19 years. Three patients had stage I TBM; 18 each had stages II and III. Twelve (31%) patients had definite TBM, 17(44%) had probable, and 10(25%) had possible TBM. At hospital discharge, 23 patients had good functional status (modified Rankin scale [mRS] score of ≤2). The mRS score at hospital discharge had a significant negative correlation with the lowest GCS score (r=−0.376; P=0.018), but not admission GCS score (r=−0.259; P=0.111). Baseline CSF concentrations of GFAP (r=−0.409; P=0.009), NSE (r=−0.479; P=0.002), and total tau (r=−0.398; P=0.011) had significant negative correlations with the lowest GCS scores. All biomarkers were able to predict functional status at hospital discharge with moderate accuracy — area under ROC curve (AUC) was 0.74 for GFAP, 0.71 for S100B, 0.79 for NSE, 0.74 for total tau, and 0.73 for pNF-H. The first PC captured 65% of variance, and all biomarkers had similar positive factor loadings on the first PC. The first PC better correlated with lowest GCS score (r=−0.465; P=0.003) than the admission GCS score (r=−0.334; P=0.038), and it better predicted mRS scores at hospital discharge than the admission GCS score (Figure; AUC 0.802 vs. 0.596).
Conclusions: CSF biomarkers of astroglial and neuroaxonal injury are predictive of on-treatment worsening in GCS score and treatment outcome in TBM.



[ROC curves depicting predictive accuracy of GCS scores and the first principal component.]

PS-35-888-02 Evaluation of a loop-mediated isothermal amplification system for the diagnosis of extrapulmonary tuberculosis

H Charifker Schindler,[1,2] R Martins Araújo,[1] R Albuquerque Montenegro,[1] MA Lopes da Silva,[3] A dos Santos Peixoto,[1] F Lopes de Melo,[4] L Maria Lapa Montenegro,[1] [1]Instituto Aggeu Magalhães, Fundação Oswaldo Cruz, Departamento de Imunologia, Recife, PE, Brazil, [2]Universidade de Federal de Pernambuco, Maternal and Child Department, Recife, PE, Brazil, [3]Instituto Aggeu Magalhães, Fundação Oswaldo Cruz, Microbiology Department, Recife, PE, Brazil, [4]Instituto Aggeu Magalhães, Fundação Oswaldo Cruz, Department of Parasitology, Recife, PE, Brazil. e-mail: haia@cpqam.fiocruz.br

Background: The present work aims to evaluate a Loop-mediated Isothermal amplification (LAMP) system in the detection of the *IS6110* target for the diagnosis of TBE, with the purpose of assisting in the diagnosis of extrapulmonary tuberculosis (EPTB).
Methods: The biological samples used in this study (peripheral blood and urine) were from patients (n = 72) from public hospitals of the health service of the state of Pernambuco (Brazil), divided into two groups: Group 1 - patients with confirmed diagnosis of EPTB (n = 41); Group 2 - Patients without TB (n = 31). The samples underwent decontamination, DNA extraction and, subsequently, submitted to the LAMP technique. The limit of detection was evaluated through four different dilution curves (1:10) using *Mtb* reference strain (H37Rv) genomic DNA.
Results: The LAMP assay was tested in 122 biological samples, 61 of Group 1 and 61 of Group 2. The results indicated that the limit of detection of LAMP was 10fg / μL, equivalent to 2 bacilli / μL. Regarding the sensitivity and specificity of the technique, were obtained values of 90.16% and 63.93%, respectively.
Conclusions: Due to its high sensitivity, associated to the good limit of detection presented, this test shows considerable diagnostic value, being able to aid in the speed

and accuracy of the final diagnosis, generating a better prognosis for the patients with suspected EPTB. Because it is a low-cost simple technique, it does not require specialized technicians and complex infrastructure, and it can be used in developing countries with high disease burden, such as Brazil.

PS-35-889-02 Endometrial PCR vs. conventional methods (histopathology, culture, AFB staining on endometrial sample and laparoscopy) for diagnosing female genital tuberculosis

K Kumarasingam,[1] U Devi,[1] A Hari,[2] A Srikantam,[3]
[1]Lepra Society, Microbiology, Hyderabad, India, [2]Gandhi Medical College, Obstetrics and Gynecology, Hyderabad, India, [3]Lepra Society, Research, Hyderabad, India.
e-mail: aparna@leprahealthinaction.in

Background: Female genital TB (FGTB) has been found to be increasing in India from 19% in 2011 to 30 % in 2015. FGTB has inherent diagnostic and therapeutic challenges due to its varied clinical presentation and difficulty in approach to the samples. The study objective was to evaluate the diagnostic accuracy of PCR versus conventional methods in detecting genital TB.
Methods: Women registered for infertility treatment at Gandhi medical college hospital and suspected with FGTB were included. Endometrial Aspirate (EA) was collected from all the subjects for testing by histopathology Examination (HPE) for granulomas, Acid Fast Bacilli (AFB), MGIT culture and a novel in house MPT 64 PCR. Any woman tested positive for TB by conventional tests were treated with anti TB treatment (ATT). All women who tested positive for EA PCR were studied further by diagnostic laparoscopy.
Results: Out of 376 patients included, 1.5% was positive for TB by one more conventional lab tests and 27.3% positive for PCR. Out of 100 PCR positive patients, 14 were subsequently pregnant and hence 86 were subjected for diagnostic laparoscopy. 02/86(2.32 %) were clinically positive for TB by laparoscopy. Conception rates were 21% and 28% respectively for PCR negative and positive women.
Conclusions: Laparoscopy and conventional tests together provide definitive diagnosis of FGTB. EA PCR seems not a suitable single test for starting ATT, since the laparoscopic findings were negative in most of the PCR positive women and conception rates are more or less the same in both PCR positive and negative women. Only patients who are PCR positive and whose laparoscopy turns positive should start ATT.

PS-35-890-02 Diagnosis of osteoarticular tuberculosis in a tertiary care centre, Pune, Maharashtra: a six-year experience

S Dharmshale,[1] A Kagal,[1] R Bhardwaj,[1] R Karyakarte,[1]
[1]B. J. Govt. Medical College, Microbiology, Pune, India.
e-mail: sujatadharmshale@rediffmail.com

Background: Microbiological diagnosis in osteoarticular tuberculosis is difficult due to deep inaccessible lesions, paucibacillary state, and initiation of empirical Anti tubercular therapy (ATT) in most of the cases. Diagnosis of osteoarticular TB evolved from clinicoradiological to serodiagnosis to detection of DNA/RNA of MTB origin.
Aims and objectives: This study was conducted to evaluate microbiological diagnostic tests for diagnosis of Osteo-articular tuberculosis.
Methods: This was a retrospective study carried out in a Department of Microbiology, B. J. Govt. Medical College & Sassoon General Hospital, Pune. From January 2013 to December 2018, a total 235 clinical samples (120 aspirate from Psoas abscess/Pott's spine/osteomyelitis, 59 joint aspirate/fluid, 41 tissue 14 bone biopsy/bone pieces and one bone marrow) from clinicoradiologically diagnosed Osteoartcular tuberculosis cases were received. All samples were processed for microscopy, culture by standard procedure. GeneXpert MTB/Rif assay was performed on 84 of these samples.
Results: : Male predominance (54.04%) was observed in the present study and average age group affected was 35.3. Among the 235 suspected osteo-articular tuberculosis, Pott's spine 80 (34.04%) was the commonest manifestation followed by synovitis/arthritis 67(31.2%) and Psoas abscess, 37(17.2%). AFB microscopy was positive in 51 (21.7%) and *Mycobacterium tuberculosis* (MTB) growth was observed in 40 (18.3%) cases. GeneXpert was positive in 38 (45.2%) out of 84 patients. GeneXpert results were 100% for bone marrow sample, 64.1% for aspirates and 27.3% for biopsy samples. Rifampicin resistant has been detected in 6 (15.8%) Pott's spine cases by GeneXpert MTB/RIF assay.
Conclusions: Among all the diagnostic tests, GeneXpert was found to be the most sensitive (94.0%) and rapid diagnostic test in Osteoarticular TB patients.

PS-35-891-02 Pattern of TB-uveitis (ocular TB) in patients with previous pulmonary or extra-pulmonary TB, reporting to a tertiary care eye clinic in eastern India

S Panigrahi,[1] S Basu,[2] [1]District Headquarter Hospital, TB and Chest Disease, Puri, India, [2]L V Prasad Eye Institute, Retina and Uveitis Services, Bhubaneswar, India.
e-mail: satyarpanigrahi@gmail.com

Background: Tuberculosis-associated uveitis (TBU) in the eye is rarely associated with microbiological evidence of TB, or with other extrapulmonary (EP) or pul-

monary TB (PTB). Yet, clinical or radiological evidence of PTB/EPTB can be crucial in linking ocular inflammation with TB, and initiation of anti-TB therapy (ATT). We aimed to compare patterns of TBU between patients with PTB and EPTB (previous or ongoing), who presented primarily with ocular symptoms.
Methods: We analysed medical records of patients diagnosed clinically as TBU, based on characteristic ocular signs, ancillary tests for TB, and exclusion of non-TB entities. All patients had presented to a tertiary care eye clinic in eastern India, between 2015-19. Details of any associated PTB and/or EPTB, including their temporal association with eye disease, past ATT, and details of ophthalmic evaluation were noted. Patterns of TBU in PTB and EPTB, were compared.
Results: Clinical data of 301 patients with TBU, were analysed. Twenty-two (7.3%) patients with PTB and 15 (4.9%) patients with EPTB were noted. Most patients (86.3% [n=19] with PTB and 66.6% [n=10] with EPTB) had received ≥6 months ATT. In PTB group, 12 and 10 patients, developed TBU following past and concurrent PTB respectively. The numbers were 8 and 6 respectively for EPTB. One patient developed EPTB after treatment of TBU. Rates of anterior (anterior uveitis, scleritis, episcleritis) and posterior segment (intermediate, posterior and panuveitis) inflammation were nearly equal in both groups.
Conclusions: Evidence of systemic TB (PTB and EPTB) is rare in patients with TBU. EPTB, previous or concurrent, can be present in isolation in a significant number of TBU patients and can progress to TBU much like PTB. Clinical and radiological investigation for EPTB merits as much rigor as PTB, in patients with suspected TBU.

PS-35-892-02 Diagnosis of extra-pulmonary tuberculosis: how good is CBNAAT?

K Venugopal,[1,2] V Sreelatha,[3] M Khama,[4] Asha Vijayan Sreeja S R [1]Govt. General Hospital, Respiratory Medicine, Alappuzha, India, [2]District TB Center, Health Services, Alappuzha, India, [3]Govt. Medical College Alappuzha, Pediatrics, Alappuzha, India, [4]GH Alappuzha, Pulmonology, Alappuzha, India.
e-mail: dtovenu@yahoo.com

Background: Globally, India is a home for more than 27% of global Tuberculosis (TB) burden. The sensitivity of smear microscopy and its inability to detect drug resistance limits its impact on TB control programs. Extra pulmonary tuberculosis diagnosis gives difficulties as lesions are paucybacillary We are trying to study on the cartridge-based nucleic acid amplification test (CBNAAT) resultsfor diagnosis of extra pulmonary tuberculosis.
Aim of the study: To study efficacy of CBNATT in detecting mycobacteria and its RIF sensitivity in different extra pulmonary sites.
Methods: The study was conducted in a Government tertiary care centre for Tuberculosis, at Alappuzha Kerala,India during 2016 May toFeb 2019. The study population included all extra pulmonarypresumptive TB cases who were subjected for further investigations including CBNAAT.
Results: Of the 690 samples received 41 (5.94 %) were positive and 4 were RIF Resistant(0.5%). 3 of the 409 CSF samples(0.73%); 9 of the 140 pleural fluid samples (6.4 %); 20 of the 140 PUS samples (40%);1 of the 4 pericardial fluid (25%). 1of the 8 Gastric Aspirate (12.5%);1 of the synovial fluid (11.11%); 5 of the 14 lymph node aspirate samples obtained by FNAC (35.71 %); 4 of the 7 joint aspirate(28.7) were positive for Mycobacteria.
Conclusions: CBNAAT is an effective rapid diagnostic tests for detection of myco bacteria and its sensitivity to rifampicine in extra pulmonary samples of different site. High yield are obtained from pus, lymph node aspirate, joint aspirate and pericardial fluid.

PS-35-893-02 Xpert Ultra for the diagnosis of extra-pulmonary tuberculosis - its role in a routine diagnostic laboratory

JS Michael,[1] D Mani,[1] MM Ninan,[1] P Rupali,[2] V Krishnan,[3] [1]Christian Medical College Vellore, Microbiology, Vellore, India, [2]Christian Medical College Vellore, Infectious Diseases, Vellore, India, [3]Christian Medical College Vellore, Spinal Surgery, Vellore, India.
e-mail: joymichael@cmcvellore.ac.in

Background: Extra pulmonary tuberculosis (EPTB) is a clinical and diagnostic challenge . Conventional techniques such as smear and culture for detection of *M.tuberculsosis* are often negative and have decreased sensitivity. Only few molecular techniques to detect DNA have been endorsed by WHO for diagnosis of EPTB , though their performance is not as effective as they are for diagnosis of pulmonary tuberculosis (PTB). Xpert Ultra has been shown to have increased sensitivity in the diagnosis of smear negative PTB and PTB in HIV positive patients. Therefore we would like to evaluate it efficacy for the diagnosis of EPTB in a routine diagnostic tertiary hospital.
Methods: 250 consecutive extra pulmonary samples sent to the Department of Microbiology for culture & drug susceptibility testing (DST)and Xpert MTB /Rif assay were included for the study. The material were ground using sterile grinder and then processed for the above 2 routine diagnostic tests as well as for Xpert Ultra. The sensitivity and specificity of Xpert Ultra was calculated against Mycobacterial Culture & DST and Histopathological findings. Percentage positivity of Xpert Ultra over Xpert MTB Rif assay was also evaluated.
Results: Out of the 250 samples tested 100 were Lymphnode, 50 were bone and joint samples and 50 were other tissue samples and 50 were fluid samples . Xpert Ultra had additional positivity over Xpert MTB Rif assay- 15

% for Lymphnodes, 10 % for other tissue samples, and 10% for CSF . The sensitivity and specificity of Xpert Ultra against conventional mycobacterial culture and Histopathology is pending as the final results are not ready for all the samples tested by Xpert Ultra.
Conclusions: Xpert Ultra is an useful molecular test which shows great potential for the diagnosis of extra pulmonary tuberculosis in a routine diagnostic setting.

PS-35-894-02 Diagnostic performance of the laboratory methods for the detection of Mycobacterium tuberculosis from extra-pulmonary specimens in Bangladesh

MKM Uddin,[1] S Kabir,[1] S Ahmed,[1] SMM Rahman,[1] A Rahman,[1] SS Ferdous,[1] M Sahrin,[1] UT Maliha,[2] PK Modak,[2] S Banu,[1] [1]ICDDR, Infectious Diseases Division, Dhaka, Bangladesh, [2]Directorate General of Health Services, National Tuberculosis Control Programme, Dhaka, Bangladesh. e-mail: shahriar.ahmed@icddrb.org

Background: Global burden of extra-pulmonary tuberculosis (EPTB) was around 14% of the notified cases in 2017 and that in Bangladesh was around 20% in 2016. Lack of sensitive diagnostics make EPTB diagnosis challenging and clinicians mostly rely on symptoms and non-specific tests often leading to mis-diagnosis. We evaluated performance of culture, Xpert MTB/RIF assay (Xpert) and Line Probe Assay (LPA) in different EP specimens for diagnosing EPTB.
Methods: Presumptive EPTB cases were enrolled between November 2015 and March 2017 from four tertiary care hospitals in Dhaka. All specimens were subjected to AFB microscopy, culture, Xpert and LPA for diagnosing EPTB. Patients were diagnosed bacteriologically when their specimens were positive in any of the tests and also clinically by the physicians. We compared performance across these methods in detecting EPTB cases. Accuracies of different laboratory tests were measured among the different types EPTB specimens considering the final diagnosis as reference standard.
Results: Among 1340 different EP specimens, 500 (37%) were finally diagnosed as EPTB cases [194 bacteriologically (39%) and 306 clinically (61%)]. Higher bacteriological positivity rate was seen in aspirated material (40%), pus (36%), and tissue (31%) among the specimens. The AFB microscopy positivity among the diagnosed cases was lower in all specimens except pus (44%). Conversely, culture, Xpert and LPA had higher positivity in aspirated material (73%, 81%, 71%), pus (74%, 88%, 88%), and tissue (57%, 89%, 78%) among EPTB cases. Accuracies of Xpert and LPA were similarly higher in ascitic fluid, CSF, tissue, pus, urine and aspirated material compared to other specimens (Table).
Conclusions: Xpert and LPA are as accurate as culture test with higher positivity rate among most of the EP specimens. Considering the turnaround time of the assays, resource limitation and improved availability of Xpert throughout the country, expanding capacity of handling EP specimens for Xpert testing should be prioritized.

PS-35-896-02 The impact of mycobacteria complex genotypes on tuberculosis phenotypes in association with risk factors

B Varghese,[1] S Al-Hajoj Al-Nakhli,[1,2] [1]King Faisal Specialist Hospital and Research Centre, Infection and Immunity, Riyadh, Saudi Arabia, [2]Alfaisal University, Infectious Disease, Riyadh, Saudi Arabia. e-mail: hajoj@kfshrc.edu.sa

Background: Genotype of Mycobacteria Complex data revealed that Saudi Arabia harbors many imported clades as a result of huge migrant population. However, the impact of these genotypes on tuberculosis phenotype and outcome never explored nor the risk factor associate with extra pulmonary tuberculosis.
Methods: A multicenter study has been carried out on a collection of 2092 (1003 extra pulmonary and 1089 pulmonary) MTBC isolates. Genotyping of all the isolates

	Bacteriological positivity among specimens tested, n (%)	Finally diagnosed as EPTB cases, n (%)***	Positivity rate of different laboratory tests with their accuracies for diagnosing EPTB cases			
Number of specimens tested (n=1340)*			Microscopy, n (%), Accuracy (%)	Culture, n (%), Accuracy** (%)	Xpert, n (%), Accuracy (%)	LPA, n (%), Accuracy (%)
Pleural fluid (n=370)	23 (6)	206 (56)	3 (2); (45)	15 (7); (49)	16 (8); (49)	15 (7); (48)
Ascitic fluid (n=242)	16 (7)	77 (31)	0 (0); (32)	8 (10); (71)	10 (13); (72)	9 (12); (72)
Cerebrospinal fluid (n=155)	12 (8)	38 (26)	0 (0); (25)	10 (26); (82)	8 (21); (81)	7 (18); (80)
Tissue (n=114)	35 (31)	37 (32)	5 (14); (72)	21 (57); (86)	33 (89); (97)	29 (78); (92)
Pus (n=178)	64 (36)	69 (39)	30 (44); (78)	51 (74); (91)	61 (88); (96)	61 (88); (96)
Urine (n=122)	5 (4)	19 (16)	3 (16); (87)	5 (26); (88)	4 (21); (88)	3 (16); (87)
Aspirated material (n=94)	38 (40)	41 (44)	8 (20); (65)	30 (73); (88)	33 (81); (92)	29 (71); (87)

*Other specimens (n=65) including bone marrow, gastric lavage, synovial fluid, pericardial fluid, endometrial fluid and the test accuracy was not measured for these specimen; ** Accuracy of culture was measured excluding the specimens with non-TB mycobacteria isolates found in culture; ***percentage among specimen tested

[PS-35-894-02 Table. Performance of AFB microscopy, culture, Xpert and LPA among different EP specimens for diagnosis of EPTB cases]

were carried out by spoligo and 24 loci based MIRU-VNTR typing. Independent risk factors for EPTB and diseases characteristics of EPTB were identified using multivariate regression model analyses.
Results: Gender was found to be significantly associated with lymph node, gastrointestinal, central nervous system and urogenital TB. Lymph node TB showed statistical association to age group below 25 years, non-Saudis and South East Asian ethnicity. Gastrointestinal TB demonstrated an association with Saudis patients above 60 years old.
Multivariate analysis showed that gender is an independent risk factor to urogenital TB and lymph node TB. On the other hands, South Asian and South East Asian ethnicities were both identified as independent risk factors significantly associated with EPTB.
Conclusions: MTB lineages influence disease phenotypes and epidemiological consequences. Further studies are needed to gain insight into the application of personalized medicine.

PS-36-E1 Effective community interventions and advocacy

PS-36-897-02 Grassroots advocacy on tuberculosis in action: experience from Australia

S Shrestha,[1] A Christie,[1] N Eberts,[1] M Rice,[1]
[1]RESULTS Australia, Global Health, Sydney, NSW, Australia.
e-mail: shivashrestha91@gmail.com

Background and challenges to implementation: Grassroots advocacy is critical to highlight voices from the community in TB advocacy. This abstract examines the following: How to mobilize volunteers on TB advocacy? What organizational processes promote volunteer engagement? What do volunteers contribute to advocacy campaigns?
Intervention or response: How to mobilize grass roots volunteers on TB advocacy?
RESULTS model of grassroots engagement can be summarized as advocacy by organised mobilization.
The theory of change is that if enough political will is built, Australia will respond with more and better investments in TB that improve the quality of diagnosis and treatment.
What organizational processes promote volunteer engagement?
RESULTS grassroots advocacy model builds opportunities for volunteers in three ways:
- Engaging with MPs:Volunteers ask MPs to support the campaign to increase funding for TB. They write letters, organize one to one meetings with MPs in their constituency.
- Engaging with Media: Volunteers write letters to the editor, Oped and get news coverage around the World TB Day.
- Fundraising:Volunteers fundraise through activities like Quiz nights, auctions, and events like the city to surf, marathon.

Results and lessons learnt: Since 2014, grassroots volunteers have:
- Conducted more than 120 meetings with members of the parliamentarians advocating for an increase in Australia's Foreign Aid and funding for TB.
- Published over 280 letters to the editors and 10 Opinion pieces
- Fund raised over AU$ 100,000 for the cause

Outcomes:
- An increase in the Australian pledge to the Global Fund in 2016 (from $200 million to $220 million)
- $75 million for product development partnerships in 2017
- Establishment of the Australian TB Caucus to its current membership of 27 MPs

Conclusions and key recommendations: Grass root advocacy is an integral part of TB advocacy when combined with advocacy with lawmakers and media. This experience demonstrates a model that both high and low burden countries can use to raise the profile of TB as well as increasing the TB funding.

Volunteers engagement	2014	2015	2016	2017	2018
Action Call with volunteers	44	33	36	36	41
Letters/Op-Eds	50/0	107/2	75/5	52/1	8 letters and 100 digital assets (videos/graphics)
Electorate Meetings	15	17	48	35	3 events 10 MP meetings
Groups (4-5 volunteers per group)	10	8	10	10	9
Funds raised	$22450	$18325	$21906	$24363	$10,889

[Output of volunteers engagement]

PS-36-898-02 Assessment of civil society and community organisations working on tuberculosis in Cambodia: a qualitative study

C Ngin,[1] C Ly,[2] S Tuot,[1,2] C Ork,[2] SC Choub,[3] AKJ Teo,[4] S Yi,[1,4,5] [1]KHANA, Center for Population Health Research, Phnom Penh, Cambodia, [2]KHANA, TB Reach Program, Phnom Penh, Cambodia, [3]KHANA, Executive Director Office, Phnom Penh, Cambodia, [4]National University of Singapore and National University Health System, Saw Swee Hock School of Public Health, Singapore, Singapore, [5]Touro University California, Center for Global Health Research, Vallejo, CA, United States of America.
e-mail: ochetra@khana.org.kh

Background: Building and sustaining a network of civil society organizations is vital in bridging stakeholders at various levels and mobilizing community resources in responding to tuberculosis (TB) epidemic. This study aims to map the existing civil society and community organization working on TB in Cambodia, identify geographical, service and coverage gaps, and describe barriers to effective collaboration of existing networks engaging in the national TB response.
Methods: We conducted 20 semi-structured interviews with representatives from the national TB program (NTP), donor agency, people living with TB, local and international non-governmental organizations (NGO/INGO) with and without active interventions on TB. Interview responses were transcribed, coded, and content analyses were performed.
Results: There were 15 NGOs working on TB in Cambodia. The NTP is the national coordinating body for TB response with funding from the Global Fund, United States Agency for International Development, and the Royal Government of Cambodia. TB coordination mechanism at the national level encompassed a TB annual conference and sub-technical working group that convenes regularly. Geographic gaps included health facilities that were inadequately reached by service providers and the long distance between villages and the health facilities. Concerns regarding the low frequency of community screenings and active case finding and the lack of consultation and treatment support were also reported.
A few key barriers in reaching key populations included distrust of public health facilities, the quality of services, competing personal priorities, and the mobility of the population. Collaboration among institutions working on TB was limited because of the absence of TB coordination institution for NGOs/INGO, irregular stakeholder meetings, and the poor communication between stakeholders and the communities.
Conclusions: A firm political will, clear policies, strategies, and guidelines are crucial in improving institutional cooperation. Concerted effort and synergies between key stakeholders are required to address gaps in the national TB response.

PS-36-899-02 Leveraging civil society organisations' work to support MDR-TB management in an urban setting: lessons from Kampala, Uganda

E Kizito,[1] T Nsubuga Nyombi,[2] S Adakun Akello,[3] H Komujuni,[1] K Mutesasira,[1] [1]University Research Co., LLC (URC), Defeat TB Project, Kampala, Uganda, [2]University Research Company, Defeat TB Project, Kampala, Uganda, [3]Mulago National Referral Hospital, Ministry of Health, Internal Medicine, Kampala, Uganda.
e-mail: ekizito@urc-chs.com

Background and challenges to implementation: Mulago hospital, a treatment initiation center (TIC) cares for 170 multi drug-resistant (MDR) TB patients receiving daily directly observed treatment (DOT) from 112 follow up facilities (FUFs) in Kampala city and the 10 catchment districts. A total of 115(67.6%) patients are from the urban districts which poses challenges to DOT implementation. The national guidelines recommend that FUFs are mentored by the TIC team monthly. TIC teams oversee DOT at FUFs, do contact tracing and return any treatment interrupters to care. Gradually, the number of FUFs with conversely limited human resources at the TIC, made these activities infrequent. Consequently, many patients went without supervised DOT, interrupted treatment, and were lost to follow up.
Intervention or response: Mulago hospital and USAID Defeat TB mapped all the MDR-TB patients by city division. A civil society organization (CSO) was selected from each of the divisions and patients distributed by division among TIC staff. CSO staff were trained in MDR-TB care (including contact tracing), attended cohort review meetings and given tools for tracking patients. Patient lists were also shared for daily DOT tracking, contact tracing and returning to care of treatment interrupters. Each CSO staff was assigned a TIC counterpart to work with virtually for smooth coordination.
Results and lessons learnt: In March 2019 three CSOs oversaw DOT for 22 patients and returned 7 interrupters to treatment. Five susceptible TB and one DR-TB patients were diagnosed through contact tracing as shown in table 1.

Parameter/CSO	Number of MDR-TB patients whose contacts were traced	Total number of close contacts	Number of MDR-TB contacts identified and screened for TB symptoms	Number of PTPs identified	Number of PTPs tested for TB	Number of DS-TB patients diagnosed	Number of DR-TB patients diagnosed	Number followed on DOT	Number of interrupters tracked -7
KHC	06	61	61	05	05	03	01	06	04
Nachwola	06	50	50	04	04	02	00	06	01
KIFAD	10	46	46	1	01	00	00	10	02

[PS-36-899-02 Table 1. CSO Contact tracing cascade and DOT support]

Conclusions and key recommendations: Mulago hospital leveraged CSO work to improve community care for MDR-TB patients through DOT follow up, returning to care of treatment interrupters and contact tracing. These efforts need to be scaled up to cover other divisions in the city and the entire country.

PS-36-900-02 Improved TB treatment outcomes: the role of community structures in the TB "continuum of response" in South Africa

G Makgopa,[1] N Kula,[1] P Dhliwayo,[2] A Moran,[3] R Matji,[4] G Jagwer,[4] [1]University Research Co., LLC (URC), Small Grants and Key Populations, Pretoria, South Africa, [2]University Research Co., LLC (URC), Monitoring, Evaluation and Learning, Pretoria, South Africa, [3]University Research Co., LLC (URC), Monitoring, Evaluation and Learning, Wisconsin, WI, United States of America, [4]University Research Co., LLC (URC), Management, Pretoria, South Africa. e-mail: gilbertm@urc-sa.com

Background and challenges to implementation: As part of a comprehensive response to TB epidemic in South Africa, community-based intervention was identified by as a core pillar in managing the scourge of TB. Key role players in community-based interventions include local non-governmental organisations.
Care Ministry NGO was funded by the USAID TB South Africa Project to provide treatment adherence support to 185 DR-TB patients in Nelson Mandela Bay District. An outcome analysis was conducted to measure impact of the NGO in improving TB outcomes.
Intervention or response: A cohort analysis was conducted for all DR-TB patients registered on TB treatment in 2015 and 2016, supported by the NGO.
In total, 105 (25 patients in 2015 cohorts and 80 patients in the 2016 cohort) patients that received treatment adherence support were included in the analysis.
Comparison was made on treatment outcomes of the 105 patients against patients not supported by the NGO.
Results and lessons learnt: Treatment success rate (TSR) in the 2015 cohort was 56% among NGO supported patients compared to 49% for non-supported patients. TSR in the 2016 cohort was 69% among NGO supported patients compared to 43% for non-supported patients. In 2015, 21% of non-supported patients were lost to follow-up, compared to 4% of NGO supported, 17,3% and 0% in 2016 respectively.
Odds of being lost to follow-up during treatment were significantly lower among NGO patients, compared to non-supported patients (OR=0.05, p<0.001, 95%CI [0.01-0.39]. NGO supported patients had significantly lower odds of death (OR=0.08, p<0.001, 95%CI [0.03-0.27].
Conclusions and key recommendations: Analysis suggests that NGO-supported patients have greater odds of treatment success than those who received standard care. The same applies to other outcome indicators, such as lost to follow-up and death rate.

PS-36-902-02 Access improvement to the TB detection in the target groups through the introduction of social mediators

O Zaitseva,[1] I Terleieva,[1] L Markovcius,[2] V Skrip,[3] [1]Public Health Center of the MOH of Ukraine, Department of TB Treatment Programs Coordination, Kyiv, Ukraine, [2]Regional Clinical Territorial Medical Association 'Phthisiatrics', TB Department, Uzgorod, Ukraine, [3]Regional Clinical Territorial Medical Association 'Phthisiatrics', Administration, Uzgorod, Ukraine. e-mail: olgazaitsva.21@gmail.com

Background and challenges to implementation: According to the estimates of the Council of Europe, the number of Roma population in Ukraine ranges from 120.000 to 400.000 people. The largest number of Roma population lives in Zacarpathian region and is one of most numerous ethnic minorities. The incidence rate of TB among Roma is 5 times higher than among the total population of the Zacarpathian region. The spread of TB among Roma occurs for a number of reasons, including due to HIV infection, injecting drug use, poor nutrition, overcrowding, low level of seeking medical care.
Intervention or response: From 2016 the complex of measures to improve the access of Roma population to the TB detection in the Zacarpathian region the activities of Roma social and medical mediators were implemented.
Mediators conducted screening by questionnaire to identify individuals with suspected TB and support to reach health facility where confirmation of diagnosis were performed.
Systematic communication with Roma and establishing close relationship between screening and early TB diagnosis demonstrate the effectiveness of the partnership between the regional TB serv ice and non-governmental organizations: during 3 years 218 TB patients were detected by questionnaire screening and 60,5% of them were smear positive.
Results and lessons learnt: Detection rate of smear positive cases among Roma with suspected TB increased by 63.6% compared to 2016, and the registration rate of TB cases of increased by 28%. In 2018, Roma was 11.1% of the 750 registered TB cases in the region, and among children 68.4% of the 28 registered, respectively.
Conclusions and key recommendations: Service delivery for the early detection and treatment of TB patients with Roma is crucial for the successful elimination of TB in the region. The activity of Roma social-medical intermediaries has led to an increase number of examinations with signs and symptoms of TB and the identification of patients, which will contributes to maintain this practice.

PS-36-903-02 How to get pro-bono support to light up buildings/landmarks red on World TB Day, 24 March: experience from Australia

S Shrestha,[1] M Rice,[1] A Christie,[1] T Eves,[1] N Poole,[1]
[1]RESULTS Australia, Global Health, Sydney, NSW, Australia.
e-mail: shiva.shrestha@results.org.au

Background and challenges to implementation: World TB Day is an opportunity to raise the profile of the disease and also create awareness among the general public. However, the low number of TB cases in Australia and limited awareness of the disease creates challenges in gaining public and media attention on Tuberculosis.
Intervention or response: RESULTS Australia designed a campaign where we reached out the local city councils to light up major buildings and landmark of significance importance on World TB Day. This was part of the Global Campaign 'Light up Red for TB' operating in multiple countries recently. RESULTS also organized a social media outreach to promote the campaign online. RESULTS with support from parliamentarians wrote to over 400 councils in the country to join the light up Red for TB campaign.
Results and lessons learnt: A total of 11 cities/towns in Australia agreed to light up 15 landmarks and locations red on the World TB Day 24 March. The relevant councils agreed to undertake this activity free of charge. The keys to success in achieving this were:
- Approaching councils in advance - Draft email/letter
- Knowing the best people to approach in the Council. Mayor and/or Marketing point person
- Emphasizing mutual benefits from the council's participation.

https://www.results.org.au/australian-landmarks-to-be-lit-red-in-honour-of-world-tb-day/
The social media posts around the campaign reached 210,000 with the engagement (engagement is defined as post clicks, likes, shares and comments) number of 1200.

[Images of Light up Red for TB campaign]

Conclusions and key recommendations: Light up Red for TB is a great opportunity for local councils to raise visibility and create awareness of Tuberculosis. Often they have the resources to be part of the campaign. This is a low resource and high leverage campaign for all to explore in their countries.

PS-36-904-02 Budget advocacy: a strategy to contribute increased funding at district and national levels to the End TB programme in Uganda

A Ocero,[1] A Nkolo,[2] J Wadulo,[3] S Turyahabwe,[4] E Birabwa,[5] [1]USAID /URC Defeat TB, Health Systems Strenghtening, Kampala, Uganda, [2]USAID Defeat TB, University Research Co., LLC, Health Systems Strenghtening, Kampala, Uganda, [3]Civil Society Budget Advocacy Group, Programs Department, Kampala, Uganda, [4]National Tuberculosis & Leprosy Control Program, National Disease Control, Kampala, Uganda, [5]USAID Uganda, TB/HIV Department, Kampala, Uganda.
e-mail: aocero@urc-chs.com

Background and challenges to implementation: The Political Declaration of the UN High-level meeting on TB expresses need for national governments to address the lack of sustainable financing for the tuberculosis response. The Uganda National TB Strategic Plan prioritizes increasing domestic funding from the current under 4% to 15% by 2019/20. Engaging national and district-level policy makers to increase government allocations for TB programming is a key strategy.
From September 2018, USAID Defeat-TB Project supported Uganda's National TB Leprosy Program to step-up advocacy activities during the months leading to the next National Budget launch in June 2019.
Intervention or response: Civil society advocates were enlisted to develop a 10-month schedule of budget activism aligned to the up-coming 2019/20 budget planning calendar. Stakeholders in national and district government influencing funding allocation were identified.
Facts and figures about the TB burden and program-funding gap were developed into position papers, flyers and burners. Budget advocacy engagements took place at: breakfast dialogue meetings with different Parliamentary Committees; a media-week of interactions with journalists and the public; health-sector-level and district-level budget framework paper (BFP) meetings; and, a civil society budget-review retreat.
Results and lessons learnt: Through the Defeat TB-CSO collaboration, 43% districts were reached through five Ministry of Finance-led district government pre-budget consultations. 30% of districts reached made commitments to fund TB activities in 2019/20. Senior managers from the Ministries of Health, and of Finance expressed a better understanding about TB. Parliamentarian participation into TB activities in their respective constituencies increased.

Despite the draft 2019/20 National BFP highlighting a US$127 Million budget-cut on pharmaceuticals for the health-sector, the National TB Leprosy Program is expected to gain a 6.3% increase in operations funding.
Conclusions and key recommendations: Increasing domestic funding for TB in resource-constrained settings is achievable through civil society-supported budget activism, closely tagged to the national budget planning and execution cycle, and well-packaged and targeted at the influencers of public funding allocation.

PS-36-905-02 Community empowerment to reduce tobacco smoking in Medawachchiya Division, Sri Lanka, through village-level tobacco prevention committees

N Rathnayake,[1] S Perera,[1] P Gunawardena,[2] TB Jayasinghe,[2] KD Senarathne,[2] M Ruwais,[2] S Dissanayake,[2] GND Guruge,[1] [1]Rajarata University of Sri Lanka, Department of Health Promotion, Anuradhapura, Sri Lanka, [2]Divisional Secretariat Office, Field Officers-Alcohol and Tobacco Prevention, Madawachchiya, Sri Lanka. e-mail: nadeeka93rathnayake@gmail.com

Background and challenges to implementation: Tobacco smoking is a major determinant for higher mortality and morbidity in Sri Lanka. The aim of the study was to empower tobacco smokers to quit or reduce through community based interventions and to evaluate the effectiveness of those interventions.
Intervention or response: This study was implemented in Medawachchiya division in Sri Lanka for a period of one year. The target group was 11 000 individuals who already use tobacco. The interventions were facilitated through 37 village level tobacco prevention committees. A committee was composed of 15 individuals including 07 government officers from police and divisional secretariat. The others were trained community members. Altogether, there were 555 members in these committees. The delivered interventions included group discussions with users on harm of tobacco use on family well-being and economy, discussions with family members of users, discussions with retail shop owners who sell cigarettes and children were equipped with skills to address tobacco smoking of family members. An evaluation was done by committees through interviewer administered questionnaires and descriptive statistics were used for analysis.
Results and lessons learnt: Results indicate that, number of tobacco smokers has been reduced to 10,108 from 11,000 users during a month. A collective decision was taken by society of retail sellers and divisional secretariat, not to permit to sell cigarettes in Medawachchiya. Prior to the interventions, 40 retail shop owners sold cigarettes in Medawachchiya, but now, 39 have stopped selling cigarettes (98%). Within a year, 10 000 000 LKR had been saved in Medawachchiya division due to reduction of smoking.
Conclusions and key recommendations: Village level committees with the inclusion of community members are capable of delivering effective interventions to reduce or quit smoking. Results reinforce to empower lay people to address tobacco epidemic in their areas with a proper guidance by trained officers.

PS-37-D6 Preventing disease: a focus on LTBI and transmission avoidance

PS-37-906-02 The effect of anti-tuberculosis treatment on the infectiousness of people with drug-susceptible tuberculosis: a systematic review and meta-analysis

CJ Calderwood,[1] J Wilson,[1] M Bergstrom,[1] S-M Johnson,[1] S Stokes,[1] N McCreesh,[1] EJ Monk,[1] J Odayar,[1] P Scott,[1] DAJ Moore,[1] LSHTM TB Centre Systematic Review Group [1]London School of Hygiene and Tropical Medicine, TB Centre, London, United Kingdom. e-mail: clairejcalderwood@gmail.com

Background: National and international guidelines recommend a period of isolation for individuals with pulmonary tuberculosis (TB) starting treatment to reduce transmission risk. We undertook a systematic review and meta-analysis to investigate dynamics of sputum sterilisation after commencement of TB therapy, as part of evidence gathering for updating the World Health Organization TB Infection Prevention and Control guidelines.
Methods: A systematic search of four databases was conducted, before two-stage sifting in duplicate. We included articles with data on patients with drug-susceptible TB receiving effective treatment (defined as at least isoniazid, rifampicin and pyrazinamide during intensive phase). The outcome of interest was sputum conversion, assessed either by smear or culture. Random effects meta-analysis was conducted.
Results: Searches identified 5290 records of which 50 articles were included. On meta-analysis smear conversion was demonstrated in 30% of baseline smear-positive patients at one month after treatment initiation, increasing to 87% at two months (2 and 9 studies). Solid culture conversion was achieved at two, four and eight weeks in 10%, 52% and 90% patients respectively (4, 11, 21 studies); at the same timepoints liquid culture conversion was achieved in 14%, 37% and 72% respectively (3, 2 and 10 studies) (table). I^2 range: 57-96%. Median quality score was 7/9 (interquartile range: 7-8).
Conclusions: The available data on dynamics of sputum conversion during effective TB treatment were surprisingly limited. Considerable heterogeneity between studies likely reflects underlying differences in disease phe-

notypes and study populations. Very few studies disaggregate culture conversion by baseline smear status or other factors thought to delay conversion such as pulmonary cavitation. 28% patients remained liquid culture-positive at two months, challenging the widely-held view that individuals are not infectious after two weeks of effective TB therapy. Sputum sterilisation is only one determinant of infectiousness; other factors including cough dynamics are probably also important.

Duration of treatment	Solid culture		Liquid culture		Smear microscopy	
	Proportion (95% CI)	N (I^2)	Proportion (95% CI)	N (I^2)	Proportion (95% CI)	N (I^2)
1 week	0.03 (0.00-0.07)	3 (57%)	-	-	-	-
2 weeks	0.10 (0.06-0.13)	4 (95%)	0.14 (0.09-0.20)	3 (95%)	-	-
3 weeks	0.18 (0.12-0.24)	2 (-)	-	-	-	-
1 month	0.52 (0.50-0.55)	11 (92%)	0.37 (0.27-0.46)	3 (95%)	0.30 (0.27-0.34)	2 (-)
2 months	0.90 (0.89-0.91)	21 (84%)	0.72 (0.70-0.74)	11 (96%)	0.87 (0.86-0.88)	9 (91%)
3 months	0.98 (0.96-0.99)	2 (-)	0.56 (0.38-0.73)	1 (-)	0.95 (0.94-0.95)	2 (-)
4 months	0.99 (0.98-1.00)	5 (78%)	0.82 (0.63-0.94)	1 (-)	0.99 (0.97-1.00)	2 (-)

Pooled estimates from random effects meta-analysis.

Abbreviations: CI = confidence interval, N = number included estimates; I^2 = I^2 statistic for heterogeneity (presented where >2 studies included)

[Summary of proportion of drug-susceptible TB patients achieving smear or culture conversion at defined time points, by detection method]

PS-37-907-02 Quantifying the rates of late reactivation TB: a systematic review

K Dale,[1,2] K Snow,[3,4] D Menzies,[5] J Trauer,[1,6] J Denholm,[1,2] [1]Victorian Tuberculosis Program, Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia, [2]University of Melbourne, Department of Microbiology and Immunology, Melbourne, VIC, Australia, [3]University of Melbourne, Centre for International Child Health, Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia, [4]University of Melbourne, Centre for Health Equity, Melbourne School of Population and Global Health, Melbourne, VIC, Australia, [5]Montreal Chest Institute & McGill International TB Centre, Respiratory Epidemiology and Clinical Research Unit, Montreal, QC, Canada, [6]Monash University, School of Public Health and Preventive Medicine, Melbourne, VIC, Australia. e-mail: katie.dale@mh.org.au

Background: The risk of tuberculosis (TB) is greatest soon after infection, but disease may develop many years or decades later. Accurately quantifying long-term TB reactivation rates is important at both the individual and population levels for estimating the benefits of preventive therapy. We performed a systematic review to find evidence for TB reactivation rates more than two years from infection (late reactivation).

Methods: We searched eight databases from inception to Dec 18, 2018, for studies that quantified TB late reactivation rates in cohorts with latent TB beyond two years after conversion or exposure, or in those with an unknown exposure history; we also included cohort studies which estimated latent TB prevalence (PROSPERO-registration: CRD42017070594). We excluded modelling studies and studies exclusively in cohorts with known risk-factors.

Results: In the majority of the 98 included studies the timing of infection was unknown. Few studies documented rates more than two years from either exposure or conversion and, since the advent of antibiotics, only seven have documented rates beyond four years. In these studies, rates declined over time, reaching ~200/100,000/year or below by the fifth year. Rates may have continued to decline beyond this (maximum follow-up was ten years), although decreasing cohorts under observation makes interpretation difficult. The effect of age remains unclear, with most studies pooling results across age groups. In study cohorts for which the timing of infection was unknown, rates declined over time to < 100/100,000/year beyond ten years. Rates were also largely ~100/100,000/year or below in studies in low incidence settings that estimated reactivation rates by considering genotypically unclustered cases and estimating latent TB prevalence.

Conclusions: To our knowledge, this is the first time evidence on late reactivation rates has been comprehensively collated. Our review highlights the significant gaps that remain in our understanding TB reactivation, and should spur prompt attempts to redress them.

PS-37-908-02 The global prevalence of latent tuberculosis: a systematic review and meta-analysis

A Cohen,[1] VD Mathiasen,[2,3] T Schön,[4] C Wejse,[2,5] [1]St. Olavs Hospital, Department of Pathology, Trondheim, Norway, [2]Aarhus University Hospital, Department of Infectious Diseases, Aarhus, Denmark, [3]Statens Serum Institute, International Reference Laboratory of Mycobacteriology, Copenhagen, Denmark, [4]Kalmar County Hospital, Department of Clinical Microbiology and Infectious Diseases, Kalmar County Hospital, Linköping, Sweden, [5]Aarhus University, Center for Global Health (GloHAU), Aarhus, Denmark. e-mail: victordahl@gmail.com

Background: In 1999, the WHO estimated that one-third of the world's population had latent tuberculosis (LTBI) which was recently updated to one-fourth. However, this is still based on controversial assumptions in combination with tuberculin skin test (TST) surveys. Interferon-gamma release assays (IGRAs) with a higher specificity than TST have since been widely implemented, but never used to estimate the global LTBI prevalence.

Methods: We conducted a systematic review and meta-analysis of LTBI estimates based on both IGRA and TST results published between 2005 and 2018. Regional and global estimates of LTBI prevalence were calculated. Stratification was performed for low, intermediate and high TB incidence countries and a pooled estimate for each area was calculated using a random effects model.
Results: Among 3280 studies screened, we included 88 studies from 36 countries with 41 IGRA (n=67 167) and 67 TST estimates (n=284 644). The global prevalence of LTBI was 24×8% (95% CI: 19×7-30×0%) based on IGRA and 21×2% (95% CI: 17×9-24×4%) and 24.1% (95% CI: 19×7-29×9%) based on a 10 and 5 mm TST cut-off, respectively. The prevalence estimates correlated well to WHO incidence rates (Rs=0.70, p< 0.001).
Conclusions: In the first study of the global prevalence of LTBI derived from both IGRA and TST surveys, we found that one-fourth of the world's population is infected. This is of relevance as both tests, although imperfect, are used to identify individuals for preventive therapy. Enhanced efforts are needed to target the large pool of latently infected individuals as it continuously constitutes an enormous source of potential active TB.

PS-37-909-02 Use of cough monitor in tuberculosis active case finding, Kimaeti Health Centre, Kenya

R Magomere,[1] [1]Ministry of Health, Health, Bungoma, Kenya. e-mail: robertmagomere@yahoo.com

Background: Kenya has recorded a decline in TB case notification since 2007. Prevalence survey done showed that approximately 40% of TB cases are missed, while three quarters of people with TB symptoms seek care in health facilities, but are not diagnosed due to lack of awareness, overwhelmed health care workers and overcrowding at the health facilities which leads to delay in diagnosis. This study aims to assess the impact of use of cough monitor in active case finding.
Methods: A trained cough monitor was placed in the waiting area of the outpatient department (OPD). The cough monitor screened all the clients visited the public health facility for symptoms of TB and identified presumptive TB patients were fast tracked to the diagnostic centre.
Results: A total of 7,683 patients were screened with 715/7683 (9.3%) of them being presumptive TB cases. Among them 529/715 (74%) submitted sputum sample for GeneXpert and 17/529 (3.2%) had bacteriologically TB. In addition 5 were diagnosed with other forms of TB using X-ray and clinical evaluation giving a total of 22. There was increase of 25% of TB case notified.
Conclusions: Cough monitors play an important role in early identification of TB patients and helps in finding the missing TB cases.

PS-37-910-02 Implementation of tuberculosis infection control practices in tuberculosis diagnostic and treatment healthcare facilities in Kampala District, Uganda, August 2015

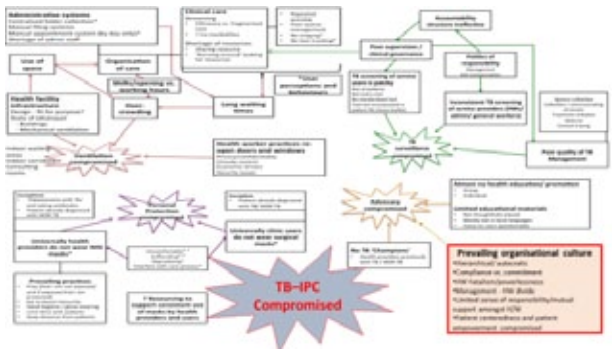
D Tugumisirize,[1,2,3] SP Katongole,[3] L Bulage,[1,4] SZ Muyanja,[5,6] RK Majwala,[6] S Turyahabwe,[1] J Moses,[1,2,7] S Muchuro,[1,6] [1]Ministry of Health, National Tuberculosis and Leprosy Program, Kampala, Uganda, [2]Ministry of Health, Supra National Tuberculosis Reference Laboratory, Kampala, Uganda, [3]Uganda Martyrs University, Faculty of Health Sciences, Kampala, Uganda, [4]Makerere University School of Public Health, Public Health Fellowship Program, Kampala, Uganda, [5]Infectious Diseases Institute, College of Health Sciences, Makerere University, Kampala, Uganda, [6]United States Agency for International Development, Defeat TB Project, Kampala, Uganda, [7]Makerere University, College of Health Sciences, Kampala, Uganda. e-mail: tdidas2013@gmail.com

Background: Tuberculosis (TB) Infection control (IC) measures are inadequately implemented in resource limited settings. We assessed the implementation of TB IC practices in TB Diagnostic and Treatment Units (DTUs) in Kampala District, which accounts for 15-20% of the total TB burden in Uganda.
Methods: We conducted a cross-sectional study in August 2015 in 25 selected DTUs including 07 Public healthcare facilities, 14 Private not for Profit (PNFPs), 03 Private for Profit (PFP), and 01 Non Government DTU. We modified and used a checklist adopted from a standardized tool for assessment of adherence to recommended TBIC from the manual for implementing TB control measures in health care facilities, and where necessary, observed the TB IC practices or reviewed healthcare facility records to ensure triangulation of the findings. We conducted univariate analysis and generated proportions in order to ascertain the extent of implementation of TB IC measures.
Results: Averagely, 73% administrative/managerial, 65% environmental, and 56% personal protective measures were implemented. However, no single healthcare facility implemented all the three levels of TB IC measures in an integrated manner. By Observation, 12% had a designated area for sputum collection, 56% were regularly opening windows, 28% had TBIC guideline, 36% had a TBIC plan, 40% had fans installed either in the waiting areas and/or consultation rooms and 24% had bio-safety cabinets fitted with UV light. Additionally, 60% had N95 respirators but only 32% of the facilities reported that their workers routinely wore them, and 36% reported that they were regularly screening health care workers for TB.
Conclusions: Implementation of WHO recommended TB IC measures was sub optimal. Interventions to improve their implementation should be developed and implemented.

PS-37-911-02 Compromised TB infection prevention and control in South African primary care facilities: a whole systems perspective

A Voce,[1] G Zwama,[2] H Macgregor,[3] A Grant,[4] K Kielmann,[2] [1]University of KwaZulu-Natal, Public Health Medicine, Durban, South Africa, [2]Queen Margaret University, Institute for Global Health & Development, Edinburgh, United Kingdom, [3]Sussex University, Institute of Development Studies, Brighton, United Kingdom, [4]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom.
e-mail: alison.grant@lshtm.ac.uk

Background: WHO guidelines on tuberculosis infection prevention and control (TB-IPC) emphasise integrated, well-coordinated, multisectoral action. However, to date, the dynamic and complex health systems context of IPC implementation has had limited consideration. The *Umoya omuhle* project applies a 'whole systems' approach to assess TB and DR-TB transmission in South African primary health care facilities, and to identify opportunities for strengthening health systems and health workers' capacity to implement IPC measures.
Methods: Focused site visits were conducted on three consecutive days in six PHC facilities across three districts of KwaZulu-Natal, South Africa to assess the influence of clinic infrastructure, organisation of care and working practices on implementation of TB-IPC. Methods included structured interviews with clinic managers, informal conversations with staff, and patients, and observations of care processes, clinic space, ventilation, and personal protective measures.
Results: Current infrastructural constraints, use of clinic space, and organisation of TB care result in sub-optimal patient flow, long waiting times and overcrowding, often in poorly ventilated areas. Implementation of cough triaging and TB surveillance is inconsistent. Climatic conditions, stigma, and low levels of perceived risk contribute to poor uptake of protective masks. Differential levels of leadership, health worker agency and organisational accountability underpin the variable implementation of TB-IPC measures.



[Compromised TB IPC in South African Primary Care Facilities]

Conclusions: Within the PHC facilities observed, systems-specific influences dynamically interact to compromise optimal implementation of TB-IPC. Successful implementation of the WHO recommendations will be contingent on whole systems change solutions that empower health workers and managers to optimise clinic space, timings, and organisation of TB care in order to reduce the risk of transmission.

PS-37-912-02 Delays in diagnosis of pulmonary tuberculosis associated with high risk of transmission in pastoralist setting, Ethiopia

F Getnet,[1] M Demisse,[2] A Worku,[3] T Gobena,[1] B Seyoum,[4] R Tschop,[5,6,7] [1]Haramaya University, School of Public Health, Harar, Ethiopia, [2]Addis Continental Institute of Public Health, Public Health, Addis Ababa, Ethiopia, [3]Addis Ababa University, Epidemiology and Biostatistics, Addis Ababa, Ethiopia, [4]Armanure Hansen Research Insitute, Infectious Diseases Research, Addis Ababa, Ethiopia, [5]Swiss Tropical and Public Health Institute, One Health and Researcher, Basel, Switzerland, [6]Armanure Hansen Research Insitute, One Health and Zoonosis, Addis Ababa, Ethiopia, [7]University of Basel, Epidemiology and One Health, Basel, Switzerland.
e-mail: b.infen4ever@gmail.com

Background: To comprehend the effect of delayed care on risk of tuberculosis (TB) transmission in TB prevalent but low case detection area, we examined the association of diagnosis delay with patient infectiousness (cavitation and smear positivity). We also assessed transmission drivers in Somali region of Ethiopia, largely populated by pastoralists.
Methods: We employed prospective strategy to recruit 434 new pulmonary TB patients aged ≥15 years in five major facilities between December 2017 and October 2018. We collected data on delays in diagnosis, sociodemographics, clinical and epidemiologic information using interview, record-review, anthropometry, sputum microscopy and Chest radiography. Log-binomial regression models were used to reveal predictors of cavitation and smear positivity at p≤0.05. C-statistics was applied to determine predictive ability and threshold delay that classifies infectiousness.
Results: Median age of participants was 30 years. Majorities were male (62.9%), nearly half (46.5%) were pastoralist and 2.3% TB/HIV co-infected. Median delay from debut of illness to diagnosis was 49 days (range, 8 to 362). Among all cases, 45.6% [95%CI: 40.9-50.4] had pulmonary cavity and 42.0% [95%CI: 37.3-46.9] were smear positive. On multivariable analysis, cavitation was higher in patients delayed over a month [P< 0.001], ≤35 years [APR (95%CI) =1.3(1.01-1.6)], with chronic diseases [APR (95%CI) = 1.8(1.2-2.6)] and low MUAC*female [APR (95%CI) =1.8(1.2-2.8)]. Smear positivity was higher in patients delayed >49 days [p=0.02], ≤35 years [APR (95%CI) = 1.4(1.1-1.8)], low BMI

[APR (95%CI) = 1.3(1.01-1.7)] and low MUAC [APR (95%CI) = 1.5(1.2-1.9)]. Delay discriminates cavitation [AUC (95%CI) = 0.67 (0.62-0.72)] at 43 days optimal cutoff and 74.6% sensitivity.
Conclusions: Our study highlights delays in diagnosis of pulmonary TB remain unduly high and is associated with increased risk of cavitation and smear positivity in pastoral settings in Ethiopia. In pastoral settings, this may call upon a socio-cultural tailored prevention and intervention TB strategy.

PS-37-913-02 Neither children nor adults: socio-demography, household exposure and nutritional status of adolescents with self-reported TB from a nationally representative survey from India

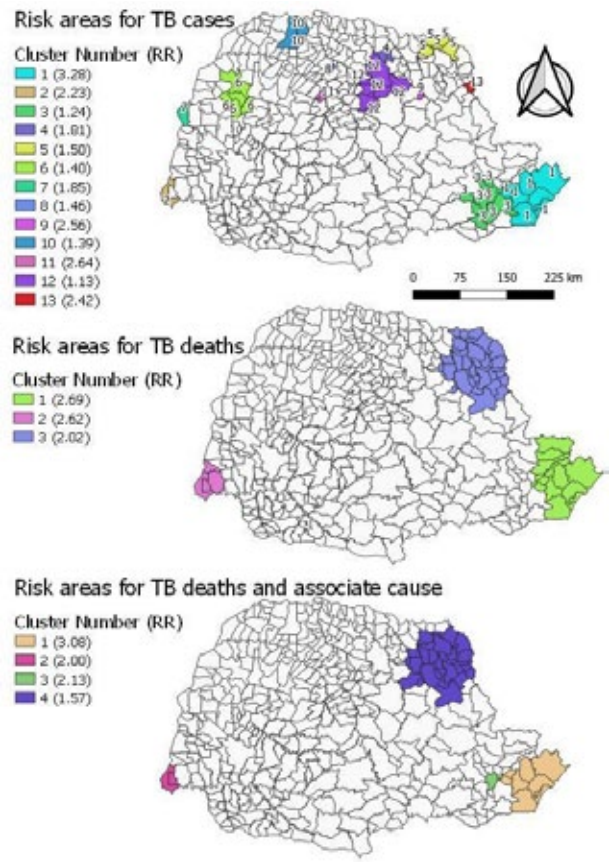
M Bhargava,[1,2] A Bhargava,[2,3] [1]Yenepoya Medical College, Community Medicine, Mangaluru, India, [2]Yenepoya (Deemed to be University), Center for Nutrition Studies, Mangaluru, India, [3]Yenepoya Medical College, Internal Medicine, Mangaluru, India.
e-mail: madhavibhargava4@gmail.com

Background: We examined the socio-demographic characteristics, household TB exposure and anthropometry as marker of under-nutrition in adolescents (15-19 years) with self-reported tuberculosis in the National Family Health Survey-4 (NFHS-4) of 2015-2016.
Methods: The NFHS-4 collected information on whether any household member was suffering from TB and if the adolescent interviewed was suffering from TB. We compared gender, economic class and urban-rural residence in adolescents with self-reported TB with the rest of the adolescents. For nutritional status we compared stunting and thinness. Height-for-age z-scores for stunting and body mass index (BMI) for age z-scores for thinness were computed by WHO Anthro-Plus software. Chi-squared tests and t-tests were used for comparisons.
Results: Of 2,77,059 adolescents interviewed, 4905 (1.8%) had household contact with TB, and of these 377 were suffering from TB. The prevalence of TB was similar in boys and girls (51.5% vs. 48.5%, p=0.959). The proportion of TB in adolescents was higher in urban households (33.7% vs.27.5%; p< 0.007), and in the poorer quintiles (p=0.004). The prevalence of stunting was 40.7% (CI: 33.5, 38) and thinness was 23.1% (CI: 16.8, 29.4) in adolescents suffering from TB, compared to 34.8% (CI: 34, 35.6) stunting and 9.6% (CI: 9.1, 10.1) thinness in other adolescents (p< 0.001). Of the 4905 adolescents with household exposure, the occurrence of TB in 377 (7.7%) represents a high rate of progression.
Conclusions: Tuberculosis in Indian adolescents is equally prevalent across gender and is strongly linked to household exposure. Apart from young children, adolescents also seem to be at an increased risk of progression from infection to active disease. Chronic undernutrition is a highly prevalent risk factor in this group, with rates of undernutrition comparable to that in under-five children. Adolescents in India may be considered for preventive therapy and nutritional interventions to reduce TB burden.

PS-37-914-02 Spatial clusters risk for occurrence of tuberculosis cases and deaths in the state of Paraná, Brazil

MAM Arcoverde,[1] AR Scholze,[2] IS Assis,[3] FM Pieri,[4] DT Santos,[3] HL Andrade,[3] LT Campoy,[3] LS Alves,[3] M Yamamura,[3] RA Arcêncio,[3] [1]State University of Western Paraná, Nursing, Foz do Iguaçu, PR, Brazil, [2]University of Northern Paraná, Nursing Setor, Bandeirantes, PR, Brazil, [3]School of Nursing of Ribeirão Preto - University of São Paulo, Maternal Child and Public Health Department, Ribeirão Preto, SP, Brazil, [4]Londrina State University, Nursing Department, Londrina, PR, Brazil.
e-mail: ricardo@eerp.usp.br

Background: Tuberculosis (TB) has been a challenge, especially for developing countries. In Brazil, although the state of Paraná, located in the South, has good social indicators (for example: Human Development Index (HDI) - 0.76), there is still difficult a coping for the TB. The proposal was to identify risk areas for tuberculosis (TB) incidence, death and lethality in the state of Paraná, Brazil.
Methods: The data were collected in the Information System for Notification of Injuries, Brazilian Ministry of Health, from 2010 to 2018, for variables: new cases, deaths from basic cause and lethality (most basic cause associated). Was performed a calculation of the relative risk for each of the variables and their respective Confidence Interval in 95%; the calculation was standardized by sex and age. Was used the SatScan software version 9.3.
Results: In the period, were reported 23176 (16.36 per 100,000) new cases of TB, 875 deaths from basic TB cause (0.62 per 100,000) and 2311 deaths from basic cause most associate of TB (1.63 per 100,000). We identified 13 risk areas with RR ranging from 1.13 to 3.28 (95%CI 1.07 - 3.51) for TB incidence. There were three risk groups with RR between 2.69 and 2.02 (95%CI 1.57 - 3.37) for TB deaths. There were four areas with RR between 1.57 and 3.08 (95%CI 1.31 - 3.53) for lethality. The RR areas for death were concentrated on the extremes with an international border, bordered by another Brazilian state and in a port area.
Conclusions: Areas of risk for deaths up to 3 times more than national data were observed. It is important to use tools that can highlight the risk areas for TB deaths in order to plan more focused actions in national sub regions. For the identified risk areas requires a more comprehensive response, involving the countries and surrounding states.



[Risk Cluster for new cases and mortality from TB, Paraná, Brazil (2010-2018)]

PS-37-915-02 Exposed but not ignored: an e-registry for MDR-TB exposed contacts

KM Gaskell,[1] K Naker,[1] R Allen,[1] W Mukhwana,[2] S Leekha,[3] D Naranzul,[4] M Dorjravdan,[4] C Roberts,[5] DAJ Moore,[1] [1]LSHTM, TB Centre, Clinical Research Department, London, United Kingdom, [2]World Vision International, Somaliland World Vision International, Hargeisa, Somalia, [3]HSIP India, Public Health Analysis and Design Team, Uttar Pradesh, India, [4]National Centre for Communicable Diseases, Tuberculosis Department, Ulaanbaatar, Mongolia, [5]LSHTM, Clinical Research Department, London, United Kingdom.
e-mail: kate.gaskell@lshtm.ac.uk

Background: Whilst the results of ongoing three RCTs of preventive therapy for MDRTB LTBI are awaited, optimal management of individuals exposed to MDRTB remains uncertain. WHO recommends surveillance of contacts for two years but countries lack the tools to achieve this; preventive therapy with an unspecified regimen for an unspecified duration is recommended for a small selected group of contacts at (not clearly specified) high risk.
Methods: Using DHIS2 we developed an electronic (e-) registry to facilitate the registration and follow-up of individuals exposed to multidrug resistant tuberculosis (MDRTB). The e-registry will be populated by data from multiple countries, simultaneously creating an international prospective observational cohort of MDRTB contacts. Our aims are to standardise data collection, improve screening of contacts, speed the diagnosis of incident TB, reduce time to appropriate TB treatment and enable follow up of contacts. WHO has rolled out a DHIS2 platform for its TB surveillance work to which this e-registry is easily linked.
Results: Pilot studies of MDRTB contact e-registries by our group in Mongolia, Peru and Somalia indicate high levels of user acceptability. In Peru 90% of contacts were satisfied with measures to ensure confidentiality and were not worried about entering their personal data onto the e-registry. In Mongolia 100% of clinicians using the e-registry were somewhat or very satisfied with the interface. In Peru 87/129 (67%) contacts were symptomatic and submitted a sputum sample, 20/44 (45%) of MDRTB contacts underwent LTBI testing and 19/120 (16%) reported previous TB treatment. In Mongolia 7/70 MDRTB contacts had laboratory confirmed TB, and 3 of 4 tested for drug susceptibility testing had identical patterns.
Conclusions: Ongoing research facilitated by this tool focuses on the risk of progression to active MDRTB in household contacts exposed to MDRTB, and identification of predictors of risk to guide future targeting of interventions.

PS-38-B1 TB Diagnostics

PS-38-917-02 Pipeline for blood transport and processing for cell-based assays to discriminate forms of TB in an endemic region of Papua New Guinea

C Rush,[1] T Diefenbach-Elstob,[1] R Dowi,[2] D Pelowa,[3] B Gula,[2] E McBryde,[1] J Warner,[1] [1]James Cook University, Australian Institute of Tropical Health and Medicine, Townsville, QLD, Australia, [2]Balimo District Hospital, Clinical Services, Balimo, Papua New Guinea, [3]Balimo District Hospital, Laboratory, Balimo, Papua New Guinea.
e-mail: catherine.rush@jcu.edu.au

Background: Tuberculosis diagnosis, drug susceptibility and response to therapy testing rely on an integrated diagnostic platform of clinical, microbiological, molecular and immune cell-based methods. Papua New Guinea (PNG), has the highest rate of TB in the Pacific region and restricted access to this breadth of testing regimens. Flow cytometry-based T cell assays can characterise leucocyte phenotype and function in response to infection and can be used to discriminate forms of TB. These cell-based assays however require live, functional cells and thus their widespread use is limited by

the requirement to maintain cell viability during transport from regions that are geographically distant from specialised reference laboratories able to perform these assays.
Methods: We designed a blood collection, preservation, transport and analysis pipeline to expand the capacity of remote, regional PNG hospitals and health districts to utilise immune cell-based diagnostics for TB. Frequencies of diverse leucocytes were compared across participant groups to identify cell types able to distinguish active from latent disease. Study groups were:
(i) community members ($IGRA^{neg}$);
(ii) latent tuberculosis ($IGRA^{pos}$);
(iii) TB suspect (suspected TB; before therapy);
(iv) TB patient (on therapy);
(v) past TB patient (treated with recovery) and;
(iv) non-TB diagnosis.
Results: We showed differences in leucocyte numbers across participant groups with T cells and related innate cells typically decreased in TB suspects and patients. Previous studies have identified CD161-expressing T cells as a useful blood biomarker of active versus latent TB. Our results confirmed this finding with TB suspects in particular having diminished $CD161^{+}$T cells compared to other participant groups.
Conclusions: Using this sample pipeline we showed that blood collected and stabilised at a remote location can be optimally transported for flow cytometric analysis at reference laboratories. This diagnostic model may be further developed for use in-country in PNG to incorporate immune-based TB diagnostics into the national TB program.

PS-38-918-02 TB-LAMP assay for diagnosis of paediatric tuberculosis: a prospective cohort study

S Sethi,[1] P Vaidya,[2] J Mathew,[2] M Singh,[2] P Daroch,[1] N Mehra,[2] P Agarwal,[3] R Khaneja,[4] R Yadav,[1] [1]PGIMER, Department of Medical Microbiology, Chandigarh, India, [2]PGIMER, Pediatric Medicine, Chandigarh, India, [3]WHO Country Office, RNTCP, Chandigarh, India, [4]State Tuberculosis Cell, RNTCP, Chandigarh, India.
e-mail: sunilsethi10@hotmail.com

Background: TB-LAMP (Loop-mediated isothermal amplification) is a manual assay and recommended by WHO for replacement for microscopy for diagnosis of pulmonary TB in adults.
No study highlights the use of TB-LAMP for diagnosis of pediatric tuberculosis. In this study, we evaluated the TB-LAMP assay for detection of *M tuberculosis* in respiratory samples of children.
Methods: A total of 187 respiratory samples including gastric aspirate/lavage (n= 96) broncho-alveolar lavage (n=27), sputum (n= 60), endotracheal aspirate (n= 4), from the suspected tuberculosis children (<15 years) were collected and were processed for MGIT culture and Xpert MTB/RIF as per manufacturer's instructions. The TB-LAMP assay were performed directly on the respiratory samples and results were interpreted as positive and negative based on manufacturer's instructions.
Results: Among 187 samples, 11 were rejected due to culture contamination, the valid results of TB-LAMP assay were received in 176/187 (94.1%). The median age of children were 7 yrs.
A total of 25/176 (14.2%) respiratory samples were positive by MGIT culture for *M tuberculosis complex* and considered as a reference standard. The smear, TB LAMP and Xpert MTB/RIF were positive in 5/176(2.8%), 26/176(14.8%) and 25/176(14.2%) samples, respectively. The sensitivity of TB-LAMP and Xpert MTB/RIF were found 80% (95% CI, 59.3-93.2%) and 84% (95% CI, 63.9-95.5%) and the specificity were 96.1% (95% CI, 91.6-98.5%) and 97.4% (95% CI, 93.4-99.3%), respectively.
The positive and negative predictive value for TB-LAMP and Xpert MTB/RIF were 76.9%(95% CI, 59.8-88.2%) and 84%(95% CI, 66.3-93.3%) or 96.7%(95% CI, 93-98.5%) and 97.3%(95% CI, 93.7-98.9%), respectively. The diagnostic accuracy of TB-LAMP and Xpert MTB/RIF were 93.8% and 95.5%, respectively.
Conclusions: The TB-LAMP assay showed a good sensitivity and specificity but slightly lower than Xpert MTB/RIF assay for diagnosis of pediatric tuberculosis. More studies are required taking clinical diagnosis and mycobacterial culture both as a reference standard.

PS-38-919-02 Tuberculosis lateral flow lipoarabinomannan test (LF-LAM) evaluation in Uganda: challenges and opportunities for optimal performance

R Makabayi-Mugabe,[1,2] S Turyahabwe,[3] S Zawedde-Muyanja,[2] P Namuwenge,[3,4] P Lusiba,[5] R Mangeni,[6] S Riese,[7] A Nkolo,[6] M Joloba,[5,8] [1]USAID/Defeat TB Project, Health Systems Strengthening Department, Kampala, Uganda, [2]Infectious Diseases Institute, Research Department, Kampala, Uganda, [3]Ministry of Health, National Tuberculosis and Leprosy Program (NTLP), Kampala, Uganda, [4]Ministry of Health, Aids Control Program, Kampala, Uganda, [5]Ministry of Health, National Tuberculosis Reference Laboratory (NTRL), Kampala, Uganda, [6]USAID/Defeat TB Project, Technical Department, Kampala, Uganda, [7]University Research Co., LLC (URC), Research Department, Maryland, WA, United States of America, [8]Makerere University College of Health Sciences, Microbiology, Kampala, Uganda.
e-mail: makrita2@gmail.com

Background and challenges to implementation: In June 2017, Uganda adopted the use of LF-LAM among adult HIV positive presumptive TB patients with a CD4 cell count ≤ 100 or very ill HIV positive presumptive TB patients regardless of their CD4 cell count.
In October 2018 an evaluation on the utilization of LF-LAM was carried out since only half of the test kits were used.

Intervention or response: A cross sectional study using semi-structured questionnaires, in-depth interviews with facility managers, focus group discussions with health workers and data abstraction were conducted across 12 Regional Referral Hospitals in Uganda from October 2018 to November 2018.

Results and lessons learnt: On average only 25% (98/387) of all eligible patients got tested with LF-LAM each month. The test was mainly carried out in the in-patient wards (9/12), 4/12 in HIV clinic with limited to no use in paediatric sections. Eligibility was sometimes extended to non-eligible groups, with varied placement of LF-LAM in the diagnostic algorithm as well as the testing processes. 15% of patients with a positive LF-LAM test were not started on TB treatment. Engagement of leadership, training and availability of initial stocks were facilitating factors while the lack of standardized procedures, data collection tools, standard operating procedures (SOPs) and stock management procedures were barriers to LF-LAM implementation. Health workers had a positive attitude towards the test noting several advantages like quick turnaround time (TAT), ease of use and when faced with challenges of obtaining sputum samples.

Conclusions and key recommendations: Despite challenges in implementation, there is potential for LF-LAM use as a diagnostic test by harnessing on its ability to greatly reduce TAT and improve treatment initiation among TB patients. For optimal performance, the NTLP should provide SOPs, standard reporting &recording tools, streamline stock management procedures, sensitize health facilities, ensure uniform communication on eligibility, place in diagnostic algorithm and management of positive patients with emphasis among children.

PS-38-920-02 Structural organisation of terminal arabinan of Mtb lipoarabinomannan isolated from mice lung granulomas and patient's urine

P De,[1] L Shi,[1] C Boot,[2] D Ordway,[1] D Chatterjee,[1]
Tuberculosis [1]Colorado State University, Microbiology, Immunology and Pathology, Fort Collins, CO, United States of America, [2]Colorado State University, Central Instrument Facility, Fort Collins, CO, United States of America.
e-mail: prithwiraj.de@colostate.edu

Background: *Mtb* Lipoarabinomannan (LAM) is a biomarker for active TB disease. Recently, there has been an upsurge in detecting urinary LAM by immunoassays. The available point-of-care (POC) TB LAM tests have poor sensitivity and only limited to HIV co-infected TB diagnosis. The anti-LAM antibodies (Abs) employed in immunoassays are presumably directed to terminal tetra-(Ara4) and hexa-(Ara6)-arabinosides-epitope recognition.

We hypothesized that there could be structural differences between isolated *in vivo* or urinary LAM and *in vitro* isolated TB LAM, which are used for optimization of any new immunoassay.

We envisage that the success, in terms of sensitivity and specificity of immunoassay based TB LAM POCs, should depend on proper definition of urinary LAM structure and employment of Abs that can recognize unique terminal structures.

Methods: We infected C3HeB/FeJ mice with *W. Beijing* SA161, isolated, extracted and purified LAM from the granulomas (Tuberculosis 2014) at the chronic stage of infection. Concomittantly, we purified LAM from a TB+ HIV- patient's urine (PloS One 2015).

The *in vivo* LAM samples (urine and granulomas) upon endoarabinanase enzyme (from soil *Cellulomonas* ssp.; CSU) digestion yielded terminal ends distinct from the *in vitro* LAM.

These enzymes were known to digest mycobacterial arabinan and release terminal Ara2, Ara4 and Ara6 epitopes with or without mannose caps.

Results: Instead of traditional $(Man)_nAra4$ and $(Man)_nAra6$ (n= 0-4), we found succinylated Ara4, Ara5 and their mannose capped variations with only trace amount of Ara6 in *in vivo* LAM.

Conclusions: Thus, our hypothesis is supported with the differences observed in terminal arabinan arrangements. This information will aid in engineering appropriate Abs, that are specific to these epitopes, and are required for the success of LAM POC assays.

PS-38-921-02 A higher-sensitivity LAM assay for TB testing in hospitalised patients with HIV: cost-effectiveness analysis

K Reddy,[1,2] C Denkinger,[3] T Broger,[4] N McCann,[1] A Gupta-Wright,[5,6] F Shebl,[1,2] K Fielding,[7,8] M Nicol,[9] R Wood,[10] R Walensky,[1,2] [1]Massachusetts General Hospital, Medical Practice Evaluation Center, Boston, MA, United States of America, [2]Harvard Medical School, Department of Medicine, Boston, MA, United States of America, [3]FIND, Tuberculosis Programme, Geneva, Switzerland, [4]FIND, R&D, Geneva, Switzerland, [5]London School of Hygiene & Tropical Medicine, TB Centre, London, United Kingdom, [6]Malawi-Liverpool-Wellcome Trust, Clinical Research Program, Blantyre, Malawi, [7]London School of Hygiene & Tropical Medicine, Infectious Disease Epidemiology, London, United Kingdom, [8]University of the Witwatersrand, School of Public Health, Johannesburg, South Africa, [9]University of Western Australia, Infection and Immunity, Perth, WA, Australia, [10]University of Cape Town, Desmond Tutu HIV Centre, Cape Town, South Africa. e-mail: kpreddy@mgh.harvard.edu

Background: Despite trial-documented benefits, the first-generation urine lipoarabinomannan (LAM) assay has suboptimal sensitivity for TB testing in hospitalized people with HIV (PWH). We examined cost-effectiveness of the higher-sensitivity Fujifilm SILVAMP TB-LAM (FujiLAM) assay for TB testing among unselected hospitalized PWH in South Africa and Malawi.

Methods: We used the CEPAC-International microsimulation model to project clinical and economic outcomes of three TB testing strategies:
1) sputum Xpert MTB/RIF alone (*Xpert*);
2) sputum Xpert plus first-generation urine Alere Determine TB-LAM (*Xpert+AlereLAM)*;
3) sputum Xpert plus urine FujiLAM (*Xpert+FujiLAM)*.
The modeled cohort matched that in the STAMP trial (median CD4 236/μL [South Africa], 219/μL [Malawi]). We applied diagnostic yields - against a composite microbiologic/clinical reference standard - from a TB diagnostics study among hospitalized PWH in South Africa (yields for *Xpert*/*Xpert+AlereLAM*/*Xpert+FujiLAM* among all patients: 21%/44%/58%; among those with CD4< 200/μL: 25%/55%/68%). Costs per test of Xpert/AlereLAM/FujiLAM were US$15/3/6 (South Africa) and $26/3/6 (Malawi).
We projected mortality, life expectancy, costs, and incremental cost-effectiveness ratios (ICERs). LAM strategies were cost-effective if their ICERs were less than those of 2nd-line antiretroviral therapy: US$940/year-of-life (YLS) saved (South Africa) and $750/YLS (Malawi). In sensitivity analysis, we varied TB prevalence (5-45%, base case 24-29%), sputum provision probability (30-75%, base case 30%), and empiric TB treatment probability (5-20%, base case 10%).

Results: Compared with *Xpert* and *Xpert+AlereLAM*, *Xpert+FujiLAM* increased life expectancy by 0.8y and 0.4y in South Africa and by 0.6y and 0.3y in Malawi. *Xpert+FujiLAM* was cost-effective in both countries (Table). *Xpert+FujiLAM* for all patients was optimal compared with CD4-stratified testing strategies. In multi-way sensitivity analysis, *Xpert+FujiLAM* remained cost-effective except in scenarios where both sputum provision and empiric treatment probabilities were very high.

Conclusions: FujiLAM for TB testing in hospitalized PWH is likely to increase life expectancy and be cost-effective in South Africa and Malawi and should be utilized in TB-endemic settings.

Country	Testing strategy	Mortality at 2 months	Mortality at 2 years	Life-years, discounted[1] (undiscounted)	Lifetime cost, 2017 US$, discounted[1]	ICER (US$/YLS)
South Africa	*Xpert*	17.3%	35.9%	8.9 (13.2)	8,190	-
	Xpert+ AlereLAM	15.5%	33.8%	9.2 (13.6)	8,410	dominated[2]
	Xpert+ FujiLAM	14.4%	31.8%	9.5 (14.0)	8,620	810
Malawi	*Xpert*	23.8%	39.9%	8.4 (12.5)	3,470	-
	Xpert+ AlereLAM	22.2%	38.2%	8.6 (12.8)	3,560	dominated[2]
	Xpert+ FujiLAM	21.2%	36.7%	8.8 (13.1)	3,650	430

ICER: incremental cost-effectiveness ratio. YLS: year-of-life saved. Displayed results are rounded. ICERs are calculated from non-rounded numbers. [1]Discount rate was 3%/year. [2]ICER of *Xpert+AlereLAM* vs *Xpert* was higher than the ICER of *Xpert+FujiLAM* vs *Xpert+AlereLAM.*

[Table. Clinical and economic outcomes and cost-effectiveness of TB testing strategies among hospitalized people with HIV in South Africa and Malawi.]

PS-38-922-02 SpeClean: urine sample treatment method for ultra-sensitive LAM diagnostics

B Hamasur,[1,2] L Ignatowicz,[3] H Ramachandraiah,[1] [1]Biopromic, R&D, Stockholm, Sweden, [2]Karolinska Institutet, MTC, Solna, Sweden, [3]Biopromic, R&D, Solna, Sweden. e-mail: beston.hamasur@biopromic.com

Background: Deleterious effect of inhibitory components presence in urine is one of the main obstacles hampering development of a lipoarabinomannan (LAM) based sensitive point of care (PoC) for the diagnosis of tuberculosis. Here we present a simple sample treatment method to overcome the problem associated with the inhibitors, hence enhancing the signal.

Methods: Inhibitory properties of urine have been demonstrated in ELISA and in in-house magnetic based immune assay. To demonstrate various levels of inhibition, urines from multiple donor at multiple times were employed. Those samples were either a non-endemic urine

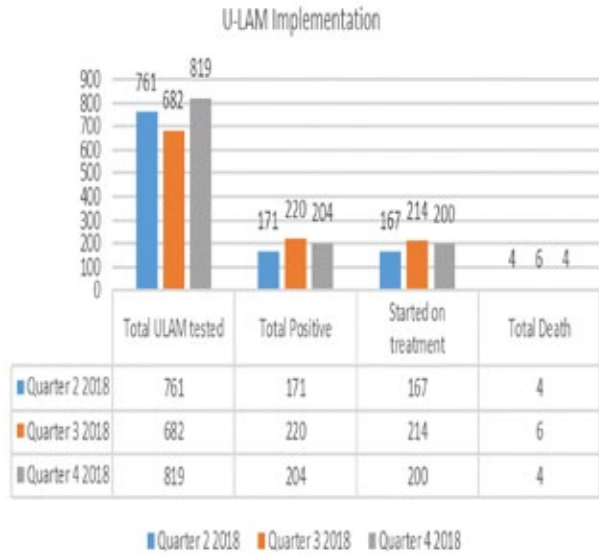
spiked with antigens, or urines from actual patients containing the antigen. Magnetic based SpeClean reagent was used to treat the samples.
Results: All urine sample exhibit inhibitory effect, though with various degree of inhibition. Sample treatment with SpeClean significantly increases the signal in comparison to the non-treated samples as well as reduces the background. Additionally, SpeClean treatment solves significantly cryo-precipitation in stored samples and increases antigen stability in not-frozen samples.
Conclusions: SpeClean treatment allows for ultrasensitive immunoassay to be performed in urine, in effect reducing the level of detection up to 20-fold in comparison to non-treated specimen. With the use of SpeClean, we are able to reach analytical sensitivity of 5pg/ml for LAM in urine both in spiked as well as in patient samples.

PS-38-923-02 Strengthening implementation of the U-LAM strategy for TB care and treatment services: the Limpopo Province, South Africa experience

D Moleba,[1] T Baloyi,[1] S Thamaga,[1] M Mphahlele,[1] E Shinwana,[2] O Baloyi,[2] R Matji,[1] G Jagwer,[1] [1]University Research Co., LLC (URC), TB South Africa Project, Pretoria, South Africa, [2]Department of Health, TB Directorate, Polokwane, South Africa. e-mail: dollym@urc-sa.com

Background and challenges to implementation: Tuberculosis is the leading cause of death among the 25 million people with HIV in sub-Saharan Africa. Early diagnosis and treatment of active tuberculosis (TB) in HIV-positive patients is challenging. Urinary lipoarabinomannan (U-LAM) is a point-of-care urine test for detecting LAM, a lipopolysaccharide present in mycobacterial cell walls, in people with active TB disease.
South Africa adopted use of U-LAM to improve TB diagnosis, allow treatment to start promptly and improve HIV-related mortality in HIV positive patients.
Intervention or response: U-LAM was introduced in Limpopo in October 2017. Hospital CEOs, nursing service managers and unit managers from 37 hospitals were trained on U-LAM implementation. Roadshows to introduce U-LAM were conducted in all five districts: Capricorn, Mopani, Sekhukhune, Waterberg and Vhembe.
In January 2018, implementers from all hospitals were trained on how to correctly perform the test, interpret, report and record results. The test was used in HIV-infected adults with signs and symptoms of TB (pulmonary or extra pulmonary) with a CD4< 100cells/ul or who are seriously ill. Those who tested positive were started on TB treatment using the national TB U-LAM algorithm.
Results and lessons learnt: Hospitals started reporting in quarter two (Q2) 2018. Of 2,262 HIV positive patients tested with U-LAM, 595 (26%) were diagnosed with TB, of whom 581 (97,6%) were initiated on treatment and fourteen died. Among TB-positive patients] , fourteen were *Rifampicin*-resistant.

Conclusions and key recommendations: Overall, U-LAM strategy improves TB case detection and reduced TB mortality among HIV positive patients in the province. Consistent political commitment and support from all levels (national, provincial, district and subdistrict) of healthcare is key in implementation of the U-LAM strategy. Involvement of all health care workers at hospital level is also important.



[LAM Implementation]

PS-38-924-02 Loop-mediated isothermal amplification test for tuberculosis: results of a two-phase local evaluation

JE Bascuna,[1] MC Ama,[1] R Basillo,[1] A Palparan,[1] D Lim,[1] M Inobaya,[2] CM Daga,[2] [1]Research Institute for Tropical Medicine, National Tuberculosis Reference Laboratory, Muntinlupa, Philippines, [2]Research Institute for Tropical Medicine, Department of Epidemiology and Biostatistics, Muntinlupa, Philippines. e-mail: rvgabuya@gmail.com

Background: The loop-mediated isothermal amplification test for tuberculosis (TB LAMP) is sputum-based diagnostic tool recommended by the World Health Organization which may find utility in the Philippine National Tuberculosis Control Program (NTP), either by being deployed in specific settings to increase coverage or by complementing existing tests being used, all to increase overall TB case-finding.
Methods: TB LAMP was evaluated in two phases: First phase involved diagnostic performance assessment in a central laboratory setting using samples from enrolled participants in participating facilities. Second Phase included performance appraisal of the technology under a hypothetical diagnostic algorithm wherein TB LAMP was deployed and used as a primary diagnostic tool while being complemented by other technologies currently used. Both phases included self-administered end-user assessment.

Results: Phase 1 (n=277) demonstrated TB-LAMP to have sensitivity better than smear microscopy (86.1% vs. 66.3%; p<0.001) and comparable to Xpert MTB/RIF (93.0%; p=0.109) in raw unprocessed samples. Of the 213 samples that tested smear-negative, 21 samples were found TB LAMP positive and culture-positive, indicating that 10% of the samples initially identified as smear negative were in fact positive for TB bacilli and correctly screened by TB LAMP.
Phase 2 (n=507) produced similar results, TB LAMP sensitivity of 73.5 (95% CI 66.1-80.0) and a specificity of 97.1 (95% CI 94.7-98.6). Sensitivity was found significantly higher than smear microscopy (65.8, 95% CI 54.0-76.3; exact McNemar's test, *p*-value=0.0013). Difference in sensitivity estimates as compared to Xpert MTB/RIF was not significant (68.9, 95% CI 58.3-78.2;exact McNemar's test, p-value=0.4545)
End-user assessment received from both phases were generally positive.
Conclusions: TB LAMP has good diagnostic performance both central laboratory and local field conditions. The technology could be integrated into the country diagnostic algorithm following further assessment covering cost effectiveness and once logistics are in place.

PS-38-925-02 A pilot field trial to evaluate the use of deep learning and mobile technologies to improve TB diagnostics processes in Peru

MJ Brunette,[1,2] C Ugarte-Gil,[1,3,4] K Villaizan,[3] Y Cao,[5] B Liu,[5] T Griffin,[5] C Liu,[5] N Zhang,[5] J Bernardo,[6]
[1]Universidad Peruana Cayetano Heredia, School of Medicine, Lima, Peru, [2]University of Massachusetts Lowell, Department of Public Health, Lowell, MA, United States of America, [3]Universidad Peruana Cayetano Heredia, Instituto de Medicina Tropical Alexander von Humboldt, Lima, Peru, [4]London School of Hygiene and Tropical Medicine, TB Centre, London, United Kingdom, [5]University of Massachusetts Lowell, Department of Computer Science, Lowell, MA, United States of America, [6]Boston University, School of Medicine, Boston, MA, United States of America.
e-mail: cesar.ugarte@upch.pe

Background and challenges to implementation: In Peru, approximately 33% of the persons with Tuberculosis (TB) are not able to begin treatment due to lack of bacteriological confirmation. Is in these situations where chest X-ray evaluation becomes critical to confirm TB. Unfortunately, the majority of primary health care centers lack of trained personnel to evaluate X-rays. Using mobile tools and technologies can help to reduce this gap in the TB cascade-of-care. A interdisciplinary team is developing a mHealth system (eRx app and web-based platform) which was introduced via a pilot study among healthcare facilities in Lima.
Intervention or response: eRx app was developed using Deep Learning techniques and only one specific computational model was tested during study. Two primary functions of eRx included the presence of abnormalities in the lung, and the prediction of certain TB manifestations. Participants in the study included physicians (n=5) and nurses (n=7) in five primary care TB clinics. Nurses were asked to take digital images of Xrays and upload them via smartphones. Physicians read X-rays and provided feedback via a web-based platform. Weekly short and semi-structured interviews were conducted with both healthcare professionals. The outcomes evaluated were user satisfaction and some human computer interaction (HCI) factors for the proposed mHealth system, with the goal to evaluate if this mHealth system could work in this setting.
Results and lessons learnt: From Sep-2018 to Feb-2019 303 X-rays were evaluated with eRx. We found three main group of challenges during the pilot study:
(a) at health worker level (i.e. high workload including extra activities outside TB clinic),
(b) at health system level (i.e. unavialibility of X-rays at TB clinic) and
(c) technological issues (i.e. mobile network stable avialibility).
Conclusions and key recommendations: Based on our results we are now able to better understand how to adapt an mHealth system to the current TB processes. This would allow for an improved socio-technical solution applied to a public health problem.

PS-38-926-02 Comparison of the new GeneXpert® MTB/RIF Ultra assay with other rapid molecular diagnostic assays for detecting tuberculosis in pulmonary and extra-pulmonary specimen

NE Maningi,[1] N Maphalala,[1] JO Sekyere,[1] LA Malinga,[2] NM Mbelle,[1,3] BP Fourie,[1] [1]University of Pretoria, Medical Microbiology, Pretoria, South Africa, [2]South Africa Department of Health, Research, Pretoria, South Africa, [3]National Health Laboratory Service, Tshwane Academic Division, Medical Microbiology, Pretoria, South Africa.
e-mail: zusiphem@gmail.com

Background: More studies are needed to evaluate the performance of the new Ultra assay in different geographical settings. The aim of the study was to compare the performance of the new Xpert® Ultra assay to the old Xpert G4 assay and the Line probe assay (LPA) for detecting TB (tuberculosis) in pulmonary and extra-pulmonary samples.
Methods: This was a prospective study to comparatively evaluate the performance of the new Xpert Ultra assay, the old Xpert G4 and Hain's LPA assay using MGIT 960 culture as a gold standard. The remnants (n=205) of pulmonary (n=120) and extra-pulmonary (N=85) specimens from TB suspects were collected from the National Health Laboratory Services in Pretoria. Each sample was divided into three for the Xpert® MTB/RIF assays, culture and for DNA extraction for the LPA.

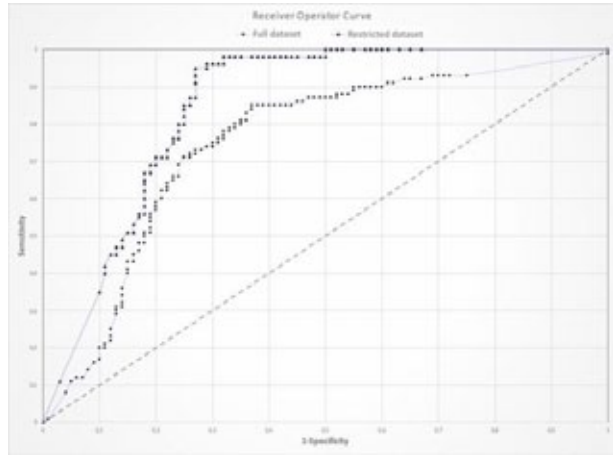
Results: In smear-positive pulmonary samples, sensitivity and specificity were respectively 97.50% and 12.50 for Xpert ultra; 92.31% and 33.33% for Xpert G4; and 92.50%, 0.00% for LPA. In smear-negative pulmonary samples, sensitivity and specificity were respectively 44.44% and 58.93% for Xpert ultra; 22.22% and 98.18% for Xpert G4; and 22.22% and 14.29% for LPA. Sensitivity and specificity for smear-positive extra-pulmonary samples for both Xpert ultra and Xpert G4 were 100.00% and 00.00%, but 85.71% and 0.00% for LPA, respectively. For smear-negative extra-pulmonary samples, sensitivity and specificity for Xpert ultra was 25.00% and 65.62%; 0.00% and 98.41% for GenXpert G4; and 60.00% and 26.56% for LPA, respectively.
Conclusions: The sensitivity of the new Xpert Ultra was superior to that of Xpert G4 and LPA in both pulmonary and extra pulmonary samples, but with very low specificity compared to the old Xpert G4. LPA had the lowest specificity compared to both Xpert assays. The zero specificity was because when culture was negative, molecular methods were TB positive.

PS-39-A1 Detection and treatment of TB

PS-39-928-02 Evaluation of Aeonose, an exhaled breath-based diagnostic, as a TB triage test for patients being admitted to a hospital in Lima, Peru

R Nathavitharana,[1] K Tintaya,[2] T Galvez Sanchez,[2] L Lecca,[2] D Tierney,[3] E Nardell,[3] [1]Harvard Medical School, Infectious Diseases, Boston, MA, United States of America, [2]Socios En Salud Sucursal Peru, TB, Lima, Peru, [3]Harvard Medical School, Global Health Equity, Boston, MA, United States of America. e-mail: rnathavi@bidmc.harvard.edu

Background: Tuberculosis (TB) transmission due to undiagnosed disease is a major driver of the epidemic. There is an urgent need for a non-sputum-based TB triage test to facilitate the evaluation of people presenting to healthcare facilities with symptoms or risk factors for TB in high-incidence countries.
We evaluated Aeonose, an exhaled breath-based diagnostic that detects volatile organic compounds, as a TB triage test as part of the FAST (Find cases Actively, Separate safely and Treat effectively) transmission control strategy.
Methods: We screened patients being admitted to Hospital Nacional Hipolito Unanue, Lima, Peru for cough, prior TB history or TB contact. Patients with a positive screen were consented for Aeonose exhaled breath testing and were offered HIV testing. All patients underwent sputum smear microscopy, Xpert MTB/RIF, mycobacterial culture (reference standard), which were performed on the same day as breath testing.
Results: Between June 2017-February 2019, we enrolled 629 patients with cough or risk factors for TB. Overall, Aeonose had a sensitivity of 85%, specificity of 63%, positive predictive value (PPV) of 40% and negative predictive value (NPV) of 93%. When patients with respiratory diseases, prior TB history and HIV (n= 323) were excluded, in the remaining 306 patients, Aeonose had a sensitivity of 93%, specificity of 73%, PPV of 43% and NPV of 98% (Receiver Operating Characteristic curves shown in Figure).
Conclusions: The optimal strategy for triage of patients with possible TB is unknown. Since patients identified to be at the highest risk (those with respiratory diseases, a history of TB and HIV) are typically recommended to undergo confirmatory testing directly, our study suggests that Aeonose could meet WHO Target Product Profile criteria (sensitivity >90% and specificity >70%) for use as a triage test for other non-high-risk patients with symptoms and risk factors for TB to determine which patients require confirmatory diagnostic testing.



[Receiver Operating Characteristic curves for the full (AUC 0.75) and restricted (AUC 0.85) datasets]

PS-39-929-02 Altered systemic levels of acute phase and antimicrobial proteins and post treatment modulation in tuberculous lymphadenitis

GR Kathamuthu,[1] K Moideen,[1] R Sridhar,[2] D Baskaran,[3] S Babu,[1] [1]National Institutes of Health-National Institute for Research in Tuberculosis - International Center for Excellence in Research, NIH-ICER, Chennai, India, [2]Government Stanley Medical Hospital, Thoracic Medicine, Chennai, India, [3]National Institute for Research in Tuberculosis, Clinic, Chennai, India. e-mail: gokul.r@nirt.res.in

Background: Pulmonary tuberculosis is characterized by elevated levels of acute phase (APPs) and antimicrobial proteins (AMPs). However, data on the association of APPs and AMPs with tuberculous lymphadenitis (TBL) is scarce.

Methods: We have examined the systemic levels of APPs and AMPs in TBL (n=44) and latent tuberculosis (LTB, n=44) individuals at baseline and in TBL before and after the completion of anti-tuberculosis treatment (ATT, n=44). We measured the plasma levelsof alpha-2-macroglobulin (α-2MG), serum amyloid A (SAA), C-reactive protein (CRP), haptoglobin (Hp), human beta defensin 2 (HBD-2), granulysin and human neutrophil peptide1-3 (HNP1-3) by ELISA. We also examined the association of these proteins with TBL lymph node (LN) size and multiple (M) versus single (S) LN involvement. Finally, we have also examined the pre and post-treatment modulation of APP and AMPs in TBL. The statistically significant difference between TBL and LTB individuals, LN size and M versus S LN involvement were analysed using Mann-Whitney U test. Wilcoxon signed-rank test were used to analyse the significance before and after completion of ATT.

Results: TBL individuals exhibit increased plasma levels of APPs (α-2MG (P=0.0096), SAA1 (P=0.0248), CRP (P<0.0001), elevated (HBD-2, P=0.0345) and diminished [granulysin (P< 0.0001), HNP1-3 (P<0.0001)] AMPs when compared to LTB individuals. In contrast, none of these proteins was significantly associated with LN size and multiple versus single LN involvement indicating a lack of association with disease severity. Following ATT,the systemic levels of α-2MG (P=0.0073), CRP (P<0.0001), Hp (P=0.0061), HBD-2 (P=0.0215) were significantly diminished and granulysin (P<0.0001) and HNP1-3 (P<0.0001) were significantly elevated when compared to pre-treatment levels.

Conclusions: Thus, altered levels of APPs and AMPs at baseline corroborates the presence of systemic inflammation and enhanced immune activation and their reversal after ATT indicates modulation after treatment in TBL disease.

PS-39-930-02 Evaluation of antibody responses for TB screening among people living with HIV

D Jaganath,[1,2,3] J Rajan,[4] C Yoon,[2,3] A Andama,[5] F Semitala,[5] I Khan,[6] R Ravindran,[7] A Cattamanchi,[2,3]
[1]University of California (UCSF), Pediatric Infectious Diseases, San Francisco, CA, United States of America, [2]University of California (UCSF), Pulmonary and Critical Care Medicine, San Francisco, CA, United States of America, [3]University of California (UCSF), Center for Tuberculosis, San Francisco, CA, United States of America, [4]University of California (UCSF), Division of Experimental Medicine, San Francisco, CA, United States of America, [5]Makerere University College of Health Sciences, Department of Internal Medicine, Kampala, Uganda, [6]University of California, Department of Medical Pathology and Laboratory Medicine, Sacramento, CA, United States of America, [7]University of California, Pathology and Laboratory Medicine, Sacramento, CA, United States of America. e-mail: devan.jaganath@ucsf.edu

Background: Current serologic tests have not been useful for tuberculosis (TB) diagnosis. Recently, multi-antigen panels have shown promising results in Pakistan and Uganda. We performed the first evaluation of antibody responses to these antigens for TB screening among people living with HIV (PLHIV).

Methods: We conducted a case-control study nested within a cohort of PLHIV initiating anti-retroviral therapy (ART) at two clinics in Kampala, Uganda. We selected a 1:1 sample of participants with and without TB confirmed by sputum Xpert MTB/RIF or culture. We measured antibody responses to 12 TB antigens (Ag85A, Ag85B, Ag85C, Rv0934-P38, Rv3881, Rv3841-BfrB, Rv3873, Rv2878c, ESAT-6, CFP-10, Rv1980, and Rv2031-HSPX) in plasma using a multiplex microbead immunoassay.

We applied machine learning methods to:

1) determine the area under the ROC curve for a known 8-antigen panel; and,

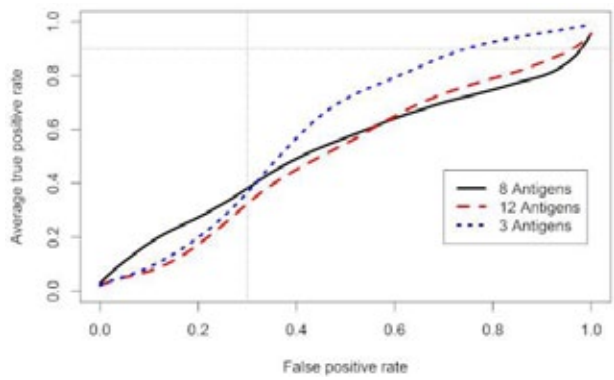
2) assess if antibody responses to all 12 antigens, or any combination, achieved the accuracy targets for a TB screening test (≥90% sensitivity and ≥70% specificity).

Results: Of 262 participants, 138 (53%) had TB and median CD4 count was 152 cells/μL (IQR 65-279). The previously reported 8-antigen panel did not meet the recommended accuracy, with mean AUC of 0.526 (95% CI 0.520-0.532). Similar results were obtained when including all 12 antigens in the panel (mean AUC 0.507, 95% CI 0.501-0.513), with mean specificity of 15.1% (95% CI 14.5-15.6) when sensitivity was at least 90%.

The best performing antibody response to a three antigen panel (Rv0934-P34, Ag85A, Rv2031-HSPX) had a mean AUC of 0.60 (95% CI: 0.594-0.606, and when sensitivity was at least 90%, mean specificity was 26.1% (95% CI 25-27.1).

Conclusions: Antibody responses to 12 TB antigens shown to be promising in prior studies did not achieve target accuracy for a TB screening test among PLHIV

initiating ART. Further research is needed to identify candidate antigens for serologic testing in TB for PL-HIV.



[Figure 1. Comparison of Antigen Panel ROC Curves.]

PS-39-931-02 Age-related defects in maturation of T-cell interferon-gamma responses in a TB-endemic region of rural Papua New Guinea

C Rush,[1] T Diefenbach-Elstob,[1] R Dowi,[2] D Pelowa,[3] B Gula,[2] E McBryde,[1] J Warner,[1] [1]James Cook University, Australian Institute of Tropical Health and Medicine, Townsville, QLD, Australia, [2]Balimo District Hospital, Clinical Services, Balimo, Papua New Guinea, [3]Balimo District Hospital, Laboratory, Balimo, Papua New Guinea. e-mail: catherine.rush@jcu.edu.au

Background: Failure to develop an appropriate T cell response following primary TB infection may explain the progression of disease and dissemination to extra pulmonary (EP-TB) sites as observed in children and individuals with co-morbidities such as HIV, diabetes and malnutrition. Furthermore, it is well established that acute TB is associated with depressed T cell mitogenic responses, reduced IFN-γ production and T cell anergy. Papua New Guinea has the highest rate of TB in the Pacific region and we have previously shown that EP-TB accounts for ~77% of all TB cases in the village of Balimo in the Western Province of PNG, which is far in excess of the global reported value of 15%. Our previous data showed the highest TB prevalence was in children < 14 years. We sought to explore relationships between T cell function and TB type and status in $IGRA^{neg}$ and $IGRA^{pos}$ community members, TB suspects (pre-treatment) and TB patients (on treatment) in this region.
Methods: We analysed peripheral blood leucocyte frequencies and T cell function by flow cytometry in Cytochex-stabilised whole blood samples collected in rural PNG and analysed remotely in Townsville, Australia.
Results: We demonstrated reduction in innate, B, CD4 and CD8 T lymphocytes and increased neutrophils in EP-TB and PTB suspects and patients, when compared to community participants. Our findings at the single cell level using mitogen-stimulated peripheral blood T cells provide evidence for an age-related defect in the ability of CD4 and CD8 T cells of uninfected children to produce IFN-γ, whilst TNF-a production remained intact.
Conclusions: Elucidation of the mechanisms underlying this dysregulated cytokine production and its influence on TB disease type and severity in this community may lead to discovery of the co-morbid conditions that contribute to TB susceptibility in this hyper endemic region.

PS-39-932-02 Conventional PCR method for detection of Beijing lineage from M. tuberculosis culture isolates

R Beenish,[1] S Singh,[1] [1]AIIMS Bhopal, Microbiology, Bhopal, India. e-mail: beenish.aiims@gmail.com

Background: CRISPR-associated genes cas2 and cas1 specifically delete among Beijing lineage has been reported previously (Rufai et al; Union-TB conference 2018). Development of molecular method for detection of Beijing strain becomes essential to identify ubiquity of the Beijing strains and their frequent association with outbreaks to accentuate their significance in drug resistance.
Methods: Novel primers were designed for CRISPR associated Cas2F (5'GCGGCACTATAGGCAAGATG3'), Cas2R (5'ACTGCCGCAACCTCTTAT3') and Cas1F (5'GCTCCGTCAGCAAGTTCAC3') Cas1R (5'CGATCAATCGAAGTACGGTGT3') gene sequences using Primer 3 (V 4.1.0) designing software. DNA isolation was performed from clinical isolates (50 Beijing strains and 50 Non-Beijing strains) were subjected to PCR and the constituents of mixtures were as follows: 2.5 µl of 10X buffer, 500 mM KCl] supplied with 1 ml of 50 mM MgCl2, 0·5 µl of stock 10mM dNTP, 20pmol of each primer and 1.25U of Taq DNA polymerase and 5µl of template DNA. Each PCR was started with a 'hot Start' for 2min at 95°C followed by denaturation (25 cycles each of 15 sec at 95°C), annealing (25 cycles each of 15 sec at 55°C) and extension (25 cycles each of 45 sec at 68°C), and a final extension for 1 cycle for 5 min at 68°C in a thermal Cycler (MJ Research, USA). Amplified products were resolved through 2% agarose gel in Tris-acetate buffer.
Results: PCR precisely amplified the corresponding targets viz, Cas1 (494 bp) and Cas2 (229 bp) from DNA isolated from 50 non-Beijing strains. Further no amplification was seen among other 50 DNA samples isolated from Beijing isolates.
Conclusions: PCR method based on cas1 and cas2 sequence deleted in Beijing lineage can be used as an epidemiological markers in geographical settings for identification of transmission outbreaks and in settings predominance of Beijing strain is doubted.

PS-39-933-02 Detection of Mycobacterium tuberculosis from guinea pig lung and spleen tissues following natural transmission using PrimeMix real-time PCR

SL Olifant,[1] MM Selamolela,[1] NE Maningi,[1] AC Stoltz,[2] PB Fourie,[1] [1]University of Pretoria, Medical Microbiology, Pretoria, South Africa, [2]University of Pretoria, Internal Medicine, Pretoria, South Africa.
e-mail: sharon.l.olifant@gmail.com

Background: The use of guinea pigs as an animal model in tuberculosis research has been widely used in vaccine and drug development. The aim of this study was to develop techniques which enhance the recovery and detection of *M. tuberculosis* from guinea pig tissues with early disease (low bacterial load). The role of PrimeStore® molecular transport medium (PS-MTM) was evaluated in comparison to 1X phosphate buffered saline solution (PBS). The detection rates of PrimeMix® real-time PCR (PM-PCR) was compared to mycobacterial culture. The most transmissible *M. tuberculosis* strain was determined using spoligotyping.
Methods: A total of 42 naturally infected, tuberculin skin test (TST) positive guinea pig lung and spleen tissues were harvested, homogenized and placed in PS-MTM and 1X PBS. Mycobacterial culture was performed on 1X PBS tissue homogenates and PM-PCR was performed on 1X PBS and PS-MTM samples. Spoligotyping was performed on lung samples.
Results: All the 1X PBS 100% (42/42) lung tissues were positive for *M. tuberculosis*. Only 95.24% (40/42) spleen tissues were positive for *M. tuberculosis*. From the PS-MTM lung samples, 95.24% (40/42) were positive for *M. tuberculosis,* and 97.62% (41/42) of the PS-MTM spleen samples were positive for *M. tuberculosis*. Mycobacterial growth was observed in only six samples, four spleen and 2 lung samples. Of the 42 strains, 41 were regarded as orphans, whereas 1 was regarded as atypical.
Conclusions: There was no difference in PM-PCR positivity between PS-MTM and 1X PBS samples. The use of PM-PCR in detecting *M. tuberculosis* is superior to culture. Spoligotyping of tissue samples requires an optimized approach. Naturally infecting guinea pigs may result in mixed strain infections which cannot be differentiated by spoligotyping. The use of real-time PCR can be advantageous in detecting *M. tuberculosis* in vaccine and drug development as opposed to culture.

PS-39-934-02 In-silico and gene knockout characterisation of oxidoreductase Rv0148 of Mycobacterium tuberculosis

G Bhargavi,[1] S Hassan,[2] S Balaji,[3] K Palaniyandi,[1] [1]National Institute for Research in Tuberculosis, immunology, Chennai, India, [2]University of Gothenburg, Department of Biological and Environmental Sciences, Carl Skottsbergs Gata, Sweden, [3]National Institute for Research in Tuberculosis, Bacteriology, Chennai, India.
e-mail: bhargavi.gunapati@gmail.com

Background: *Mycobacterium tuberculosis (M. tb)* resides inside the host macrophages during infection and adapts to resilient stresses generated by the host immune system. In response, *M. tb* codes for short- chain dehydrogenases/ reductases (SDRs). These SDRs are nicotinamide adenine dinucleotide (NAD) reliant oxidoreductases involved in cell homeostasis. The precise function of oxidoreductases in *M. tb* was unclear studies to be explored to find the significant role of oxidoreductases.
Methods: In this study we have chosen oxidoreductase family member Rv0148 a conserved hypothetical involved in intermediary metabolism of *M. tb*. The study deals with *in-silico* modelling of Rv0148 and predicted interacting partner as Htdy (Rv3389) through bio-informatics analysis and further through protein protein interactions. Gene knockout mutant of Rv0148 was performed to predict the significant functional role of Rv0148 in *M. tb*. Further, interactome analysis revealed that Rv0148 involved in drug resistance.
Results: *In-silico* analysis revealed Rv0148 is interacting with Htdy and the protein interactions were confirmed. Construction of gene knockout mutant Rv0148 in *M. tb* was produced by specialized transduction. The macrophage cell line infection with this knockout mutant showed increased expression of pro-inflammatory cytokines IL-1β, TNF-α & IL-6 and it is sensitive to rotenone, oxaloacetic acid, DMSO, DTT, H_2O_2, Cumene Hydroperoxide oxidative & nitrogen stresses. Drug susceptibility testing of the mutant showed resistance to first- line drugs streptomycin, ethambutol, and second line aminoglycosides amikacin and kanamycin. Increased expression of *htdy* was observed in knockout mutants and further interactome analysis of Rv0148 predicted that other 220 interacting partners might be activated and causing drug resistance.
Conclusions: The current study on oxidoreductases has brought to light the possibility to predict the function of oxidoreductase genes involved in drug resistance using protein protein networking. Furthermore, Rv0148 and Htdy are functionally interconnected involved in drug resistance and cell homeostasis of *M. tuberculosis*.

PS-39-935-02 Development of new C-2 bridged analogues of ethambutol as effective anti-tuberculosis agents

V Valcheva,[1] I Slavchev,[2] Y Nikolova,[2] G Dobrikov,[2]
[1]Institute of Microbiology, Bulgarian Academy of Sciences, Infectious Microbiology, Sofia, Bulgaria, [2]Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Laboratory "Organic Synthesis and Stereochemistry", Sofia, Bulgaria.
e-mail: violeta_valcheva@mail.bg

Background: The active circulation of drug resistant variants of *Mycobacterium tuberculosis* strains globally, assisted by mass migration, suggests an urgent need to develop and implement new anti-tuberculous compounds - non-toxic and effective against drug-resistant strains. Nowadays, there is a rising interest and demand for new anti-tuberculous substances. A good alternative would be the production of active synthetic analogs of already existing drugs in clinical use. Herein we present a small series of new C-2 bridged analogues of ethambutol (EMB), bearing R- and S-2-aminobutanol moieties.
Methods: Modern synthetic methods are used that allow the modification of the compounds by a small number of synthetic steps (2 to 4), with high yields and enantioselectivity. This avoids the expensive and unreasonable use of the methods of total organic synthesis for the purpose of obtaining the final products. The *in vitro* antimycobacterial activity and cytotoxicity of all compounds against reference strain *Mycobacterium tuberculosis* H37Rv and human embryonic kidney cell line HEK-293 were evaluated using the resazurin microtiter assay (REMA) and MTT-dye reduction assay.
Results: Using cheap and commercially available chemicals, six new (R)-2-aminobutanol derivatives have been synthesized. Their *in vitro* antituberculosis activity against *Mycobacterium tuberculosis* $H3_7Rv$ was evaluated. Most of the compounds showed remarkable activity - up to 15 fold higher than activity of EMB.
Conclusions: It is interesting to note, that for all compounds there is no activity against other microorganisms. This indicates that all compounds act specifically *Mycobacterium tuberculosis*. These results can be considered an important starting point for design of new leads for anti-TB compounds.

PS-39-936-02 Longitudinal profiling of gut microbiome among tuberculosis patients during anti-tuberculosis therapy

B Xu,[1,2] W Shi,[1] Y Hu,[1] Y Hu,[3] S Prast-Nielsen,[3] X Zheng,[1] Z Ning,[4] [1]Fudan University, Epidemiology, Shanghai, China, [2]Karolinska Institutet, Public Health Sciences, Stockholm, Sweden, [3]Karolinska Institutet, Centre for Translational Microbiome Research, Stockholm, Sweden, [4]Zigong Center for Disease Control and Prevention, Tuberculosis Control Center, Zigong, China.
e-mail: yhu@fudan.edu.cn

Background: Anti-tuberculosis treatment requires at least six months of continuous combined administration of antibiotics. The long-term exposure to antibiotics could cause consequent changes of gut microbiota, which may alter gastrointestinal function and drug absorption, thereby affect the outcome of treatment. Previous studies have observed changes in the gut microbiome between tuberculosis (TB) patients and healthy people while longitudinal effect of anti-tuberculosis treatment on it is seldom studied.
Methods: A prospective cohort of TB patients was conducted in a Chinese designated TB hospital. 84 stool samples from 24 patients were collected at five time points (before and ten days, two, five, six months after treatment initiation). The microbiota composition was analysed through 16S ribosomal RNA gene sequencing. Shannon index and unweighted Unifrac matrix were used to measure alpha and beta diversity. Differential abundance analysis was carried out using STAMP. Wilcoxon rank sum tests were performed for comparison between groups, and p-values were adjusted for multiple testing.
Results: Lower alpha diversity before treatment was associated with male gender, low-income, concomitant chronic obstructive pulmonary disease and older age (over 50 years). The alpha diversity of the gut microbiome decreased over treatment time, and more pronounced in individuals with higher alpha diversity ($p\text{-value} < 0.05$). After five months of treatment, significant alteration of community structure was observed ($q\text{-value} < 0.05$). Relative abundance of members of genera *Phascolarctobacterium*, *Coprococcus* and *Flavonifractor* increased after two months of treatment, while many members of genera *Gemella*, *Escherichia/Shigella*, *Ruminiclostridium*, *Lachnospiraceae_UCG-010*, *Lactobacillus*, *Streptococcus*, *Atopobium* significantly decreased during the long-term anti-TB treatment (5 months).
Conclusions: Dysbiosis of the gut microbiota in TB patients during anti-TB treatment was observed in our pilot study. Functional studies in a larger cohort are necessary to identify potential microbial biomarkers for designing appropriate treatment regimen.

PS-39-937-02 The potential impact of new, urine-based tests for TB: a modelling study

S Ricks,[1] C Denkinger,[2] S Schumacher,[2] N Arinaminpathy,[1] [1]Imperial College London, Infectious Disease Epidemiology, London, United Kingdom, [2]FIND, TB Programme, Geneva, Switzerland.
e-mail: saskia.ricks12@imperial.ac.uk

Background: Urine-based diagnostic tests such as the lateral flow (LF) LAM assay may offer new opportunities for diagnosing TB, including the potential for being used as point-of-care tests. However, current assays, such as Alere Determine™ TB LAM Ag (AlereLAM), are only able to detect TB amongst those with advanced HIV immunosuppression. Future LF-LAM assays may have improved sensitivity, such as Fujifilm SILVAMP TB LAM (FujiLAM), which is currently in development. We aimed to estimate the potential epidemiological impact of such diagnostics, in high-HIV-burden settings such as South Africa.
Methods: We developed a mathematical model to capture the TB/HIV co-epidemic in South Africa, along with the differential performance of LF-LAM with respect to CD4 immunosuppression. We modelled the following implementation scenarios: (1) At hospital admission, all PLHIV with advanced immunosuppression (CD4 cell count < 200 cells/μL) regardless of TB symptoms, are offered TB diagnosis with LF-LAM alongside Xpert. (2) In addition to scenario 1, PLHIV initiating ART at outpatient HIV clinics with advanced immunosuppression, as well as TB symptomatics, are offered TB diagnosis with LF-LAM alongside Xpert. In both scenarios, for the LF-LAM assay we considered AlereLAM, as well as a future assay such as FujiLAM.
Results: Between 2019 and 2035, AlereLAM could avert 0.1% of total TB mortality if implemented only in inpatient settings, and 16.78% if additionally implemented in outpatient settings. A FujiLAM-like assay, that is with improved sensitivity, would avert 0.16% and 20.12% in these settings, respectively.
Conclusions: In a high-HIV burden setting such as South Africa, tests such as AlereLAM could have meaningful impact on overall TB mortality, if deployed in outpatient as well as inpatient settings. In future, however, this impact could be substantially increased by next-generation assays having improved performance.

PS-40-D3 Fresh air: occupational and environmental threats to lung health

PS-40-938-02 Frequency of bronchial asthma symptoms among hairdressers in the city of Parakou, Benin

M Adjobimey,[1,2] S Ade,[3] A Adanto,[4] R Mikponhoue,[2] V Hinson,[2] G Agodokpessi,[1] [1]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Prevention, Cotonou, Benin, [2]Unité de Recherche et d'Enseignement en Santé au Travail de la Faculté des Sciences de la Santé de Cotonou, Pathologies Professionnelles, Cotonou, Benin, [3]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Pneumologie, Cotonou, Benin, [4]Faculte de Médecine, Médecine, Parakou, Benin. e-mail: menoladjobi@yahoo.fr

Background: Bronchial asthma is a very common disease, affecting more than 300 million people worldwide. Occupational asthma accounts for approximately 15% of all asthma cases. Hairdressing, a common profession for females in Benin, exposes people to risk factors that may trigger or worsen asthma attacks. The objective of this study was to determine the prevalence of asthma-like symptoms in female hairdressers in 2018 in Parakou, Benin.
Methods: This was a cross-sectional study conducted from 29 September 2018 to 9 November 2018 in the hairdressing salons of Parakou, Benin. Using a questionnaire, we collected information regarding the presence of asthma symptoms in the previous 12 months, their onset in the workplace, and their improvement during days off work.
Results: In total, 72 hairdressing salons and 266 female hairdressers were included. The mean (SD) age of the hairdressers was 25.7 (15.9) years. The average (SD) duration of work in hairdressing was 2.0 (3.1) years. There were 166 (62.4%) apprentices, 78 (29.3%) managers, and 22 (8.3%) post-apprenticeship hairdressers. The main products handled were fixing agents, shampoos, and straightening products. In the previous 12 months, 27 (10.2%) participants had frequent chest wheezing, 40 (15.0%) had chest tightness, and 51 (19.2%) had cough. At least one of these three symptoms was found in 66 (24.8%) and all three symptoms were found in 11 (4.1%). Overall, 14 (5.3%) reported having had asthma attacks and 49 (18.5%) believed their asthma symptoms were work-related.
Conclusions: A high rate of asthma symptoms was found among hairdressers in Benin. Screening and monitoring of asthma in hairdressers are a necessity given the number of people working this profession in Benin.

PS-40-939-02 Preventing tuberculosis with silica dust controls in the workplace

P Gottesfeld,[1] MM Nota,[2] [1]Occupational Knowledge International, NA, San Francisco, CA, United States of America, [2]Occupational Knowledge International, NA, Dar es Salaam, Tanzania, United Rep..
e-mail: info@okinternational.org

Background: For more than 100 years silica dust exposure in the workplace has been recognized as a significant risk factor for Tuberculosis (TB) but few efforts have been made to implement preventative measures to reduce TB incidence. More than 230 million people are exposed to silica in the workplace with the highest exposures occurring in high burden countries. Silica dust exposure, even without clinically evident silicosis, has been demonstrated to increase the life-long risk of TB. Furthermore, silica dust exposure among workers who are HIV positive in high-burden TB countries is a deadly combination increasing the risk of active TB by 15-fold. We report on a successful pilot program to reduce silica dust exposures in artisanal small-scale mining in Nigeria.
Methods: We worked cooperatively with artisanal miners to introduce wet methods to reduce respirable silica dust. Following extensive outreach and training, wet spray misting and other controls were implemented to reduce exposures.
Results: Pre-post air monitoring indicated an 80% reduction in respirable silica dust exposures were achieved with low-cost wet spray misting. The project demonstrated that artisanal small-scale miners will work cooperatively to take measures to reduce exposures to protect themselves and their communities. This pilot program can be implemented to protect silica-exposed workers from TB and co-morbidities including silicosis, lung cancer, and other chronic lung disease. Investments in dust controls to prevent disease are more cost effective than programs to identify and treat cases of TB.
Conclusions: Primary prevention for TB is possible with low cost initiatives even in resource constrained informal sector workplaces. The UN General Assembly TB Declaration calls on countries to implement "primary prevention in high-risk occupations by reducing silica dust exposures in mining, construction and other dusty workplaces." Global health funders should expand opportunities to prevent TB in high-burden countries with investments in workplace dust controls.

PS-40-940-02 Prevalence and correlation of breathing and skin problems among informal workers in textile industries

B Maurya,[1] [1]International Institute for Population Science, Development Studies, Mumbai, India.
e-mail: bharati.iips@gmail.com

Background and challenges to implementation: Chemical fumes and cotton/fibres dust (Airborne dust) workers inhale at the workplace, and they have more opportunity to vulnerable to occupational disease. Overexposure to airborne dust can cause respiratory and non-respiratory morbidity, temporary and permanent disabilities, and deaths. Occupational health hazards also create a negative influence on the quality of products, the burden of the health economy.
Intervention or response: The study indicates the prevalence of respiratory problems due to exposure to chemical fumes and cotton/fibre in textile industries. This study was primary and cross-sectional, conducted from 409 male migrant workers in 20 textile industries in Surat district. Multistage stratified cluster random sampling was used to collect the information from yarn, weaving and processing units workers of the industries. This study is self-reported, uni-variate and bi-variate analysis has done.
Results and lessons learnt: significant findings reveal that 2.4 per cent of workers uses the proper mask for proper protection. While another are using only chemical based textile material to cover their face, nearly 13 % (N=55) reported excessive dust in their workplace which is spread over the air. 16.4 % (N=67) reported breathing problems where 32.7% cough, 43.3% chest tightness, 19.4 % wheezing and breathlessness, 40.3% shortness of breath at rest. Apart from 20 per cent (N=82) reported skin related problems past six months period which is suspected to be caused by textiles associated works. 47.6 % reported erythema, 75.6% of workers reported itching and 13.4 % workers suffering from fungal and skin related allergy.
Conclusions and key recommendations: The continuous and long duration of work in the contact of chemical fumes and cotton dust invite the other non-respiratory health problems. It's essential to provide personal protective equipment and proper air ventilation to minimise the airborne dust.

PS-40-941-02 Pulmonary conditions and health literacy status of young adult stonecutters in Addis Ababa, Ethiopia

HM Hassen,[1] [1]Dire Dawa University, Biological Sciences, Dire Dawa, Ethiopia.
e-mail: hailemariammamo5@gmail.com

Background: Occupational lung diseases (silicosis, allergic alveolitis, pneumoconiosis, asthma and co-infections) affect stone boulders, preventable improving health literacy with safety cultures. In Ethiopa, stone boulders activities release dust particles that affect pulmonany functions. Investigating the status of these effects and workers health literacy status is essential for timely due attention and actions. Purpose of the study was determining status of pulmonary conditions and health literacy status of young adult stone boulders in Addis Ababa, Ethiopia.
Methods: Comparative cross-sectional design and random sampling was used among stone boulders (18-35 years) worked for one and more years. Matched controls were taken from non-smoking, normal college students within same age range. Anthropometric measurements was taken, then pathophysiologic indicators of lung health/pulmonary function indices was done using digital spirometer. Stone boulders health literacy related to awareness on health impact and practice on safety measures was assessed using questionnaire.
Results: Mean % predicted values of pathophysiologic indicators of lung health/pulmonary functions indices (FVC, FEV1, FEV1/FVC, PEFR, PIFR and FEF25-75) were significantly lower ($p<0.05$) in stone boulders compared to the control groups. About 18.1% and 17.4% of stone boulders had obstructive and mixed condition. Health literacy status on impact of nature of the work and practice to utilize safety devices were very lower, most of workers had never used and they did not care for their health, and for workmates. There was low health literacy status related to awareness on effect and poor practice to use safety devices. Working conditions and settings were uncomfortable and risky.
Conclusions: Pulmonary function indices were reduced probably, because of accumulation, inflammation or co-infection that entails further vigorous researches on particles nature, mechanisms, effect magnitude changing concentration and exposure duration. Health literacy status was lower and need to create awareness with safety regulations and conditions in coordination.

PS-40-942-02 Occupational air pollution and respiratory function among workers in a cement plant in Togo

M Adjobimey,[1,2] KS Adjoh,[3] R Mikponhoue,[1] B Mouzou,[1] V Hinson,[1] G Agodokpessi,[2] P Ayelo,[1]
[1]Unité de Recherche et d'Enseignement en Santé au Travail de la Faculté des Sciences de la Santé de Cotonou, Pathologies Professionnelles, Cotonou, Benin, [2]Centre National Hospitalier de Pneumo-Phtisiologie de Cotonou, Prevention, Cotonou, Benin, [3]Service de Pneumo-Phtisiologie du Centre Hospitalier Universitaire Sylvanus OLYMPIO de Lomé, Pneumologie, Lome, Benin.
e-mail: menoladjobi@yahoo.fr

Background: Cement plants create an environment that constantly exposes workers to dust in many developing countries. These dusty environments may have an impact on the respiratory function of the workers exposed. Our objectives were to measure exposure to cement dust and the lung function of workers in a cement plant in Togo.
Methods: This cross-sectional study of 74 workers at a cement plant in Togo was conducted from 25 July 2018 to 15 September 2018. The level of cement dust was measured using an aerodynamic chimney monitoring system by the Quality, Health, Safety, and Environment department. Each worker had spirometry performed using Spirobank II and had various demographic and employment information collected. Spirometric results were interpreted by an occupational physician and a pulmonologist. We performed logistic regression to identify risk factors (e.g. age, smoking, dust exposure duration) associated with respiratory disorder.
Results: The average (SD) age was 49.1 (10.1) years, and 72 of the 74 workers were male. Among the workers, 56.8% had more than 15 years experience in the cement plant and 32.4% worked in maintenance. The average dust content was 80 mg/m^3 with extreme values of 9.6 and 268.9 mg/m^3. The dust level at all stations was above the set limit of 5 mg/m^3. Cough was present in 10.8% of workers, rhinitis in 9.5%, and dyspnea in 5.4%. Staff spirometric results showed 68.9% had completely normal respiratory function, 13.4% had small track syndrome, 10.8% had restrictive syndrome, 5.4% had obstructive syndrome, and 1.5% had mixed impairment. In regression analysis, only experience of more than 15 years was associated with respiratory disorder.
Conclusions: In this high-dust environment, nearly one-third of workers had a respiratory disorder. Regularly monitoring the respiratory function of workers with a spirometer coupled with routine dust level measurement and subsequent corrective action may prevent respiratory morbidity in this population.

PS-40-943-02 A study of prevalence of impaired pulmonary function and its associated factors amongst residents of an urban village of Delhi, India

A Saxena,[1] A Khokhar,[1] JC Suri,[2] [1]Vardhman Mahavir Medical College and Safdarjung Hospital, Department of Community Medicine, New Delhi, India, [2]Vardhman Mahavir Medical College and Safdarjung Hospital, Department of Respiratory and Sleep Medicine, New Delhi, India. e-mail: 27.anirudh@gmail.com

Background: According to a World Health Organization (WHO) report, respiratory diseases account for 11% of the total deaths in India. There is a lack of literature on lung function impairment studies amongst the general population in India, especially those done in an urban village setting which is a mix of residential and commercial establishments. The present study, hence, was designed against this background to study the prevalence of pulmonary function impairment and determine the factors associated with it.
Methods: A cross-sectional study was carried out in an urban village (Aliganj) in Delhi. Sample size of 287 residents was covered by systematic random sampling technique. A pre-designed, semi-structured questionnaire was used to elicit relevant information and Pulmonary Function Test (PFT) was done using a portable advanced desktop Spirometer. Data analysis was done using licensed SPSS software (version 21). Statistical tests of significance for difference between proportions and multiple linear regression model were applied and the calculated results were considered significant at a p-value< 0.05. Ethical clearance was duly obtained from the Institutional Ethical Committee.
Results: Mean age of participants was 35.07±13.46 years. Impaired pulmonary function was seen in 152 (53%) of the participants. Out of 152 participants with impaired pulmonary function, 135 (88.8%) had a restrictive pattern, 2 (1.3%) had an obstructive pattern and 15 (9.9%) had a mixed pattern of impairment. Out of the factors with statistically significant association with impaired pulmonary function, significant odds were found between impairment of pulmonary function and female sex (OR=5.57), absence of a separate kitchen (OR=3.06) and underweight BMI category (OR=2.77) using multiple linear regression model.
Conclusions: The prevalence of impaired pulmonary function is high among residents of Aliganj, Delhi. A questionnaire-based screening for respiratory symptoms along with spirometry at the community level for general population may help in early detection & management of respiratory morbidities.

PS-40-944-02 Delayed diagnosis of sarcoidosis

Z Laushkina,[1] [1]Novosibirsk Research TB Institute, Pulmonary TB Department, Novosibirsk, Russian Federation. e-mail: zlaosh@list.ru

Background: Sarcoidosis is a systemic granulomatous disease of unknown etiology; it can mimic many other diseases including tuberculosis. Sometimes it is difficult to distinguish between these two diseases.
Methods: We retrospectively analyzed the medical records of 58 patients with biopsy-proven sarcoidosis (29 men) with a median age of 44 (range 21-76) yrs. All patients have been hospitalized in TB hospital with wrong diagnosis "pulmonary TB". Clinical, radiological, laboratory data of all admitted patients were collected.
Results: The period from the disease manifestation up to establishment of true diagnosis was 181±209 (mean±SD) days. Median delay time was 123 (30-1015) days. Patient delay was related to the length of time between the onset of the symptoms and the first contact with a health facility. Median patient delay was 24 (14-280) days. 22 % of patients were previously treated of an assumed community-acquired pneumonia before hospitalization in TB hospital, 52 % of patients up to making a true diagnosis received antituberculous treatment, median tuberculosis treatment 90 (30 -720) days. In 3.4 % of all cases a few acid-fast bacilli were found in sputum by luminescent microscopy (that we suppose as false-positive result). Delayed diagnosis is associated with male sex (p=0.001), acute attack of the disease (p=0.005), complaints: low body weight (p=0.005), fever (p=0.01), weakness (p=0.018); destructive cavities on chest X-ray (p=0.000), detection of AFB in sputum (p=0.026), biopsy delay (p=0.000).
Conclusions: We found the tendency to overdiagnosis of pulmonary TB in sarcoidosis patients. Many patients with sarcoidosis are misdiagnosed with and treated for tuberculosis. The use of antituberculous therapy in sarcoidosis patients increased the diagnostic delay. Other important reasons for delay were non-typical symptoms. Diagnosis of sarcoidosis requires histological confirmation.

PS-40-945-02 Species identification of non-tuberculous mycobacteria (NTM) from sputum samples of TB suspects in a tertiary care centre from North India

R Sharma,[1] BK Singh,[1] SK Sharma,[1] I Mani,[1] V Upadhyay,[1] P Jorwal,[1] R Ramachandran,[2] P Kumar,[3] [1]All India Institute of Medical Sciences (AIIMS), Medicine, New Delhi, India, [2]World Health Organization, Public Health, New Delhi, India, [3]National Tuberculosis Institute, Public Health, Bangalore, India. e-mail: rohinisharma9500@gmail.com

Background: Non-tuberculous mycobacteria (NTM) infections are often misdiagnosed as tuberculosis due to the similar clinical and radiological presentations. NTM infections can be differentiated from tuberculosis only through species identification.
Here we performed a species-level identification of NTM from sputum samples using ITS sequencing of the 16S-23S rRNA gene.
Methods: Twenty-one immunochromatographic assay negative isolates from smear-positive patients were collected and evaluated. The isolates were then subjected to mycolic acid extraction for HPLC, DNA isolation for line probe assay (LPA), *hsp65* and 16S-23S rRNA gene ITS sequencing.
Results: After evaluating all the diagnostic modalities for NTM, it was observed that the *Mycobacterium intracellulare* was the predominant slow-growing NTM (9/20, 45%), while *Mycobacterium abscessus* (*subsp. bolletii*) was the dominant rapid grower (5/20, 25%). One isolate, which could not be identified either by LPA or by HPLC, was detected as *Nocardia cyriacigeorgica*,by sequencing a non mycobacterial species predominantly found in pulmonary infection. The results of HPLC and LPA were 100% concordant. One isolate was identified as *M.abscessus* by sequencing, but HPLC and LPA detected it as *Mycobacterium chelonae*.
Conclusions: NTM should be considered as the key pathogen in immunocompromised patients and in patients with manifestations similar to tuberculosis. In such cases, species identification is critical for initiation of appropriate therapy. The 16S-23S rRNA gene ITS sequencing method is a rapid and accurate technique for NTM species identification.

PS-40-946-02 Assessment of airborne infection control and practices in healthcare institutions in Kerala, southern India

A Raj,[1] [1]Amrita Institute of Medical Sciences and Research Centre, Community Medicine & Public Health, Ernakulam, India. e-mail: arunrajkadayara@gmail.com

Background: Nosocomial transmission of airborne infections like H1N1, drug resistant TB, Nipah virus disease have been reported recently and have been linked to the limited airborne infection-control strategies. The objective of the current study was to assess the gaps in facilities and practices for preventing air borne infection transmission, with reference to the National Air Borne Infection Control (NAIC) guidelines, 2010.
Methods: A cross sectional study was conducted in 25 public and 25 private hospitals selected from 5 randomly selected districts in the state of Kerala. A checklist with 62 components was developed based on the NAIC guidelines. Frequencies, percentages and mean with standard deviation were used to summarize facility risk assessment and compliance to guidelines.
Results: Most of the facilities had infection control committees 35(70%). Annual infection control trainings were held for staff in 21(42%) facilities. Twenty (40%) facilities were not familiar with NAIC guidelines. Counseling on cough etiquette at registration was practiced in 5 (10%) institutions. Cross ventilation was present in OPDs in 27(54%) institutions. Sputum was disposed properly in 43 (86%) institutions. N 95 masks were available in high risk settings in 7 (14%) health facilities.
Conclusions: There exists lacunae in the air borne infection control practices in health care facilities in Kerala. Dissemination of National Airborne Infection control guidelines has to be given due importance in Kerala state with clear monitoring mechanisms to prevent nosocomial transmission of air borne infections.

PS-40-947-02 Association of knowledge and practice of infection prevention and control among healthcare personnel in Gauteng, South Africa

S Masuku,[1] S Olorunju,[2] M van der Walt,[1] D Peu,[3] S Mogale,[3] [1]South Africa Medical Research Council, TB Platform, Pretoria, South Africa, [2]South African Medical Research Council, Biostatistics, Pretoria, South Africa, [3]University of Pretoria, Health Care Sciences, Pretoria, South Africa. e-mail: smasuku@mrc.ac.za

Background: Tuberculosis (TB) remains an occupational health risk among Health Care Personnel (HCP) globally, with the risk of transmission present throughout the health care settings. Good knowledge of and practice towards Infection Prevention and Control (IPC) guidelines can greatly reduce to risk to the HCP. The study aim was to assess if knowledge of IPC leads to good practices.
Methods: HCP, employed for 2 years, from a hospital were invited to participate in a cross-sectional survey conducted between September 2017 to March 2018. Knowledge and practices towards IPC guidelines (WHO Policy on TB Infection Control in Health-Care Facilities, Congregate Settings and Households, 2009) were assessed through a self-administered questionnaire consisting of 3 domains (Demographic/employment/Qualification, Knowledge and Practice) with 19 structured and 2 open ended questions. Data was captured using REDCap database and analysis done on Stata 15 soft-

ware. Good knowledge was scoring correctly in at least 5/9 questions and self-reported good practice as doing correctly in at least 5/10 questions.
Results: 102/190 HCP returned questionnaires of which 23% were male. Ages ranged between 26-61 years. Mean years of employment in this facility was 8 years, with 32% having >10 years of service. Twenty-nine HCP had a degree, 47 a diploma and 26 a Certificate. The majority (85/102) of the respondents were nurses, and they also scored significantly higher on knowledge (P=0.04) compared to rest, being 2 doctors, 4 pharmacy staff, and 8 ancillary staff. Knowledge of IPC was overall high, 92%, but only 58% of HCP reported good practices, the majority being nurses. Knowledge scores were similar across age groups but older HCP scored higher on good practices (P=0.01). HCP with higher qualifications showed better knowledge but not significantly.
Conclusions: Good knowledge of IPC did not result in good practice. Older HCP with lower qualifications scored higher on good practices.

PS-41-C4 Strengthening TB detection and management in children

PS-41-948-02 Childhood TB diagnostic capacities in primary healthcare facilities in high TB-burden countries: results from the TB-Speed cross-sectional descriptive survey

E Wobudeya,[1] S Niangoran,[2] L Borand,[3] TE Mao,[4] J-V Taguebue,[5] R Moh,[2] C Khosa,[6] J Mwanga Amumpaire,[7] M Bonnet,[8] O Marcy,[9] TB-Speed Study Group [1]Makerere University, John Hopkins University, Research Collaboration, MU-JHU Care Limited, Kampala, Uganda, [2]Treichville - University Teaching Hospital, PACCI, Abidjan, Côte D'Ivoire, [3]Institut Pasteur in Cambodia, Epidemiology and Public Health Unit, Phnom Penh, Cambodia, [4]Ministry of Health, CENAT, Phnom Penh, Cambodia, [5]Fondation Chantal Biya, Centre Mère Enfant, Yaounde, Cameroon, [6]Ministry of Health, Instituto Nacional de Saude, Maracuene, Mozambique, [7]Epicentre, Mbarara Research Center, Mbarara, Uganda, [8]IRD, UMI 233 TransVIH-MI, Montpellier, France, [9]Universite de Bordeaux, Inserm U 1219 - Bordeaux Population Health Research Center, Bordeaux, France. e-mail: ewobudeya@mujhu.org

Background: Globally, more than 50% of childhood TB cases are not diagnosed, especially at primary health care level. As part of the TB-Speed Decentralization study, we conducted a baseline survey of childhood TB diagnostic capacities in primary health centers (PHCs) of 5 high TB burden countries: Cambodia, Cameroon, Côte d'Ivoire, Mozambique, and Uganda.
Methods: We conducted a cross-sectional assessment (January - June 2018) in 6-10 rural/semi-urban districts per country and 5-6 PHCs per district, selected in collaboration with NTPs, using a standardized tool for data collection from routine registers, physical counts and interviews with PHCs staff.
Results: Overall, 179 PHCs (Cambodia 40, Cameroon 45, Côte d'Ivoire 30, Mozambique 30, Uganda 34) were assessed in 32 districts. They reported 5905 TB cases in 2017 (1281 Cambodia, 64 Cameroon, 235 Côte d'Ivoire, 3241 Mozambique, 904 Uganda), including 796 (13.5%) children (19.7% Cambodia, 4.7% Cameroon, 5.5% Côte d'Ivoire, 13.8% Mozambique, 6?2% Uganda); 584 (73.4%) children had pulmonary TB including 111 (13.9%) bacteriologically confirmed, and 212 (26.6%) had extra-pulmonary TB. 135 (75.4%) PHCs had dedicated TB staff and 53 (29.6%) had staff trained in paediatric TB care. 83 (46.4%) PHCs diagnosed TB while 96 (53.6%) referred children to another level for diagnosis.
Of 125 (69.8%) collecting microbiological samples on-site, only 12 (6.7%) PHCs specifically collected paediatric samples (7 gastric aspirate, 8 induced sputum, 1 stool). 82 (45.8%) PHCs had on-site laboratory; 6 (3.3%) had Xpert MTB/RIF available, 78 (43.6%) only smear microscopy. 7 (3.9%) PHCs had on-site Chest X-Ray (CXR) while 6 (3.3%) had access to nearby CXR services. 107 (59.8%) PHCs assessed initiated TB treatment in children.
Conclusions: This study highlights limited but heterogeneous childhood TB diagnostic capacity in PHCs from 5 high TB burden countries. Access to specific paediatric sample collection and access to molecular testing for TB, as well as CXR remains very limited.

PS-41-949-02 Prevalence of pulmonary TB in children aged 0-5 years old with severe acute malnutrition (SAM) at the Macia Health Center, Mozambique

DV Osorio,[1] I Munyangaju,[2] A Muhiwa,[3] E Nacarapa,[4] I Ramiro,[5] AV Nhangave,[6] B Maculuve,[6] [1]Macia Health Center, Clinical, Macia, Mozambique, [2]Elizabeth Glaser Pediatric AIDS Foundation, Clinical, Maputo, Mozambique, [3]Elizabeth Glaser Pediatric AIDS Foundation, SI&E, Maputo, Mozambique, [4]Carmelo Hospital, Clinical, Chokwe, Mozambique, [5]Health Alliance International, Management, Maputo, Mozambique, [6]Provincial Health Directorate, Provincial Research Nucleus, Xai Xai, Mozambique. e-mail: dulceosorio92@gmail.com

Background: Mozambique has one of the highest rate of HIV in adults at 13.2% (24.4% in Gaza, 13 000 newly infected children) and for TB at 551/100,000; chronic undernutrition is 43% for < 5 years old (Gaza notified 3935 cases of SAM in 2017). The interactions between SAM and TB further complicate diagnosis of TB in children. We aimed to determine the prevalence of pulmonary TB in children with SAM using different diagnostic methods - clinical diagnosis, GeneXpert MTB/RIF® and culture (nasopharyngeal aspirate (NPA) and feces), TB LAM (urine) and radiography.

Methods: Cross-sectional retrospective analysis conducted at the pediatric inpatient of Macia Health Center between February - August 2018. All children with SAM (Weight/Height <- 3DP and/or bilateral edema) in this period were included in the study. All children were evaluated for clinical diagnosis of TB, GeneXpert and culture (NPA and feces), TB LAM and chest X-ray results.
Results: A total of 45 pediatric cases with SAM were admitted to the ward between 02/2018 - 08/2018; 17 had kwashiorkor, 20 marasmic-kwashiorkor and 8 marasmus. Of the 45 cases, 17 (37.8%) were clinically diagnosed with TB. All 45 cases submitted NPA and fecal specimens, 100% were GeneXpert MTB not detected; 4(8.9%) of the NPA were TB culture positive. Of the 45 cases 17 (37.8%) had TB LAM positive, 23 (51.1%) TB LAM negative and 5 (11.1%) did not do the test. All 17 clinically diagnosed cases had a positive TB LAM (Table 1). All cases had a chest x-ray, 17 (37.8%) had a suggestive and 28 (62.2%) had non-suggestive x-ray.
Conclusions: Despite the small sample size of our study, TB was diagnosed and treated in more than 1/3 of the SAM cases. TB LAM test showed high correlation with clinical diagnosis and more research on its use in pediatric TB is needed.

	N*	HIV positive	HIV negative	Cough	Fever	LOW**	FTT***	lethargy	Edema
SAM	28	4 (14%)	24 (85%)	15 (54%)	9 (32%)	14 (50%)	13 (46%)	26 (93%)	23 (82%)
SAM + TB	17	6 (35%)	11 (65%)	12 (71%)	12 (71%)	14 (82%)	14 (82%)	17 (100%)	13 (77%)
Total	45	10 (22%)	35 (78%)	27 (60%)	21 (47%)	28 (62%)	27 (60%)	43 (96%)	36 (80%)

*N = patients; Median age of patients = 30 months old **LOW = Loss of weight
***Failure To Thrive

[Table 1. Clinical details of the TB diagnosed patients, Macia Health centre, Feb. - Aug. 2018]

PS-41-950-02 Addressing gaps in childhood TB case detection and management through targeted contact management: lessons from South Africa

G Jagwer,[1] P Mugoni,[1] N Kula,[1] A Moran,[2] C Dlamini,[3]
[1]University Research Co., LLC (URC), USAID TB South Africa Project, Pretoria, South Africa, [2]University Research Co., LLC (URC), USAID TB South Africa Project, Washington, DC, United States of America, [3]USAID/South Africa, Health, Pretoria, South Africa. e-mail: gregoryj@urc-sa.com

Background and challenges to implementation: Childhood TB is a marker for ongoing TB transmission in the community and an indicator of the level of adult TB control within the population. Despite a well-functioning National TB programme in South Africa, childhood TB remain grossly under-detected in South Africa. According to the NTP, the proportion of childhood TB among all reported cases is only 10-12% compared to 15-20% estimated for other high-burden countries. TB infected children, if not appropriately identified and treated, create a pool from which future adult cases can arise posing a significant threat for South Africa as a TB high burden country.
Intervention or response: Targeted contact management among children of TB index patients were conducted by the USAID TB South Project between October 2017 and August 2018, in 15 of the 20 TB high burden districts of South Africa. To strengthen the efforts of the government, the project contracted 39 community institutions to provide targeted contact management which includes TB awareness and education, TB screening and intensified case finding, improved linkage to care and treatment, initiation for diagnosed patients as well as treatment adherence support to improve TB outcomes.
Results and lessons learnt: A total of 3006 children were reached of which 97% were screened for TB. Of those screened 1067 were found presumptive and tested for TB. A total of 75 patients were detected of which 96% were initiated on treatment. This represents a case notification rate of 2459/100,000 among children screened. The notification rate is six-times the national TB notification rate of 398/100,000.
Conclusions and key recommendations: Targeted contact management conducted through community structures is a highly effective strategy for TB case finding among children. These observations highlight the need to strengthen screening of children from historical index cases. Thus, this intervention should be scaled up in TB high burden areas to increase yield among children.

PS-41-951-02 Strengthening childhood TB management in Nepal: challenges, progress and lessons learned

SK Shrestha,[1] T Chhetry,[1] R Bhattrai,[1] A Thapa,[2]
BS Tinkari,[2] [1]Save the Children, Global Fund, Kathmandu, Nepal, [2]National Tuberculosis Center, NTP, Kathmandu, Nepal. e-mail: suvesh.shrestha@gmail.com

Background and challenges to implementation: Childhood tuberculosis has been neglected as Nepal's Tuberculosis Program focused on adult TB, resulting in underdiagnose, with less than 10% of total TB cases notified being children. The major gaps observed were lack of political commitment and absence of childhood focused NTP.
Intervention or response: Assessment of childhood TB services was done using bench-marking tools and gaps were identified. Childhood TB was prioritized in National TB strategic plan (2016-21). Collaboration with both international and national child health experts, public and private organizations was initiated to develop childhood TB guidelines, building capacity of health care providers and establishing a national working group.

	Active national working group on childhood TB	National guidance for childhood TB	The childhood TB strategy is fully implemented	All providers of Paediatric care are involved in childhood TB management	Investigation of childhood contacts of infectious TB patients is part of the national strategy	All eligible children have access to preventive treatment	Special approaches for diagnosis of TB in children are included in the national guidance on TB	Special diagnostic approaches for TB in children are applied
Gap Identified on Jan 2017	Not Met	Not Met	Not Met	Not Met	Not Met	Not Met	Not Met	Not Met
Current Status as of February 2019	Met	Met	Partially Met	Partially Met	Met	Partially Met	Met	Partially Met

[PS-41-951-02 Table. Current Status of Childhood TB program compared to initial assessment]

Childhood TB interventions were implemented in 40 high burden districts from March 2017 focusing on contact tracing, diagnosis, and preventive therapy. Malnourished children in the community and major hospitals were also targeted for TB screening.

Results and lessons learnt: Political commitment and multi-sectorial involvement to manage childhood TB were achieved. A total of 93 doctors were trained in childhood TB management training and they became focal persons to manage childhood TB in their respective regions.

Child focused interventions from March 2018-19 resulted in TB diagnosis of 521 TB cases among 38,987 malnourished children, 1,764 children were started on IPT after contact tracing of 59,742 family members. In the year 2018 the childhood TB diagnosed was 5.5% of total case notified.

Conclusions and key recommendations: Nepal has shown that childhood TB management can be strengthened when it becomes a priority. Intervention that pay attention on child TB can be implemented in collaboration with the ministry's Child health division, pediatrics association, other government and non-government organizations to increase and strengthen the program.

PS-41-952-02 Healthcare professionals' perceptions on barriers and facilitators to childhood tuberculosis diagnosis in Côte d´Ivoire and Mozambique

E De Carvalho,[1] J Orne-Gliemann,[2] R Moh,[3] L Adonis Koffy,[4] N Bhatt,[5] C Khosa,[5] M Bonnet,[1] E Wobudeya,[6] E Ouattara,[2] O Marcy,[2] [1]IRD, UMI 233 TransVIH-MI, Montpellier, France, [2]Universite de Bordeaux, Inserm U 1219 - Bordeaux Population Health Research Center, Bordeaux, France, [3]Treichville - University Teaching Hospital, PACCI, Abidjan, Côte D'Ivoire, [4]Yopougon University Teaching Hospital, Pediatric Department, Abidjan, Côte D'Ivoire, [5]Ministry of Health, Instituto Nacional de Saude, Maracuene, Mozambique, [6]Makerere University, John Hopkins University, Research Collaboration, MU-JHU Care Limited, Kampala, Uganda. e-mail: oliviermarcy@gmail.com

Background: Childhood tuberculosis (TB) remains largely under-diagnosed in resource-limited settings, especially at primary healthcare level. As part of the TB-Speed project, we aimed to identify barriers and facilitators to decentralized childhood TB diagnosis in two high TB burden countries with different models of care for pediatric TB - standalone services (Côte d´Ivoire, CI) and integrated services (Mozambique, MZ).

Methods: In a cross-sectional qualitative study (May-July 2017) we interviewed HCPs (17 in CI, 16 in MZ, mostly nurses, and laboratory, health or X-ray technicians) working within rural district hospitals and primary healthcare facilities. We conducted semi-structured interviews in French or Portuguese and analysed data using a thematic framework.

Results: HCPs reported difficulties in diagnosing childhood TB, particularly clinical evaluation, cough being rarely perceived as a TB symptom by parents. CI-HCPs highlighted limited experience, inadequate tools for clinical diagnosis; MZ-HCPs had more experience in managing TB but obtaining pediatric bacteriological samples, delays to laboratory results, poor access to quality chest X-ray, and diagnosing TB in HIV-infected or malnourished children were common challenges.

Transportation and stigma were barriers to TB diagnosis at community-level. CI-HCPs perceived TB as less prioritized compared to HIV or malaria; families usually faced additional costs for TB diagnosis. MZ-HCPs mentioned staff turnover and insufficient TB training, and perceived lack of sustainability of TB activities dependent on development partners.

Regarding key facilitators to childhood TB diagnosis, CI-HCPs highlighted engagement and collaboration between HCPs, and motivation of caregivers; MZ-HCPs mentioned shared resources with HIV activities implementation partners, easy-to-read algorithms, and cough officers operating at triage. HCPs called for strengthened TB leadership, easier sample collection procedures and better decentralized laboratory capacity.

Conclusions: Challenges with childhood TB diagnosis could be addressed by decentralizing new diagnostic tools and improving local capacity. Social and structural barriers including family resources, stigma, workload, and supervision mechanisms require multidisciplinary policy decisions.

PS-41-953-02 Healthcare providers' perceptions of barriers to TPT uptake and adherence among children in Eswatini

Y Hirsch-Moverman,[1] JE Mantell,[2] S Shongwe,[3] A Mafukidze,[3] M Strauss,[4] G George,[4] F Xaba,[3] N Shongwe,[3] J Frieze,[5] AA Howard,[5] [1]MSPH at Columbia University, ICAP, New York, NY, United States of America, [2]NYS Psychiatric Institute and Columbia University, HIV Center for Clinical & Behavioral Studies, New York, NY, United States of America, [3]ICAP Eswatini, ICAP, Mbabane, Eswatini, [4]University of Kwazulu Natal, HEARD, Durban, South Africa, [5]Columbia University Mailman School of Public Health, ICAP, New York, NY, United States of America. e-mail: yh154@columbia.edu

Background: Isoniazid preventive therapy initiation and completion rates are suboptimal among children. Shorter tuberculosis preventive treatment (TPT) regimens have demonstrated safety and efficacy in children and may improve adherence but are not widely used in high TB-burden countries. We used qualitative methods to elicit TPT regimen preferences to identify attributes for a discrete choice experiment (DCE) and understand how they may influence decision-making and service delivery in Eswatini.

Methods: We conducted semi-structured in-depth interviews with healthcare providers (HCP). We used inductive and deductive coding and grouped coded excerpts in themes.

Results: Of 20 HCP, 75% were female; mean age was 35 years. Key attributes impacting adherence to TPT regimens in children included pill-related characteristics (size, number, and taste/formulation), visit costs, side effects, and treatment duration (Table).

TPT Attribute	Illustrative Quotes
Visit Cost	If I can diagnose a mother and ask her to come and bring the kids... they'll complain about how much it cost to come from far away... because the transport is not so frequent... they'll have to come with the kids and they'll have to have money to feed the kids.
Pill-related Characteristics	If a pill is bitter, that child won't take it.
	I am thinking of my throat that 'is it going to fit in my throat?'
	...the lesser the number [of tablets], the better the outcome.
Treatment Duration	...even the parent would say 'my child is not sick why should it be six months just like TB treatment?'
Side Effects	When...a child is being brought with some side effects, that parent will say, 'Let's just stop, my kid is suffering'.

[Attributes and Illustrative Quotes]

HCP felt it was challenging for children to take medication and multiple pills were overwhelming. HCP suggested pills should be as small as possible and not bitter, with dispersible tablets as a potential solution. They voiced concerns that crushing pills may affect their integrity and cutting pills in half result in inaccuracies in measurement. Visit costs included transport, travel time and transport difficulties. HCP noted that TPT side effects might lead to poor adherence and patients sometimes attribute symptoms they have to their medications. HCP reported that a long treatment duration - generally as long as TB treatment itself - is difficult for healthy children and can be stigmatizing for children in school.

Conclusions: HCP are gatekeepers to information and delivery of new health interventions and their perceptions and preferences matter to the successful roll-out of new treatment regimens. Our data elucidated which attributes HCP felt were important in determining adherence to TPT among children. These attributes will be incorporated into the DCE to systematically assess TPT regimen preferences of HCP and children.

PS-41-954-02 Enhancing paediatric tuberculosis diagnosis and treatment in India's private healthcare sector: findings of a scoping study

KS Veesa,[1] R Dugyala,[1] S Rangisetty,[1] Y Amrutha,[1] K Khillare,[1] D Balasubramanian,[2] SK Mattoo,[2] M Casenghi,[3] J Cohn,[3] SK Angappan,[1] [1]Solidarity and Action Against The HIV Infection in India, Public Health, Hyderabad, India, [2]Ministry of Health and Family Welfare, Central TB Division, New Delhi, India, [3]Elizabeth Glaser Pediatric AIDS Foundation, Innovations, Geneva, Switzerland. e-mail: karunsandeep@saathii.org

Background: India, with an annual 2.74 million TB cases, contributes to over a quarter of the global TB burden, with two-thirds being treated in the private sector. An estimated 224,000 children have TB, of which only 59% were reported to the National TB Programme (NTP) in 2018. A 2017 review highlights the heterogeneity of TB treatment regimens in the private sector, with associated risks of drug resistance. Strategies to end TB in India require intensive engagement with the private sector to ensure appropriate diagnosis, treatment and reporting.

Methods: The study assessed private sector pediatric TB management in three districts of Andhra Pradesh, Maharashtra and Telangana as part of the 'Catalyzing Pediatric TB Innovations' initiative of Unitaid-EGPAF, implemented by SAATHII, in partnership with the NTP. A total of 1,994 private facilities were mapped and validated through individual site visits during Aug 2018 - Mar 2019. Data were collected through surveys of available TB services with these mapped facilities and examined using summary statistics.

Results: 634 (32%) facilities provided any pediatric services, 322(51%) by pediatricians and 312 (49%) by general practitioners. 320(50%) managed pediatric TB in-house and the rest (314) referred outwards, mostly to public health sector. Most (9 /10) providers of pediatric TB services are in urban areas.

Facilities with pediatricians were more likely to treat pediatric TB than those with general practitioners (chi-square= 56.9, $p<0.001$).

Among 320 in-house providers, only 61 (19%) used CB-NAAT, 45 (14%) prescribed WHO-approved pediatric FDC drugs provided at no cost by the government, 103 (32%) notified cases to the NTP and 64 (20%) were aware of government incentives for TB notification.

Conclusions: Targeted strategies are needed to engage the private sector for pediatric TB. Ongoing technical support is needed to ensure standardised diagnosis and treatment, with linkages with the government to ensure CBNAAT testing and WHO-approved FDCs.

PS-41-955-02 Increasing detection of childhood tuberculosis by engaging the public and private sectors in Bangladesh

MT Rahman,[1] MM Rahman,[1] F Hossain,[1] MA Alahi,[1] TI Tanha,[1] MM Rahman,[2] MS Islam,[2] T Roy,[3] H Hussain,[4] [1]Interactive Research and Development, TB REACH Project, Dhaka, Bangladesh, [2]DGHS, National Tuberculosis Control Program, Dhaka, Bangladesh, [3]Interactive Research and Development, Country Director, Dhaka, Bangladesh, [4]Interactive Research and Development, IRD Global, Singapore, Singapore. e-mail: toufiq.rahman@ird.global

Background and challenges to implementation: An estimated 1 million children fall ill with tuberculosis (TB) each year. TB in children is often missed due to non-specific symptoms and difficulties in diagnosis. In 2018, only 11,334 (32%) of the estimated 35,000 child TB cases were notified in Bangladesh. Active case finding (ACF) can increase the case detection in children to minimize notification gap.
Intervention or response: All children visiting the outpatient department (OPD) of two tertiary hospitals, two sub-district hospitals and 30 private pediatricians in Mymensingh district with any illness were verbally screened from November 2018 to March 2019. At each setting, trained health workers screened children for symptoms of TB using a structured screening tool. Children identified as presumptive were referred to the physicians for clinical evaluation and laboratory investigations (Smear microscopy, GeneXpert, Chest X-ray, Histopathology, etc.). Children diagnosed with TB were initiated on treatment according to the national child TB guidelines.
Results and lessons learnt: During the period, 88,202 children were screened, and among them, 2,911 (3.3%) were identified as presumptive and evaluated clinically by the physicians. Of them, the diagnostic tests were advised for 2,086 (72%), children and 189 (9%) were diagnosed with TB and treatment started for 188 (99%). A total of 87 (46%) of the cases were detected from the private sector. The mean age for children diagnosed with TB was 10.5 years, and 104 (55%) of them were female. The pulmonary and extra-pulmonary TB were 107 (57%) and 82 (43%), respectively. To detect each child TB patient, we screened 467 children and tested 11. ACF increased child TB detection in Mymensingh district by 43% (52) compared to the corresponding period in the previous years.
Conclusions and key recommendations: Increased child TB detection in the intervention area demonstrates the effectiveness of public and private mix ACF for minimizing the notification gap in high burden and high child TB missed settings like Bangladesh.

PS-41-956-02 Excellent treatment outcomes amongst children with drug-resistant tuberculosis: a cohort study from Tajikistan

J Achar,[1] J Kliescikova,[2] B Pirmahmadzoda,[3] M Sayfullo,[2] G Dymov,[2] A Rajabzoda,[3] ZS Dusmatova,[2] AP Cavalheiro,[1] JA Seddon,[4] P du Cros,[5] [1]MSF UK, Manson Unit, London, United Kingdom, [2]Médecins Sans Frontières, Operational Centre Amsterdam, Dushanbe, Tajikistan, [3]Ministry of Health and Social Protection, National TB Programme, Dushanbe, Tajikistan, [4]Imperial College London, Department of Paediatrics, London, United Kingdom, [5]Burnet Institute, TB Elimination and Implementation Science, Melbourne, VIC, Australia. e-mail: jay.achar@london.msf.org

Background: Few children are diagnosed with drug-resistant (DR) tuberculosis (TB) and data from Central Asia is particularly scarce. This limits the development of evidence-based recommendations. We describe a cohort of children treated for DR-TB from a collaborative programme between Médecins Sans Frontières and the National TB Programme in Dushanbe, Tajikistan.
Methods: We conducted a historical cohort study including all children < 18 years treated for DR-TB in Dushanbe, Tajikstan between 1st November 2011 and 31st December 2016. Drug-susceptibility test (DST) results were recorded from Xpert MTB/RIF, Hain MTBDR plus, and MGIT960 performed at the national reference laboratory. Where DST results were unavailable from the child, results were assumed from the identified source.
Results: Of 119 children included, 4 (3%) were younger than 2 years, 14 (12%) were between 2 and 5 years, 23 (19%) were between 5 and 12 years, and 78 (66%) were between 12 and 18 years. Seventy-one (60%) were female, and 99 (96%) of 103 children with an HIV test result were sero-negative. Eighty-five children (71%) were classified as "new" cases, while 94 (79%) were diagnosed with pulmonary disease. Eighty-two (69%) children were diagnosed with rifampicin-resistant/multidrug-resistant TB, 15 (13%) with pre-extensively drug-resistant-TB, and 20 (17%) with extensively drug-resistant-TB. One hundred and two (86%) children were successfully treated, 7 (6%) died, 9 (7%) failed and 1 (1%) was transferred out.

Drug	Number (percent)
Levofloxacin or moxifloxacin	117 (98)
Pyrazinamide	116 (98)
Prothionamide	110 (92)
Cycloserine	108 (91)
Capreomycin	89 (75)
Linezolid	20 (17)
Clofazimine	18 (15)
Delamanid	5 (4)
Bedaquiline	4 (3)

[Drugs used in initial regimen of children treated for drug-resistant tuberculosis (n=119)]

Conclusions: Despite limited availability of newer DR-TB drugs during the study period, results from our study show that high treatment success and low rates of loss to follow-up are possible. Our results support findings from other geographical regions and highlight the importance of improving detection amongst children to reduce global treatment gaps.

PS-41-957-02 Paediatric and adolescent tuberculosis mortality in South Africa, 2004-2016

M Osman,[1] K Du Preez,[1] J Seddon,[1,2] R Dunbar,[1] A Welte,[3] A Hesseling,[1] P Naidoo,[4] [1]Stellenbosch University, Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Cape Town, South Africa, [2]Imperial College London, Department of Paediatrics, London, United Kingdom, [3]Stellenbosch University, SACEMA, Stellenbosch, South Africa, [4]Bill and Melinda Gates Foundation, TB Program, Seattle, WA, United States of America. e-mail: muhammadbinyusuf@gmail.com

Background: Despite the decline in overall tuberculosis (TB) incidence in South Africa, the overall disease burden remains high with an estimated incidence of 567/100,000 in 2017. In South Africa, TB remains the leading cause of mortality, accounting for 6.5% of all deaths. While children and adolescents contribute a smaller proportion of TB disease and mortality than adults, the burden of mortality remains high, with TB a leading cause of death among children and adolescents. We aimed to describe the changes in TB mortality amongst children and adolescents in South Africa, and identify risk factors for mortality.
Methods: Retrospective analysis of all TB patients under the age of 20 years routinely recorded in the electronic TB register in South Africa (2004-2016) with adolescence defined as those aged 10-19 years. We developed a multivariable Cox regression model to evaluate predictors of mortality and estimate the hazard ratio of death.
Results: During the period of review, 726,639 children and adolescents were recorded on treatment, with definitive treatment outcomes in 84% (609,420) of patients: 81% were successfully treated, 4% moved, 12% were lost to follow up, and 2.5% (18,463) died during this period. Mortality decreased from 3.3% in 2007, to 1.9% in 2016. Youngest children (< 5 years) had the steepest decline in mortality (3.4% in 2007 to 1.3% in 2016), while mortality amongst children 10-14 years did not decrease (3.7% in 2007 to 3.2% in 2016). In the multivariable model (Table1), age, HIV status, previous TB treatment history and site of TB disease were associated with mortality.
Conclusions: The overall burden of TB mortality is declining but remains significant with 2% of children and adolescents on treatment dying in 2016. Compared to those 5-9 years old, children below 5 years have increased mortality and older adolescents (15-19 years) have the highest mortality.

Predictor variable	Hazard ratio and 95%CI
0-4 years vs 5-9 years	1.46 (1.39-1.52)
10-14 years vs 5-9 years	1.42 (1.34-1.50)
15-19 years vs 5-9 years	1.78 (1.70-1.86)
HIV unknown vs HIV negative	1.92 (1.82-2.03)
HIV positive vs HIV negative	4.64 (4.42-4.88)
Previous TB treatment	1.72 (1.64-1.80)
Extra pulmonary TB	1.52 (1.46-1.58)

[Multivariable Cox regression model of predictors of mortality in children and adolescents]

PS-41-958-02 Role of genetic factors in anti-tubercular therapy-induced liver injury in children

PC Vaidya,[1] D Jayaraman,[1] VV Borkar,[2] N Mehra,[1] M Kalia,[1] DC Vaidya,[3] S Phulke,[4] R Gautam,[5] J Menon,[6] BR Thapa,[6] [1]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Pediatrics, Advanced Pediatrics Centre (APC), Chandigarh, India, [2]Global Hospital, Department of Hepatology and Liver Transplantation, Parel, Mumbai, India, [3]Malla Reddy Institute of Medical Sciences, Department of Pathology, Hyderabad, India, [4]Maharishi Markandeshwar Institute of Medical Sciences and Research, Department of Opthamology, Mullana, Ambala, India, [5]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Biochemistry, Chandigarh, India, [6]Postgraduate Institute of Medical Education and Research (PGIMER), Department of Gastroenterology, Chandigarh, India. e-mail: moyna1794kalia@gmail.com

Background: Tuberculosis (TB) can affect any age group and continues to be an important cause of morbidity and mortality for children worldwide. The estimated burden of childhood TB worldwide is approximately 1 million. Severity of anti-tubercular treatment (ATT) induced liver dysfunction can vary from mild elevation of liver enzymes to acute and fulminant liver failure. The incidence of ATT induced Hepatitis in children is 2-10%. There is dearth of evidence in literature on the prevalence of ATT induced Hepatitis in children. The aim of the present review was to investigate genetic factors involved in ATT induced hepatotoxicity leading to hepatitis in children.
Methods: A literature search was undertaken through PubMed till 21st April 2019 with the keywords "Anti-tubercular drugs (ATDs), hepatotoxicity, hepatitis in TB pediatric patients, CYP2E1, NAT2" with limitation to "title". The relevant published articles related to ATT induced hepatitis in pediatric population were included for the review.
Results: The incidence of hepatotoxicity in children is less when compared to adults. In children, Drug Induced Hepatotoxicity (DIH) is associated with age younger than 5 years, extra pulmonary TB, use of High pyrazinamide and isoniazid dose. Genetic factors such as poly-

morphisms also act as a key factor in DIH. It has been reported that polymorphism in N-acetyl transferase2 (NAT2), CytochromeP4502E1 (CYP2E1) and Glutathione S-Transferase (GSTM1) are associated with the ATT induced hepatitis in pediatric as well as in adult population. There was a higher prevalence of N-acetyl transferase2 (NAT2) and CYP2E1c1/c1 slow-acetylator genotypes in DIH compared to non-DIH genotypes.
Conclusions: It has been postulated that certain genetic factors are attributed to coincide to produce toxic metabolites causing varied alterations in liver functions. The genotyping of the NAT2 and CYP2E1 polymorphism in pediatric as well as in adult population could possibly identify the groups at highest risk of developing ATT-induced hepatitis prior to medication.

PS-41-959-02 Risk factors for unfavourable outcomes in children treated for drug-susceptible TB between 2008 and 2017 at the Indus Hospital, Karachi, Pakistan

J Ahmed,[1] A Malik,[1,2,3] S Siddiqui,[1] K Asif,[1] A Khan,[1,4] F Amanullah,[1,5] [1]Global Health Directorate - Indus Health Network, The Indus Hospital, Karachi, Pakistan, [2]Emory University Rollins School of Public Health, Epidemiology, Atlanta, GA, United States of America, [3]IRD Global, Infectious Diseases, Karachi, Pakistan, [4]IRD Global, IRD Global, Karachi, Pakistan, [5]IRD Pakistan, Infectious Diseases, Karachi, Pakistan.
e-mail: junaid.fuad@ghd.ihn.org.pk

Background: In 2017, 10 million people developed TB disease of which 1 million were children. Few studies have described the treatment outcome and experience of children being treated for TB especially from high-burden low-resource settings. The objective of this study is to understand the factors predicting unfavorable outcomes in children with TB.
Methods: We conducted a retrospective cohort study among children (<15 years) being treated for TB at The Indus Hospital between 2008 and 2017. Treatment outcomes were evaluated using chi-square statistic. Unfavorable outcomes included the following treatment outcomes: lost-to-follow-up, died and treatment failure.
Results: The pediatric TB program enrolled 2843 children 63% of whom were females. Children between the ages of 11 to 14 years constituted 45% of the cohort followed by 5 to 10 years (37%), 1 to 4 (17%) and <1 (2%). Among statistically signifcant risk factors for unfavorable outcomes were age and baseline weight (p-values<0.01). Children <1 year of age had a treatment success rate of 70% in comparison to 79% or greater for the older age groups. Children with a baseline weight under 6kg had the lowest treatment success rate of 58% followed by >6 to 10 kg at baseline (70%).
Conclusions: We found that the youngest children with TB comprised the smallest cohort and were most likely to have poorer outcomes under programmatic conditions. Children < 5 years are at highest risk for developing active TB disease following exposure. TB preventive therapy can save young children from unnecessary morbidity and mortality.

LATE BREAKER PRESENTATIONS FRIDAY 1 NOVEMBER 2019

The HIV-TB and diabetes late-breaker session

LB-2861 CheXaid: deep learning assistance for physician diagnosis of tuberculosis using chest x-rays in patients with HIV

P Rajpurkar,[1] C O'Connell,[2] A Ng,[3] R Griesel,[4] G Maartens,[4] M Mendelson,[4] D van Hoving,[4] M Lungren,[5] T Boyles,[6] [1]Stanford University, Computer Science, San Francisco, CA, United States of America, [2]Standford University, School of Medicine, San Francisco, CA, United States of America, [3]Standford University, San Francisco, CA, United States of America, [4]University of Cape Town Faculty of Health Sciences, Cape Town, South Africa, [5]Standford University, AIMI Group, San Francisco, CA, United States of America, [6]University of the Witwatersrand, Department of Medicine, Johannesburg, South Africa. e-mail: tomboyles@yahoo.com

Background: Shortcomings in diagnostics are an important barrier to reducing morbidity and mortality from tuberculosis (TB), particularly in HIV-positive patients. Chest x-ray (CXR) is an important diagnostic tool, but presents additional challenges due to atypical radiographic presentation and radiologist shortages in regions where co-infection is common. Current approaches to autonomous interpretation of CXR have focused on ambulatory patients and often exclude clinical variables. Our goal was to develop and deep learning algorithm, including chest x-ray and clinical variables to assist in TB diagnosis in seriously ill patients with HIV
Methods: We gathered data from 677 seriously ill patients with HIV who were admitted to 2 hospitals in South Africa with suspected TB. A deep learning algorithm, CheXaid, was developed from a pre-trained chest X-ray reading algorithm (CheXnet) using a 121-layer DenseNet architecture plus 8 readily available clinical variables. The dataset was randomly split into a training set (n = 563) and a held out test set (n = 114) used for evaluation. The reference standard was a positive culture from any anatomical site. Results were compared with those of physician who were given identical information
Results: CheXaid had a sensitivity, specificity, and accuracy of 0.67, 0.87, and 0.79 respectively at a cut-off of 50% probability, which was less sensitive but more specific and accurate than physicians (0.73, 0.61, and 0.65 respectively). The c-statistic for the full CheXaid model was 0.831 (95% CI 0.75, 0.91) indicating excellent discrimination.
Conclusions: CheXaid is the first deep learning algorithm to combine interpretation of chest X-ray images with clinical variables to diagnose TB in seriously ill adults with HIV. The algorithm has excellent discrimination and performs better than clinicians given identical information. These results suggest that deep learning assistance can significantly improve clinician accuracy in TB diagnosis particularly in settings where radiological expertise is scarce.

LB-2895 Incidence and affecting factors for tuberculosis among patients with type 2 diabetes mellitus using health insurance big data in Korea

HM Lee,[1] SD Song,[2] CT Kim,[3] [1]Gyeongsangbuk-do Center for Infectious Disease Control and Prevention, Andong-si, Korea, Republic of, [2]International Tuberculosis Research Center, Korea, Changwon-si, Korea, Republic of, [3]Korean National Tuberculosis Association, Seoul, Korea, Republic of. e-mail: fire-cloud@daum.net

Background: Diabetes mellitus(DM) is known as a risk factor for tuberculosis (TB). Soaring prevalence of DM globally would have a negative impact on TB control strategy is predicted.
The present study evaluated the incidence rate of TB and affecting factors on TB from patients with type 2 Diabetes Mellitus (T2DM) in Korea.
Methods: We used customized big data provided by the National Health Insurance sharing service to conduct a retrospective cohort study. Type 2 diabetic cohort and Non-diabetic (NDM) cohort comprised 428,858 and 486,673 subjects aged 45-64, respectively. Baseline data was evaluated with national health examination and medical use database between 2010 and 2011.
The incidence of TB was calculated through follow-up from Jan 2012 to Dec 2017. Cox′s proportional hazard model was used to identify affecting factors on TB.
Results: The mean annual incidence of T2DM cohort was 76.5[hazard ratio (HR) 1.85 (1.80-1.91)], male 83.0 [HR 1.94 (1.86-2.02)], female 66.9 [HR 1.67(1.59 -1.74)] per 100,000. It indicate higher TB incidence than the NDM cohort. The risk factors for TB incidence in the two cohorts were sex(male), age(increase), low income, low BMI, current smoking, and inactive. Compared to NDM cohort, the T2DM cohort had a higher risk of TB incidence in the following factors: sex(male), age(increase), and chronic complications.
Nevertheless, body mass index (BMI) ≥25 kg / m2 showed a preventive effect for tuberculosis, but the effect disappeared in women with stage 2 obesity(BMI ≥30 kg / m2).
Conclusions: The risk of TB in the T2DM cohort was higher than that of the non-diabetic cohort. Sex(male), increasing age, low BMI and growing number of chronic diabetic complications were risk factors for TB . Preventing diabetes mellitus, diabetic complications and un-

derweight could help to prevent TB in the middle-aged adults. Also, regular physical activity and smoking cessation are needed.

LB-2908 The prevalence of Tuberculosis (TB) among pregnant women and the sensitivity of symptomatic screening versus Xpert MTB/RIF: a cross-sectional study in seven health facilities, Botswana

S Hamda,[1] JG Tshikuka,[1,2] D Joel,[3] G Monamodi,[1] V Setlhare,[1] B Tembo,[4] F Mulenga,[4] B Mbeha,[5] T Agizew,[1] [1]University of Botswana, Family Medicine and Public Health, Gaborone, Botswana, [2]National Pedagogic University, Faculty of Health Sciences, Kinshasa, Congo (Democratic Rep.), [3]University of Botswana, Paediatrics, Gaborone, Botswana, [4]Ministry of Health and Wellness (MoHW), Botswana National Tuberculosis Reference Laboratory, Gaborone, Botswana, [5]Ministry of Health and Wellness/MoHW, Botswana National Tuberculosis Reference Laboratory, Gaborone, Botswana.
e-mail: shhamda@gmail.com

Background: Delayed or undiagnosed TB in pregnancy can lead to poor maternal outcomes, including premature birth and perinatal death. This study aimed at determining (1) the prevalence of TB and TB/HIV co-infection, and (2) the sensitivity of symptomatic screening versus Xpert MTB/RIF in detecting active TB among pregnant women using TB culture, as gold standard.
Methods: From November 2017 to March 2018 pregnant women presenting to seven antenatal care (ANC) clinics were randomly enrolled and screened using TB symptoms (i.e. cough>2 weeks, fever, night sweating and weight loss). Two sputum specimens were collected from all clients and each client was tested using Xpert MTB/RIF and culture, at the National Tuberculosis Reference Laboratory (NTRL) in Botswana. HIV-status was determined from ANC client record. Fisher exact test was used to compare prevalence of TB between HIV-infected and HIV un-infected.
Results: Out of 429 pregnant women enrolled 407 (95.0%) were included in the analysis; and 8 (2.0%) had one or more TB symptoms, of which 4 (0.98%) were presumptive TB cases, but all clients with one or more TB symptoms were tested negative both with Xpert MTB/RIF and culture. While, two (0.5%) asymptomatic clients tested positive for TB with both Xpert MTB/RIF and culture. The prevalence of TB among HIV infected was not significantly different (Fisher exact test P < 0.312) compared to HIV un-infected [1.45 % (1/69) vs 0.3% (1/336)]. Xpert MTB/RIF demonstrated a 100% sensitivity and 100.0% specificity, while symptom screening had 0.0% sensitivity but 98% specificity.
Conclusions: Tuberculosis prevalence among pregnant women in Botswana was estimated to be 0.5% with no significant difference between HIV-infected and uninfected. Symptom screening has limited ability to detect TB among pregnant women calling for an urgent action to consider alternative TB screening algorithm, including Xpert MTB/RIF, irrespective of the presence or absence of TB symptom/s and HIV-status.

The Union student late-breaker session on lung health

LB-2922 Non-coverage of tuberculosis and diabetes mellitus screening among household contacts of active tuberculosis patients in Southern Thailand

N Safira (on behalf of fourteen students in TB research training PSU),[1] E McNeil,[1] V Chongsuvivatwong,[1] [1]Prince of Songkla University, Epidemiology Unit, Hat Yai, Thailand.
e-mail: safiraa25@gmail.com

Background: The rising incidence of diabetes mellitus (DM) complicates tuberculosis control in low-to-middle-income countries (LMIC). Annual diabetes screening should be done in high-risk individuals as a nationwide guideline. However, the coverage of tuberculosis screening among household contacts and unawareness of DM status has rarely been investigated simultaneously. The objective of this study was to assess non-coverage in such screenings among tuberculosis contacts in Southern Thailand.
Methods: A cross-sectional household survey was carried out in a community from January 18 to 20, 2019. Index tuberculosis cases were retrieved from the registry of Phatthalung Hospital. Face-to-face interview with prior consent was done during home visits.
Results: Of the 95 index cases identified, 61 consented for home visit (64%).
For tuberculosis screening, among 174 household contacts the non-coverage of tuberculosis screening was 60% in 55 children and 50% in 119 adults. Among those screened, 4% of adults and 32% of children did not get a chest x-ray.
For DM screening, of 95 contacts aged ≥35 years, 85% had been screened for DM and 23 adults (28%) had been diagnosed and were receiving treatment. Fourteen (15%) had never been screened for DM.
Conclusions: Both screenings were far from the national target. Non-coverage of tuberculosis screening was more common than non-coverage of DM screening among household contacts. This indicates the need to further improve the of tuberculosis contact tracing program.

LB-2892 Change of the incidence of chronic bronchitis after the adoption of the federal anti-tobacco law in the Russian Federation

M Peredelskaya,[1] G Sakharova,[2] N Antonov,[2] O Salagay,[3] N Nenasheva,[1] I Demidov,[4] [1]Russian Medical Academy of Continuing Professional Education, Allergy, Moscow, Russian Federation, [2]Central Research Institute of Organization and Informatization of Health Care, Pulmonological, Moscow, Russian Federation, [3]Ministry of Health Care, Moscow, Russian Federation, [4]Weborama, Big Data, Moscow, Russian Federation. e-mail: concy1984@gmail.com

Background: One of the risk factors for the development of chronic bronchitis (CB) is tobacco smoking. In 2013, the federal law "On protecting the health of citizens from the effects of second hand tobacco smoke and the consequences of tobacco consumption" (FL) came into force all over the territory of the Russian Federation (RF).

Methods: The analysis of the incidence of CB has been carried out based on official statistics of the RF for the period from 2009 to 2017, the analysis included data for the RF as a whole, for eight federal districts and 83 regions. To analyze the impact of the law, the incidence rate trend lines for the different periods of time were build: the trend line n. 1 for 2009-2013 years (before the introduction of the FL) and the trend line n.
2 for 2014-2017 (after the introduction of the FL). Trend lines were build using linear regression method, with the calculation of coefficients k for the slope of approximating lines. Statistical significance was assessed with a modified Student coefficient, for a significance level of p less0.01.

Results: Analysis of trends in the incidence of CB revealed a statistically significant difference in the values of coefficients: in the trend n. 1 the k coefficient was 60.5, which describes the increase in incidence of CB during the period of maximum exposure to a risk factor. The value of the coefficient k in the trend 2 - 43.8 - corresponds to a decrease in incidence rate.

Conclusions: The analysis shows a steady downward trend in the incidence of chronic bronchitis among the population of the RF after the adoption of the FL. Thus, integrated measures of state anti-tobacco policy produced a positive impact on the health of citizens.

The HIV-TB and diabetes late-breaker session

LB-2948 Investigation of associations between comorbidities including diabetes, undernutrition and anaemia and health-related quality of life in persons with TB attending TBDOTS clinics in the Philippines

S Cox,[1,2] L White,[1] C Garfin,[3] M Castro,[4] J Solon,[4] T Edwards,[1,5] MAL-TB DOTS Study Group [1]Nagasaki University, School of Tropical Medicine & Global Health, Nagasaki, Japan, [2]London School of Hygiene and Tropical Medicine (LSHTM), London, United Kingdom, [3]National TB Program, Manila, Philippines, [4]Nutrition Center of the Philippines, Manila, Philippines, [5]London School of Hygiene and Tropical Medicine, Tropical Epidemiology Group, London, United Kingdom. e-mail: sharon.cox@lshtm.ac.uk

Background: TB treatment may improve quality of life (QOL) but co-existing health related factors could negatively impact QOL. We investigated associations in persons with TB attending TBDOTS clinics, in particular co-morbidity with undernutrition, diabetes and anaemia.

Methods: Participants were enrolled in public facilities in Metro Manila (3 centres) and Negros Occidental (2 centres). Multivariate linear regression was used to model the four correlated domain score outcomes derived from responses to the WHOQOL-BREF questionnaire (physical, psychological, social, environmental). A forward-stepwise approach was used to select a final multivariable model with inclusion based on global tests of significance with $p< 0.1$.

Results: In 446 drug-sensitive adults, the mean domain scores (standard deviation) on a scale of 4-20 were physical: 13.4 (2.4), psychological 13.7 (2.2), social: 14.6 (2.0), environmental: 13.3 (2.0). Diabetes (HbA1c >=6.5% or current diabetes medication) and moderate/severe anaemia (haemoglobin< 11g/dL) were not associated with QOL ($p>0.1$). After adjustment for age, treatment adherence, inflammation (C-reactive protein>5g/L), category I or II TB treatment, frequency of TBDOTS clinic attendance, employment, handgrip strength, treatment phase and previously stopping working due to TB, moderate/severe undernutrition (BMI < 17 kg/m^2) was associated with lower QOL ($p=0.010$) resulting mostly from a reduced psychological domain score (coefficient=0.89, 95% CI: -1.41, -0.38) and physical score (coefficient=-0.51 (-1.03, 0.01). Moderate and severe food insecurity were also associated with a significant reduction in all domains. In 219 patients with known HIV status enrolled in Metro Manila, HIV was associated with QOL ($p< 0.001$) with a more notable reduction in psychological domain score (coefficient=-0.96, 95% CI:-1.69, -0.23). Diabetes, undernutrition and anaemia were not associated with QOL ($p>0.3$).

Conclusions: Nutritional status and food insecurity represent modifiable risk factors for poor QOL that may be alleviated through interventions via TBDOTS clinics, supporting further research of the potential benefit of nutritional interventions in persons with TB.

The Union student late-breaker session on lung health

LB-3003 Using health promotion approach for deciding actions to reduce tobacco consumption among undergraduates in Rajarata University of Sri Lanka

N Sewwandi,[1] D Ranasinghe,[1] A Madhumali,[1] N Karunarathne,[1] N Rathnayake,[1] S Kumara,[1] D Guruge,[1] All Undergraduates in Rajarata University of Sri Lanka [1]Rajarata University of Sri Lanka, Health Promotion Department, Anuradhapura, Sri Lanka.
e-mail: nadeeshaswgamage@gmail.com

Background: Evidence shows that around 80% of lung cancer deaths are caused by smoking and smoking is a major risk factor for lung cancers. So, initiation of tobacco smoking during young ages is highly prevalent in Sri Lanka and this study aimed to identify the determinants of tobacco smoking and to decide actions to reduce tobacco consumption among undergraduates in Rajarata university of Sri Lanka.
Methods: This program was conducted with first year undergraduates (n=135, 80 girls and 55 boys) in Faculty of Applied Sciences, Rajarata University of Sri Lanka. A team of undergraduates in the Department of health promotion in Rajarata University of Sri Lanka facilitated the whole program. Participants were divided into groups according to their preferences. Focus group discussions were conducted to enable undergraduates to identify tobacco consumption as a problem in this university. Facilitators guided them to identify superficial and hidden determinants for tobacco consumption. Facilitators improved their skills and involvement required to address selected determinants and to reduce tobacco smoking in the university. Data were collected by facilitators through focus group discussions and analyzed pre and post data using thematic analysis and using descriptive statistics.
Results: In-terms of immediate changes, 70% of participants identified that the availability and easy accessibility for cigarettes as major determinants for tobacco smoking among undergraduates. Undergraduates decided different actions to reduce accessibility for cigarettes in the university and 52% of undergraduates suggested to avoid smoking in common functions in the university. 54% of undergraduates suggested to take actions to stop selling and buying cigarettes within university premises as a rule in the university.
Conclusions: Availability and easy accessibility are major determinants for tobacco smoking among university undergraduates in this university and health promotion approach can be used to enable undergraduates to identify determinants of tobacco consumption and to decide actions to reduce it.

LB-3014 Empowering construction workers to reduce tobacco smoking through a community based intervention at a selected construction site at Mahakanadarawa, Sri Lanka

R Karunarathne,[1] S Young,[2] D Guruge,[1] Construction Site Workers at Constructing Water Plant [1]Rajarata University of Sri Lanka, Department of Health Promotion, Anuradhapura, Sri Lanka, [2]University of Colombo, Environmental Technology, Colombo, Sri Lanka.
e-mail: ruwanmali.karunarathne@gmail.com

Background: Construction workers have higher prevalence of smoking. Specially, their false attitudes and beliefs influence them to increase tobacco smoking. Majority of these are either socially learned or constructed by the tobacco industries. Accordingly, the intervention was carried out to address false attitudes and beliefs of workers regarding smoking.
Methods: Study conducted during four months in a selected construction site at Kanadarawa village in a water plant constructing site. Determinants caused for their smoking were derived from the study group (n=48) itself through the intervention. Changes of attitudes towards smoking among workers were assessed through ‚pocket meeting' discussions. Presentations, videos and posters were used to change their false attitudes by revealing them the ‚company strategies' as well.
Results: The changes were assessed using an interviewer administer questionnaire and analyzed by using SPSS software.
(a) The beliefs; "smoking reduces the sleepiness", "smoking gives a mental relief", "smoking is good for health" and "smoking gives a stimulation to health" were accepted as correct, before the intervention with a percentage of 52.%, 52.15, 6.3% and 12.5% respectively. After the intervention, it was 6.3%, 2.1%, 0% and 0% respectively.
(b) Attitudes related to effects of smoking; "smoking can be stopped", "possible to reduce daily consumption of smoking", "smoking is a foolish, worthless work", before the intervention; the percentage who accepted those as "yes" was 43.8%, 91.7% and 81.3% and after it was 95.8%, 95.8%, 95.8% respectively. Number of workers who are not using cigarette was improved from 29.2% to 43.8% and not using ‚bidi' was improved from 43.8% to 56.3%.
Conclusions: Community based interventions are effective in changing false attitudes on smoking among construction workers and showed a significant change

(P>0.000) in attitudes. Smokers themselves are capable of changing determinants affect for their own usage and able to reduce or to quit tobacco smoking among them.

LB-2965 Progress in the development of small protein biosignature based tests for the diagnosis of TB disease

H Mutavhatsindi,[1] G van der Spuy,[1] JS Sutherland,[2] H Mayanja-Kizza,[3] E Nepolo,[4] A Miheret,[5] D Kassa,[6] AC Crampin,[7] G Walzl,[1] NN Chegou,[1] [1]Stellenbosch University, Biomedical Sciences, Cape Town, South Africa, [2]Medical Research Council Unit Gambia @ London School of Hygiene and Tropical Medicine, Faraja, Gambia, [3]Makerere University, Medicine, Kampala, Uganda, [4]University of Namibia, Biochemistry and Microbiology, Windhoek, Namibia, [5]Armauer Hansen Research Institute, Immunology, Addis Ababa, Ethiopia, [6]Ethiopian Health and Nutrition Research Institute, Infectious and Non-Infectious Diseases Research Directorate, Addis Ababa, Ethiopia, [7]Karonga Prevention Study, Chilumba, Malawi. e-mail: hygon@sun.ac.za

Background: The development of non-sputum based point-of-care tests is a high priority in the fight against TB. Previous studies identified various host blood biomarker signatures of up to seven proteins, which showed potential as tools for the diagnosis of active TB. There is a need to validate these protein signatures and identify the most useful candidate biomarkers which could be developed further into point-of-care tests. The aim of this project was to validate recently identified host protein biosignatures and identify new biosignatures as tools for the diagnosis of TB.
Methods: We recruited adults presenting with symptoms suggestive of pulmonary TB at primary healthcare clinics in six African countries. Using the Luminex technology, we measured the levels of 20 previously identified host biomarkers in serum samples from study participants and assessed the accuracy of combinations between the biomarkers in the diagnosis of TB.
Results: Out of 1004 study participants included in the study, 278 (27.69 %) were diagnosed with TB and 199(19.82 %) were HIV infected. The previously identified 7-marker biosignature continued to perform well. However, we identified small protein bio-signatures comprising of three analyse (NCAM, CRP and I-309) which diagnosed TB in all study participants with AUC of 0.90 (95% CI 0.86-0.93). When participants were stratified according to HIV infection status, the small signature diagnosed TB in HIV uninfected participants with an AUC of 0.90 (95% CI 0.86-0.94) and an AUC 0.90 (95% CI 0.82-0.96) in HIV infected participants.
Conclusions: We have identified a small three-protein signature in specimens from multiple African countries, with potential in the diagnosis of TB disease. Our findings hold promise for the development of point-of-care triage test as the biosignature meets the WHO Target Product Profile minimum requirements such a test.

The HIV-TB and diabetes late-breaker session

LB-3021 Diabetes and tuberculosis- partners in crime

G Mishra,[1] R Munje,[1] M Dawkore,[1] [1]Indira Gandhi Government Medical College, Respiratory Medicine, Nagpur, India. e-mail: gpmishra81@gmail.com

Background: Diabetes mellitus (DM) is an important and recognized risk factor for tuberculosis (TB). India is a high TB burden country along with an increased prevalence of diabetes in its population. The current study aimed to study the diagnostic profile and treatment outcomes of tuberculosis in diabetics (TBDM) as compared to that in non-diabetics.
Methods: A retrospective analysis from clinical records of TB patients diagnosed between November 2016 to April 2018 (eighteen months) was carried out in a tertiary care teaching institute.
Results: Out of a total 1592 TB patients diagnosed during the study period, 66 (4.15 %) patients were diabetics. Amongst them, 49 patients had declared outcomes and were analyzed further. 98 TB patients without diabetes, diagnosed during the same period, were selected randomly in 1:2 ratio as the control group. There were 26(53%) microbiologically confirmed TB patients and 23(47%) clinically diagnosed TB cases among diabetics as compared to 43(43.87%) microbiologically confirmed TB patients and 55(56.12%) clinically diagnosed TB cases among non-diabetics. There were 41(83.63%) pulmonary and 8(16.32%) extra-pulmonary TB cases among diabetics as compared to 56 (57.14%) pulmonary and 41(42.85%) extra-pulmonary TB cases among non-diabetics. Among diabetics, 39 (79.59%) patients were newly diagnosed and 10(20.40%) patients were retreatment cases of TB whereas 80(81.63 %) patients were newly diagnosed and 18(18.36 %) patients were retreatment cases of TB among non-diabetics. Poor treatment outcome of TB was seen in 14 (28.57%) diabetics as compared to 10(10.2%) non-diabetics.
Discussion: Diabetics are at an increased risk of developing pulmonary TB. TB is associated with poor treatment outcome in diabetics.
Conclusions: A robust screening of diabetics for TB is imperative and the healthcare provider must be well aware of the diagnostic spectrum and possible poor treatment outcomes of TB in these patients.

LB-2990 Outcomes and risk of mortality among TB/HIV co-infected patients on anti-retroviral therapy in the era of test and start in Uganda

R Ssebunya,[1] W Akobye,[1] M Kagwisagye,[1] A Maganda,[1] A Kekitiinwa,[1] [1]Baylor College of Medicine Children's Foundation, Uganda, Kampala, Uganda.
e-mail: rssebunya@baylor-uganda.org

Background: Benefits of starting antiretroviral therapy (ART) early among HIV/TB co-infected individuals has been widely documented. However TB treatment outcomes and the risk of mortality in the test and start era has not been evidenced. We therefore sought to bridge this knowledge gap using secondary data from four large HIV clinics in Rwenzori, western Uganda.
Methods: A retrospective cohort review of 443 charts was conducted for all HIV/TB co-infected individuals started on TB treatment between January 2016 and December 2017. Time from starting TB treatment to death as documented in registers was the main outcome. Risk of mortality stratified by timing of ART among patients on TB treatment was assessed using Kaplan Meier curves and estimates measured as number of deaths per 1000 person-years.
Results: A TB treatment success rate of 73.6% (326/443) and a seventeen percent (17.4%, 77/443) overall mortality were registered at 12 months after starting TB treatment. Adolescents and clients 30 years and above were disproportionately affected; mortality rate (20%, 4/16) and (19.2%, 59/77) respectively. Of the 67 registered deaths, 55/67 (82.1%) had been on ART two weeks and more before started anti-TB drugs. Risk of mortality was higher among those who were on ART before starting anti-TB drugs (1.45 person-years, 95%CI: 1.14 - 1.85) compared to those who started both HIV and TB treatment on the same day (1.04 person-years, 95%CI: 0.34 - 3.22) and those who started ART after starting TB treatment (0.34 person-years, 95%CI: 0.16 - 0.71).
Conclusions: Results indicate significantly higher mortality among clients initiating TB treatment while on ART and particularly those who start within 3 months signifying high rates of un-masking TB IRIS in the era of test and start. Further investigations are needed to determine the optimal timing to start TB treatment among patients already on ART.

LB-3050 Can CRP help to distinguish live vs dead bacilli detected by Xpert-Ultra? Results from the TREATS TB prevalence survey

M Ruperez,[1] K Shanaube,[2] L Mureithi,[3] C Wapamesa,[2] JM Burnett,[3] B Kosloff,[1,2] P de Haas,[4] S Floyd,[1] E Klinkenberg,[4] H Ayles,[1,2] TREATS Study Group [1]London School of Hygiene and Tropical Medicine (LSHTM), London, United Kingdom, [2]Zambart, Lusaka, Zambia, [3]Health Systems Trust, Cape Town, South Africa, [4]KNCV Foundation, The Hague, Netherlands.
e-mail: maria.ruperez@lshtm.ac.uk

Background: C-reactive protein (CRP) testing is used extensively in clinical practice in resource-rich settings and has been proposed as a screening test for TB in high-burden countries. National TB prevalence surveys (TBPS) attempt to measure "active TB", but those using Xpert face the challenge of < 100% specificity, possibly explained by the presence of DNA from non-viable bacilli. We evaluated whether a point-of-care (POC)-CRP could help to detect "active TB" in 3 communities in Zambia and South Africa that have high HIV prevalence
Methods: POC-CRP testing was performed in all participants who were screened as sputum-eligible (SE) (abnormal Chest-X-ray and/or symptoms) and in 5% of those non-sputum-eligible (NSE). In SE participants two sputum samples were tested with Xpert-Ultra on the same day and a third one was sent for culture on the following day. We calculated the positive-predictive-value (PPV) of Xpert-Ultra compared with culture in participants with raised and normal levels of CRP.
Results: As of 26/07/2019, CRP was measured in 1361 participants (1129 SE, 232 NSE). A higher proportion of participants had a raised CRP (≥10mg/dl) among SE (15%) compared to NSE (9%, p=0.010) and among HIV-positive (24%) compared with HIV-negative individuals (12%, p< 0.001).

Test		CRP≥10mg/dl n (%)	CRP<10mg/dl n (%)	p-value
*Xpert +		17 (10%)	21 (2%)	<0.001
Xpert -		147 (90%)	907 (98%)	
**Culture +		6 (10%)	12 (4%)	0.044
Culture -		56 (90%)	308 (96%)	
***CRP		Culture +	Culture -	Total
≥10mg/dl	Xpert +	6 (100%)	0	6
	Xpert -	0	56 (100%)	56
<10mg/dl	Xpert +	5 (56%)	4 (44%)	9
	Xpert -	7 (2%)	301 (98%)	308

Individuals were classified as Xpert-positive if in ≥1 sputum sample MTB was detected, with trace calls classified as negative, as culture-positive if there was growth identified as M. tuberculosis on ≥1 of two MGIT tubes, and as culture-negative if there was no growth or the growth was identified as non-tuberculous-mycobacteria.

*Individuals with available CRP and Xpert results, N=1092
**Individuals with available CRP and culture results, N=382
*** Individuals with available CRP, Xpert and culture results, N=379

[Xpert-Ultra and culture results by CRP levels in sputum eligible participants from the TREATS TBPS]

There was an association between a CRP≥10mg/dl and both positive culture (p=0.044) and Xpert-Ultra (p< 0.001). Among 15 individuals with an Xpert-posi-

tive test result, 6 (40%) had a CRP≥10mg/dl and all 6 were also culture-positive (PPV=100%), while 9 (60%) had a CRP< 10mg/dl of whom 5 were culture-positive (PPV=55%). Comparable results were found when stratifying by HIV status.
Conclusions: Individuals with raised CRP were more likely to have clearly identified "active TB". Though limited by the small numbers, in participants with Xpert-positive results a raised CRP indicated "active TB", but a normal CRP could not accurately differentiate between "active" and "inactive" TB.

The Union student late-breaker session on lung health

LB-3062 A scalable model of community-based active case finding for TB using point-of-care GeneXpert versus same-day smear microscopy: a randomised controlled trial

A Esmail,[1] J Limberis,[1] A Pooran,[1] P Randall,[1] G Calligaro,[1] L Mottay,[1] K Dheda,[1] [1]University of Cape Town Lung Institute, Cape Town, South Africa.
e-mail: a.esmail@uct.ac.za

Background: There are ~350 000 TB cases globally, residing predominantly in peri-urban slums and informal settlements, that remain undiagnosed and perpetuate transmission (‚the missing cases'). Feasibility and optimisation of mobile low-cost active case finding (ACF) models using portable molecular tools is urgently required.
Methods: We performed intensified community-based ACF in Cape Town, South Africa, and compared POC sputum Xpert-MTB/RIF with same-day sputum smear-microscopy (performed at a microscopy centre within a 10km radius) in a pragmatic randomised (1:1) parallel-group trial with individual randomisation. 5247 individuals were rapidly screened (<5 minutes) using a HIV status and a questionnaire, and a scalable model (low-cost panel van with portable battery-operated GeneXpert and staffed by 2 minimally trained health care workers), and targeted for intensified ACF. M. tuberculosis culture positivity was used as a reference standard. The primary endpoint was the proportion of culture-positive TB patients initiating treatment with 60 days of diagnostic testing.
Results: 608/5247 (11.6%) individuals with at least one TB symptom and/or HIV co-infection were randomised [61/608 (10%) participants had culture confirmed TB]. 302/608 (49.7%) were assigned Xpert and 306/608 (50.3%) to the smear-microscopy group. Significantly more patients in the Xpert compared to the smear-microscopy group-initiated treatment by 60-days when specifically excluding culture-only based treatment initiation (17/33 [51.5%] versus 7/28 [25%]; p=0.04). The difference (95%CI) in the proportion of patients initiating treatment between groups was 26.5% (9-50, p=0·0047) and 70.8% more patients initiated treatment in the Xpert versus the smear-microscopy arm. Xpert detected all likely infectious cases (11/ 11 [100%] i.e. smear-positive and/or cough aerosol culture-positive and/or with cavitory disease).
Conclusions: Community-based ACF using a portable molecular tool nested within a low-cost mobile health unit is feasible and had a very high detection rate of infectious TB cases. These data inform community-based active case finding strategies in TB endemic settings.

The HIV-TB and diabetes late-breaker session

LB-3065 Understanding the TB-DM cascade-of-care in Lima: identifying gaps and barriers in a public health system

N Hilario-Huapaya,[1,2] J Inolopu,[1,2] C Ugarte-Gil,[1,3] [1]Universidad Peruana Cayetano Heredia, Instituto de Medicina Tropical Alexander von Humboldt, Lima, Peru, [2]Universidad Peruana Cayetana Heredia, Facultad de Salud Pública, Lima, Peru, [3]Universidad Peruana Cayetana Heredia, Facultad de Medicina, Lima, Peru.
e-mail: cesar.ugarte@upch.pe

Background: Amongst Latin American countries, Peru reports a high tuberculosis (TB) burden, with more than 80% patients living in urban areas. Diabetes (DM) prevalence is increasing, particularly in urban areas. Understand the cascade-of-care among persons with TB-DM can help to identify potential gaps and barriers faced by the patients, and can reduce the burden of this syndemic
Methods: Mixed methods approach were used: we analyzed data from National TB Program of persons with TB who received TB treatment in 333 health centers between 2015-2016 in Lima. Deep-interviews and analysis of national guidelines and documents on TB, DM and TB-DM were used to understand the barriers and gaps identify in the quantitative analysis.
Results: 8991 adults were affected with TB during the study period in Lima, predominantly male (63.7%). Mean age was 32.0 years and 87.0%(n=7825) of them was their first TB episode. 93.4% had pulmonary TB and 6.4% reported smoking 6.4%. 7.1%(n=637) reported previos DM diagnosis and 17.6%(n=1585) didn´t have a glucose test for DM screening. Among those with DM diagnosis information(n=7408; 82.4%), 9.3% were identified as persons with TB-DM(n=684). Complete laboratory test were less frequent among TB-DM patients (86.8% vs. 91.9%), but have similar frequency of health insurance (94.3% vs. 94.2%). Both groups had

similar rates of TB treatment success (TB-DM:88.5% vs.TB-non-DM:87.4%), however only 58.9%(n=403) among TB-DM patients had DM screening, complete laboratory tests, health insurance and successful TB treatment.

The barriers identified by the interviews were the lack of integration between TB and DM care(primary care vs. tertiary care), lack of DM information provided to the patient and often stockout of medicines and diagnostic tests for DM.

Conclusions: Regardless the efforts to provide adequate care for TB-DM, intrinsic weakness in our health system make integrate care very difficult. A patient-centered care should be the correct approach for persons with TB-DM comorbidity.

LATE BREAKER PRESENTATIONS SATURDAY 2 NOVEMBER 2019

The Union/CDC late-breaker session on TB

LB-2904 A novel blood-based triage test, ImmiPrint®-TB, to rule out active tuberculosis: a prospective multicentre study

A Trajman,[1,2] M Cordeiro-Santos,[3] A Brito de Souza,[3] A Esmail,[4] M Lipman,[5] M Santin,[6] A Noguera-Julian,[7] K Dheda,[4,8] [1]Federal Univeristy of Rio de Janeiro, Internal Medicine Post-Graduation Program, Rio de Janeiro, RJ, Brazil, [2]McGill University, McGill International TB Centre, Montreal, QC, Canada, [3]State University of Amazonas, Fundação de Medicina Tropical do Amazonas, Manaus, AM, Brazil, [4]University of Cape Town, Cape Town, South Africa, [5]University College, UCL Respiratory, London, United Kingdom, [6]University of Barcelona, Department of Infectious Diseases, Bellvitge University Hospital-IDIBELL, Barcelona, Spain, [7]University of Barcelona, Infectious Diseases Department, Hospital Sant Joan de Déu, Barcelona, Spain, [8]London School of Hygiene and Tropical Medicine (LSHTM), London, United Kingdom.
e-mail: a.esmail@uct.ac.za

Background: WHO and FIND have identified target product profiles (TPPs) for TB triage/rule-out tests, which ideally should be a point-of-care (POC) non-sputum-based test with at least 90% sensitivity and 70% specificity. ImmiPrint®-TB (ProteinLogic, Cambridge, UK) is a blood-based rapid immunoassay utilising a TB panel with 5 biomarkers. It is a < 2 hour POC assay using a table top immunosensor device.
Methods: We prospectively evaluated the accuracy and negative predictive value (NPV) of ImmiPrint®-TB in 635 participants ≥16 years old with suspected pulmonary TB in South Africa and Brazil. Pulmonary TB was confirmed by Xpert® and/or culture positivity in sputum (n=289). Non-TB patients (n=346) had active TB excluded or another confirmed alternative diagnosis. ImmiPrint®-TB results were analysed according to HIV and smear status.
Results: In those with suspected TB, the sensitivity, specificity and NPV (95% CI) were 0.91 (0.87-0.94), 0.68 (0.63-0.73) and 0.90 (0.86-0.93), respectively. Among 104 persons living with HIV and 119 smear-negative participants with confirmed TB, sensitivity was 0.96 (0.90-0.99) and 0.84 (0.76-0.90), respectively.
Conclusions: These preliminary findings suggest that ImmiPrint®-TB, a POC triage test with high NPV, is a promising community-based test for ruling out active TB, including in persons living with HIV and those who are smear-negative. Next steps include evaluation of ImmiPrint®-TB in larger cohorts in different community-based settings, including in those with extrapulmonary TB, presumed latent TB infection, and children. Abstract also submitted to TBScience2019

	TB cases	TB excluded	Prevalence	Sensitivity	Specificity	NPV	PPV
Overall	289	346	0.46 (0.42-0.49)	0.91 (0.87-0.94)	0.68 (0.63-0.73)	0.90 (0.86-0.93)	0.70 (0.65-0.75)
Smear-positive	150	79	0.66 (0.59-0.72)	0.97 (0.92-0.99)	0.61 (0.49-0.72)	0.91 (0.79-0.97)	0.82 (0.76-0.88)
Smear-negative	119	249	0.32 (0.28-0.37)	0.84 (0.76-0.90)	0.7 (0.64-0.76)	0.90 (0.85-0.94)	0.57 (0.49-0.65)
HIV-positive	104	84	0.55 (0.48-0.63)	0.96 (0.90-0.99)	0.67 (0.56-0.77)	0.89 (0.84-0.93)	0.78 (0.7-0.85)

[Diagnostic performance of the ProteinLogic ImmiPrint®-TB blood test among 635 patients with respiratory symptoms]

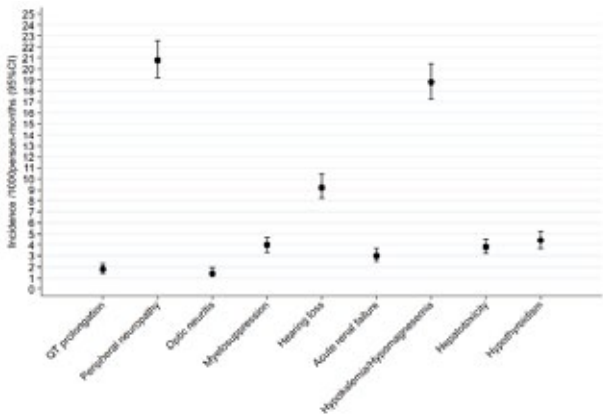
LB-2909 Bedaquiline and delamanid are safe: results from the endTB prospective observational study

M Bastard,[1] C Hewison,[2] U Khan,[3] CD Mitnick,[4] M Franke,[4] M Rich,[5] P Khan,[6] H Huerga,[7] KJ Seung,[5] [1]Epicentre - Médecins Sans Frontières, Geneva, Switzerland, [2]Médecins Sans Frontières, Paris, France, [3]Interactive Research and Development (IRD), Dubai, United Arab Emirates, [4]Harvard Medical School, Boston, MA, United States of America, [5]Partners In Health, Boston, MA, United States of America, [6]Interactive Research and Development (IRD), Karachi, Pakistan, [7]Epicentre - Médecins Sans Frontières, Brussels, Belgium, Fax: 0140215500. e-mail: cathy.hewison@paris.msf.org

Background: Multidrug-resistant tuberculosis (MDR-TB) requires long treatment using drug combinations known to cause toxicity. Bedaquiline and delamanid, the first new TB drugs in 40 years, as well as other commonly used drugs, may cause QT interval prolongation, a risk factor for sudden death. The endTB study aimed to assess the safety of MDR-TB regimens containing bedaquiline or delamanid.
Methods: Patients from the 17-country endTB project were included in this study if they started an MDR-TB regimen containing bedaquiline or delamanid between April 2015 and June 2018. We collected safety data from monitoring of a predefined set of nine adverse events, called adverse events of special interest (AESIs) because they have particular importance for patients receiving MDR-TB treatment containing bedaquiline, delamanid, and other select drugs. AESIs were clinically relevant if they required either a treatment change or supplements (e.g., potassium for hypokalemia). We reported frequency and incidence of clinically relevant AESIs.
Results: Of 2,315 patients included during the study period, 60.7% received bedaquiline only, 28.6% delamanid only and 10.6% both. A majority were previously treat-

ed with second-line drugs (72.7%) and had resistance to a fluoroquinolone (52.9%). The most common clinically relevant AESIs were peripheral neuropathy (25.1%), electrolyte depletion (23.4%) and hearing loss (12.3%). Among 953 patients receiving an injectable, 33.3% experienced hearing loss, acute renal failure or electrolyte depletion. QT interval prolongation was rare, occurring in 64/2,315 patients (2.8%), at an incidence rate of 1.8 events/1000 person-months (95%CI 1.4-2.3).

Conclusions: Bedaquiline and delamanid are safe. Clinically relevant QT interval prolongation is infrequent even with concomitant use of other QT-prolonging drugs. Since AEs associated with other drugs in MDR-TB regimens are common, close toxicity monitoring and management is required in patients treated for MDR-TB; the emphasis of this monitoring should be on clinically relevant AEs that occur at high frequency.



[Incidence and 95% CI of clinically relevant adverse events of special interest (N=2315)]

LB-2921 The PanACEA HIGHRIF 1 trial: do we now have the optimal dose of rifampicin?

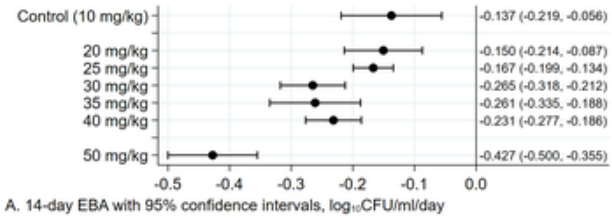
MJ Boeree,[1] L te Brake,[2] V de Jager,[3] K Narunsky,[4] P Phillips,[5] S Gillespie,[6] M Hoelscher,[7] R Dawson,[4] AH Diacon,[3] R Aarnoutse,[2] PanACEA [1]Radboudumc, Lung Diseases, Nijmegen, Netherlands, [2]Radboud University Medical Centre, Pharmacy, Nijmegen, Netherlands, [3]TASK Applied Science, Cape Town, South Africa, [4]University of Cape Town Lung Institute, Cape Town, South Africa, [5]University College of California, San Francisco, CA, United States of America, [6]University of St Andrews, St Andrews, United Kingdom, [7]University of Munich, Division of Infectious Diseases and Tropical Medicine, Munich, Germany.
e-mail: martin.boeree@radboudumc.nl

Background: The standard dose of rifampicin (10 mg/kg) was selected for pragmatic reasons in the 1970s but a maximum tolerated dose was never identified. Accumulating data indicate higher doses are more effective, may shorten treatment and prevent emergence of resistance.

The HIGHRIF1 study aimed to evaluate the safety/tolerability, pharmacokinetics, and extended early bactericidal activity (EBA) of increasing doses of rifampicin. Here we report the outcome of the final cohorts.

Methods: We performed a 14-day multiple-dose, dose-escalation study in treatment-naive adult smear-positive pulmonary tuberculosis patients in South Africa. Consecutive cohorts of patients received 40 or 50 mg/kg rifampicin once daily in monotherapy (day 1-7), supplemented with standard treatment between day 8-14. Safety and tolerability was assessed daily; full pharmacokinetic profiles were collected on day 7 and 14. The decrease in viable mycobacterial load was assessed by the daily fall in sputum colony forming unit counts and increase in MGIT time to culture positivity.

Results: Adverse events (AEs) in both cohorts were mostly mild (grade 1) or moderate (grade 2). In the 50 mg/kg group (n=17), all participants experienced AEs during monotherapy, and there were more AEs (n=93) compared to 40 mg/kg (n=36). Eleven patients in the 50 mg/kg group withdrew or stopped study medication. Increased bilirubin was observed in 9 patients without transaminitis. There was a supra-proportional increase in rifampicin exposure with dose. The EBA increased considerably with dose with the best effect seen in the 50 mg/kg cohort.



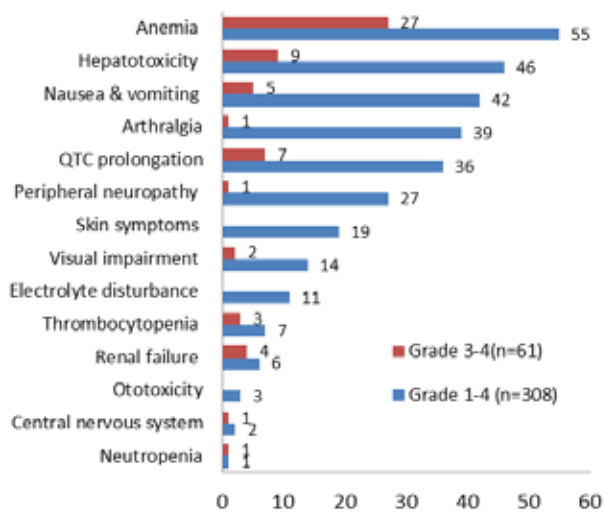
[14-day EBA with 95% confidence intervals, log10CFU/ml/day]

Conclusions: Rifampicin of 40mg/kg was safe and well-tolerated while 50 mg/kg was not. A remarkable increased fall in bacterial load was observed. Despite the better bactericidal effect of the higher dose, 40 mg/kg is likely to be the optimal balance between efficacy and tolerability and should be tested for treatment shortening potential in a phase IIB/C trial.

LB-2957 All-oral, bedaquiline-based, shorter treatment for RR/MDR-TB in rural South Africa shows promising early results

I Tack,[1] A Dumicho,[1] L Ohler,[1] AB Bulti,[1] K White,[1] A Shigayeva,[1] J Ngozo,[2] G Van Cutsem,[3,4] J Furin,[5] P Isaakidis,[3] [1]Medecins Sans Frontieres, Eshowe, South Africa, [2]Department of Health, TB Control Programme, Pietermaritzburg, South Africa, [3]Medecins Sans Frontieres Southern Africa Medical Unit, Cape Town, South Africa, [4]University of Cape Town, Cape Town, South Africa, [5]Harvard Medical School, Department of Global Health and Social Medicine, Boston, MA, United States of America.
e-mail: msfocb-eshowe-cliniccoord@brussels.msf.org

Background: In 2018, South Africa introduced an all-oral, bedaquiline-based,shorter treatment regimen for RR/MDR-TB, leaving the toxic injectables behind. We report on preliminary outcomes of a cohort of patients in a high HIV burden setting.
Methods: This retrospective analysis of routinely collected programmatic data included patients initiated on a bedaquiline-based shorter regimen in King Cetshwayo District between July 2018 and April 2019. In this all-oral regimen, bedaquiline replaces the injectable, ethionamide is omitted and linezolid is added for the first 2 months. Median time to smear and culture conversion was calculated for patients with positive baseline samples. Adverse events were extracted from clinical chart review and graded according to internationally accepted grading scale.



[Frequency and severity grading per adverse event experienced in RR/MDR-TB patients started on standardized, short, all-oral bedaquiline-based treatment regimen in King Cetshwayo District, KZN from 1 July 2018 to 30 April 2019.]

Results: We evaluated 123 RR/MDR-TB patients, median age of 34 (IQR: 26-43 years); 61.8% were male. 69.1% were HIV positive, of whom 78.8% on ART at initiation of their treatment.
At the time of assessment, 89 patients completed at least 4 months of DR-TB treatment of whom 43 (48.3%) had positive smear and 42 (47.1%) positive culture samples at baseline. Smear and culture conversion rates at 4 months were 88.4% (38/43) and 83.3% (35/42) respectively. The median time to smear and culture conversion was 5.1 (IQR: 4.1-7.9) and 7.6 (IQR: 4.1-8.1) weeks.
A total of 308 adverse events (AEs) were reported by 112 (91.1%) patients, with a median of 2 AEs per patient. Forty-three (34.9%) patients experienced at least one severe AE, being grade 3 or more. Frequency and grading of AEs are depicted in Figure 1.
Conclusions: Replacing the injectable by bedaquiline and adding linezolid to RR/MDR-TB treatment shows exciting early results. Adverse events remain common: the most frequent being anemia.
We recommend scaling up the use of bedaquiline and linezolid in regimens for RR/MDR-TB patients to achieve rapid treatment response, given continuous safety monitoring is ensured.

LB-2976 Short, simplified regimen for the treatment of children with multidrug-resistant tuberculosis in Karakalpakstan, Uzbekistan

D Lister,[1] YD Lin,[1] T Abdrasuliev,[2] H Tasnim,[1] J Cajazeiro,[3] J Singh,[4] M Tillashaikhov,[5] P Du Cros,[6] J Achar,[7] [1]MSF, Sydney, NSW, Australia, [2]MSF, Nukus, Uzbekistan, [3]MSF, Amsterdam, Netherlands, [4]MSF, Tashkent, Uzbekistan, [5]Ministry of Health, Tashkent, Uzbekistan, [6]Burnet Institute, Melbourne, VIC, Australia, [7]MSF UK, London, United Kingdom.
e-mail: jay.achar@london.msf.org

Background: Standardized shorter multidrug-resistant tuberculosis (MDR-TB) regimens (SR) of 9-12 months' duration are recommended by the WHO for use in children. Experience in children is limited. We describe the safety and outcomes of treating children and adolescents with a modified SR in Uzbekistan.
Methods: Between 2013-18,[DL1] children with MDR-TB were enrolled into a prospective, single-arm observational cohort study. Exclusion criteria included resistance to ofloxacin or both kanamycin and capreomycin, extrapulmonary involvement (except lymphadenitis or pleuritis) and previous treatment with second-line TB drugs. Outcomes are reported at end of treatment and following 12 months post-treatment follow-up.
Results: Forty-eight children received the SR. Following treatment commencement, five children were withdrawn from the study due to ineligible DST results. Median age was 16 years (range 6 months to 17 years and 91% (39/43) had pulmonary disease. Baseline culture was positive in 77% (33/43). Baseline resistance to pyrazinamide was detected in 51% (22/43), ethambutol in 49% (21/43) and kanamycin in 35% (15/43). No baseline ofloxacin resistance was detected.

At the end of treatment, 88% (38/43) were successfully treated, 7% (3/43) failed, 2% (1/43) were LTFU and 2% (1/43) died. Amongst 27 children who have completed 12 months post-treatment follow-up, 85% (23/27) were successfully treated, 1 failed, 1relapsed, 1 died and 1 LTFU. Seventeen grade 3 or 4 adverse events occurred in 10 patients. Six severe AEs were related to QTc prolongation, 4 renal impairment, 2 abdominal pain, and one each for nausea, anxiety, hepatitis, light headedness and haemoptysis.

Conclusions: We provide a detailed description of children treated using a modified SR for MDR-TB under operational research conditions. Our results support the effectiveness of the SR in children in this region. Severe adverse events occurred, but only affected treatment in one child. The lack of younger and clinically diagnosed children highlights the challenge of case-finding in this group.

LB-3037 Effect of vitamin D supplementation against TB infection: results of a randomized controlled trial

D Ganmaa,[1] G Gantsetseg,[2] D Khulan,[2] S Ariunzaya,[2] B Delgerekh,[2] E Sumiya,[2] M Tunsag,[3] B Amarsaikhan,[4] X Zhou,[5] A Martineau,[6] [1]Brigham and Women Hospital, Harvard Medical School and Harvard T.H. Chan School of Public Health, Boston, MA, United States of America, [2]MHI- Harvard T.H. Chan School Subcontractor, Ulaanbaatar, Mongolia, [3]National Center for Communicable Diseases of Mongolia, Ulaanbaatar, Mongolia, [4]Mongolian National University of Medical Sciences, Ulaanabaatar, Mongolia, [5]Yale School of Public Health, New Haven, CT, United States of America, [6]Queen Mary University of London, London, United Kingdom.
e-mail: gdavaasa@hsph.harvard.edu

Background: Vitamin D has immunomodulatory effects on both adaptive and innate immune responses. We wanted to test the hypothesis that improving vitamin D status among previously TB-uninfected healthy children will enhance immune responses to and protect against TB infection in a high transmission setting.

Methods: We designed a double-blind, placebo-controlled, randomized clinical trial of vitamin D supplementation to reduce the risk of latent TB infection (LTBI) among children ages 6 to 13 in Ulaanbaatar, Mongolia. 8851 schoolchildren were randomized to either 14,000 IU vitamin D3 weekly ('active treatment') or identically appearing capsules ('placebo').

We followed these children for three years and compared LTBI incidence among those on vitamin D treatment vs. placebo.

Results: A total of 8,117 (91.7%) children completed the study. Mean age at baseline was 9.4 years and mean serum 25(OH)D level was 11.9 ng/ml. Supplementation with weekly vitamin D elevated mean 25(OH)D levels to 29.8 ng/ml in the active treatment group compared to 9.7ngml in the placebo group (p=0.001). The proportion of children who were QFT positive at the 0.35 IU/ml IFN-gamma threshold was not different between treatment and placebo group (relative risk [RR] 1.10, 95% CI 0.87 to 1.38). The same was true when we used stable conversion at QFT+ at >4.0 IU/ml IFN-γ threshold (RR 0.66, 95% CI 0.39 to 1.13). Vitamin D supplementation at this regimen reduced LTBI in vitamin D deficient children (< 10ng/ml) RR 0.41, 95% CI 0.17 to 0.99 (p=0.04) for the 4.0 threshold but not for the 0.35 threshold.

Conclusions: Vitamin D supplementation was effective in correcting deficiency, but it did not influence risk of QFT conversion at the 0.35 IU/ml threshold in the study population as a whole. Supplementation was protective against QFT conversion at the 4.0 IU/ml threshold in the subgroup of children who had 25(OH)D levels < 10 ng/ml at baseline.

LB-3052 Preventing TB Overseas Pilot Study (PTOPS): latent tuberculosis infection treatment for U.S.-bound immigrants

A Khan,[1,2] C Phares,[3] HL Phuong,[4] P Nahid,[5] H Phan,[6] C Merrifield,[5] C Tran,[7] NV Nhung,[8] J Oeltmann,[9] PTOPS Study Group [1]London School of Hygiene & Tropical Medicine, Public Health and Policy, London, United Kingdom, [2]Stop TB Partnership/TB REACH, Geneva, Switzerland, [3]Centers for Disease Control and Prevention, Division of Global Migration and Quarantine, Atlanta, GA, United States of America, [4]Cho Ray Hospital, Visa Medical Clinic, Ho Chi Minh City, Viet Nam, [5]University of California San Francisco, San Francisco, CA, United States of America, [6]University of California San Francisco, Hanoi, Viet Nam, [7]Centers for Disease Control and Prevention (CDC), Division of Global HIV/AIDS and Tuberculosis, Atlanta, GA, United States of America, [8]Vietnam National Tuberculosis Program, Hanoi, Viet Nam, [9]Center of Disease Control and Prevention, Division of Global HIV/AIDS and Tuberculosis, Atlanta, GA, United States of America.
e-mail: amerak@stoptb.org

Background: Seventy percent of tuberculosis (TB) cases in the U.S. occur in persons born outside the U.S. Over 80% of these cases resulted from reactivation of latent TB infection (LTBI) acquired prior to U.S. arrival. Strengthening efforts to address LTBI would further U.S. TB elimination goals. The required overseas medical examination for U.S. immigration focuses on identifying TB disease. As a new strategy, we assessed uptake of overseas voluntary testing for infection and treatment for LTBI.

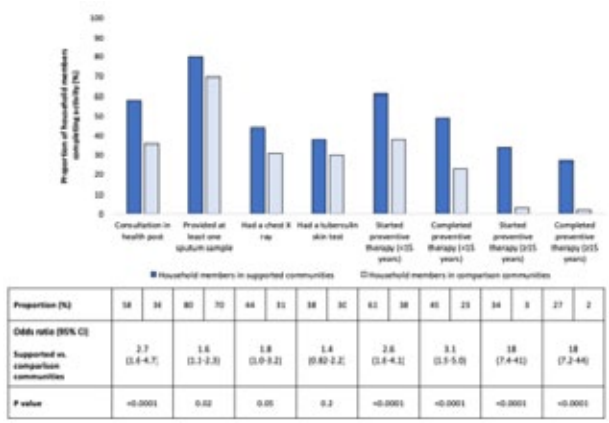
Methods: We conducted a prospective study among U.S. immigrant visa applicants aged ≥12 years undergoing the required medical examination at Cho Ray Hospital, Vietnam, from October 2018-July 2019. For those 12-14 years, the exam includes an interferon-gamma release assay (IGRA); consenting participants ≥15 years received an IGRA. Eligible participants with LTBI were offered 12 doses of weekly isoniazid-rifapentine (3HP). Participants accepting treatment received at least 8 directly

observed doses in Vietnam and, if needed, up to 4 self-administrated doses with weekly follow-up calls in the U.S. To assess uptake, we determined the proportion of immigrants willing to initiate and complete treatment.
Results: Of 5233 immigrants approached to participate, 2208 (40%) consented and had an IGRA result; 467 (21%) had positive results, 422 (90%) were eligible for treatment. Of those eligible, 287 (68%) accepted treatment. As of July 2019, 159 (55%) completed treatment [125 (79%) in Vietnam and 34 (21%) in the U.S.], 102 (36%) participants are still taking 3HP, and 26 (9%) did not complete treatment.
Conclusions: Treatment acceptance among eligible participants (68%) was similar to studies conducted within the U.S. Among those who started treatment and had time to complete treatment, completion rates were high (159/(159+26)=86%). The majority completed treatment prior to US arrival. Scale-up of routine IGRA testing and options to offer treatment for LTBI should be considered to support US TB elimination efforts.

LB-3028 Socioeconomic support to improve tuberculosis screening and preventive therapy completion in tuberculosis-affected households in Peru: a cluster randomised trial

MJ Saunders,[1,2] S Datta,[1,2,3] T Wingfield,[2,3,4] D Huff,[2,3] R Montoya,[2,3] E Ramos,[2,3] M Tovar,[2,3] J Lewis,[5] R Gilman,[6] CA Evans,[1,2,3] [1]Imperial College London, Infectious Diseases & Immunity and Wellcome Trust Imperial College Centre for Global Health Research, London, United Kingdom, [2]Innovación Por la Salud Y Desarrollo (IPSYD), Asociación Benéfica PRISMA, Lima, Peru, [3]Innovation For Health And Development (IFHAD), Laboratory of Research and Development, Universidad Peruana Cayetano Heredia, Lima, Peru, [4]University of Liverpool, Department of Clinical Infection, Microbiology and Immunology, Institute of Infection and Global Health, Liverpool, United Kingdom, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom, [6]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States of America.
e-mail: matthew.saunders@ifhad.org

Background: Socioeconomic interventions have become an important component of international tuberculosis policy, but impact and operational evidence are needed.
Methods: The Community Randomised Evaluation of a Socioeconomic Intervention to Prevent Tuberculosis (CRESIPT) study is a cluster randomised trial assessing socioeconomic support for tuberculosis-affected households (patients with tuberculosis and their household members) in 32 desert shantytown and urban communities in Peru. In 16 randomly selected supported communities, socioeconomic support package activities are led by peer mentors (recovering patients with tuberculosis) and consist of integrated social support constituting household visits and tuberculosis clubs providing information, peer support, and assessment of tuberculosis risk; and economic support constituting cash transfers as incentives and enablers. These are compared with 16 randomly selected comparison communities that do not receive the socioeconomic support package. All healthcare is provided free of direct charges by the Peruvian National Tuberculosis Program. The initial outcomes reported here are measures of tuberculosis screening and preventive therapy completion in household members, recorded after six months follow up for household members, on an intention to treat basis.
Results: From 18/11/2016 until 18/11/2018, 6,900 participants were recruited: 2,893 household members of 826 patients were recruited in supported communities; and 2,355 household members of 826 patients were recruited in comparison communities. Compared with household members in comparison communities, household members in supported communities were more likely to attend a screening consultation in health posts, provide at least one sputum sample for testing, and have a chest X-ray. The odds of completing preventive therapy were three times higher among contacts aged <15 years and eighteen times higher among contacts aged ≥15 years.
Conclusions: This cluster randomised trial provides rigorous evidence demonstrating the potential of socioeconomic interventions to improve access to tuberculosis care and prevention, increasing the optimal completion of tuberculosis screening and preventive therapy among household members in tuberculosis-affected households.



[Completion of tuberculosis screening and preventive therapy among household members]

LB-2991 High minimum inhibitory concentration of bedaquiline naive clinical Isolates of Mycobacterium tuberculosis from Mumbai, India

K Nilgiriwala,[1] A Papewar,[1] N Gala,[1] V Chitalia,[1] S Shah,[1] A Mandal,[1] S Kanth,[1] C Rodrigues,[2] N Mistry,[1] CRyPTIC Consortium [1]Foundation for Medical Research, TB Department, Mumbai, India, [2]P. D. Hinduja Hospital and Research Centre, Microbiology, Mumbai, India, Fax: +912224932876. e-mail: fmr@fmrindia.org

Background: Eliminating the wave of drug resistant TB (DR-TB) globally and developing effective and shorter treatment regime has become crucial. New drugs like bedaquiline have recently been approved for the treatment of DR-TB cases. Monitoring of resistance against bedaquiline needs to be closely monitored in order to understand the effectiveness of the drug in future.
Methods: A total 1,000 clinical isolates (treatment naive for bedaquiline) from a tertiary care centre in Mumbai, India were used for performing microtitre drug susceptibility testing by using UKMYC5 plates to determine minimum inhibitory concentration (MIC) of bedaquiline (0.015-2μg/mL). Whole genome sequencing was performed by Illumina NextSeq500. *Mykrobe Predictor* (v0.5.6) was used for determining lineage and drug susceptibility. Genomic variants in resistance associated genes (RAGs) for bedaquiline (depth≥5; quality≥30) were obtained using Samtools of Clockwork pipeline.
Results: Fourteen isolates were found to have high MIC (≥0.25μg/mL) (based on the MIC distribution for H_{37}Rv). The aggregate frequency of variants in the RAGs was ~5 times higher for isolates with high MIC (≥0.25μg/mL) than the isolates with low MIC (< 0.25μg/mL). Novel variants in the RAGs were observed in 8/14 isolates and majority of the isolates (9/14) had variant(s) in at least one RAG (Rv0678/*pepQ*/*atpE*). More than one-third (36%) of the isolates were of Beijing lineage. It was noteworthy that 64% (9/14) of these isolates were drug resistant (1 MDR, 5 pre-XDR and 3 XDR).
Conclusions: This study highlights the trend of the TB isolates with high MIC for bedaquiline, which is alarming. Importantly, the isolates were from patients who were treatment naive for bedaquiline, which makes it furthermore concerning. The presence of novel mutations in RAGs (and absence of mutations in these genes in some isolates with high MIC - indicating potential new target genes) calls for stringent monitoring system for evaluation of the efficacy of bedaquiline in DR-TB treatment.

TBSCIENCE2019 ORAL ABSTRACT-DRIVEN PRESENTATIONS

Oral Session: New diagnostics to reach the missing millions

CONCISE WHOLE BLOOD TRANSCRIPTIONAL SIGNATURES FOR INCIPIENT TUBERCULOSIS: A SYSTEMATIC REVIEW AND INDIVIDUAL PARTICIPANT DATA META-ANALYSIS

Gupta, Rishi, Dr; Turner, Carolin, Dr; Venturini, Cristina, Dr; Esmail, Hanif, Dr; Rangaka, Molebogeng, Dr; Lipman, Marc, Prof; Abubakar, Ibrahim, Prof; Noursadeghi, Mahdad, Prof

Background: Blood transcriptional signatures may predict risk of tuberculosis (TB). While multiple candidate signatures for active and incipient TB have been identified, it is not known which signature performs best, or whether any meets World Health Organization target product profile (WHO TPP) benchmarks for incipient TB biomarkers.

Methods: We performed a systematic review to identify candidate mRNA signatures for incipient TB, along with genome-wide transcriptomic datasets with sampling prior to TB diagnosis. We reconstructed each signature model and directly compared biomarker performance for incipient TB diagnosis in the pooled RNAseq dataset, in a one-stage individual participant data meta-analysis.

Results: We tested 17 candidate mRNA signatures in a pooled dataset from four studies conducted in South Africa, Ethiopia, The Gambia and the UK. We included 1,126 samples, with 183 samples from 127 incipient TB cases, Eight signatures (comprising 1-25 transcripts), predominantly reflecting interferon-inducible gene expression, had equivalent diagnostic accuracy for incipient TB over a two-year period with areas under the receiver operating characteristic curves from 0.70 (95% confidence interval 0.64-0.76) to 0.77 (0.71-0.82). The sensitivity of all eight signatures declined with increasing disease-free time interval. Using a threshold derived from two standard deviations above the mean of uninfected controls, giving specificities of >90%, the eight signatures achieved sensitivities of 24.7-39.9% over 24 months, rising to 47.1-81.0% over 3 months. Based on pre-test probability of 2%, the eight signatures achieved positive predictive values from 6.8-9.4% over 24 months, rising to 11.1-14.3% over 3 months. Using biomarker thresholds maximising sensitivity and specificity with equal weighting to both, no signature met the minimum WHO TPP parameters for incipient TB biomarkers over a two-year period.

Conclusions: Multiple transcriptional signatures perform with equivalent diagnostic accuracy for incipient TB. These biomarkers reflect short-term risk of TB and only exceed WHO benchmarks if applied to 3-6 month intervals.

ORAL SWAB ANALYSIS FOR DIAGNOSIS OF ADULT AND PEDIATRIC PULMONARY TUBERCULOSIS

Cangelosi, Gerard, Dr; Nicol, Mark, Dr; Luabeya, Angelique, Dr; Wood, Rachel, Ms; Olsen, Alaina, Ms; Ortega, Corrie, Ms; Zar, Heather, Dr; Hatherill, Mark, Dr

The most common specimen used for diagnosis of pulmonary tuberculosis (TB) is sputum, a viscous material derived from human airways. Collection of sputum is occupationally hazardous and incompatible with active screening. Good-quality specimens are challenging to collect with consistency and difficult to standardize, process, and analyze.

To address these issues we hypothesize that *Mycobacterium tuberculosis* analytes are deposited on the oral epithelium during active TB disease, and can be detected by oral swab analysis (OSA). In OSA the dorsum of the tongue is gently scraped with a sterile disposable swab. The swab head with collected material, consisting of bacterial biofilm and host cells, is ejected into a sample buffer and eluted as a semi-clear, non-viscous suspension suitable for testing by nucleic acid amplification (NAA) targeting *M. tuberculosis* DNA. Tongue swabbing is fast, painless, and does not require accommodations for privacy or aerosol control. Sputum-scarce patients such as children and HIV-positive adults are easily swabbed.

In a blinded study on 209 South African adults (Luabeya et al, 2019), sensitivity of OSA (2 swabs per subject) relative to sputum GeneXpert (1 sputum per subject) was 93%. Specificity was 92%. In a more recent study on 52 Ugandan adults using a higher-capacity swab, sensitivity was 90% relative to sputum GeneXpert Ultra with just 1 swab per subject. Within a cohort of 201 pediatric TB patients in South Africa, OSA detected only 43% of sputum culture-positive subjects, but it also detected 31% of sputum-negative subjects who were clinically diagnosed with TB. Compared to sputum, DNA purification requirements are very simple for tongue swabs, a finding that could facilitate the development of new point-of-care tests. With further development OSA could become a useful adjunct or alternative to sputum testing for diagnosing active TB, both in standard patient care and for active case-finding.

BUCCAL SWAB ANALYSIS FOR THE DIAGNOSIS OF TUBERCULOSIS IN CHILDREN

Mesman, Annelies, Dr; Calderon, Roger, Mr; Mendoza, Milagros, Ms; Pollock, Nira, Dr; Soto, Martin, Mr; Coit, Julia, Ms; Holmberg, Rebecca, Dr; Franke, Molly, Dr

As part of a large pediatric tuberculosis (TB) diagnostic study in Lima, Peru evaluating alternative sample types for the diagnosis of TB in children, we examined the sensitivity and specificity of *Mycobacterium tuberculosis* (*Mtb)* detection in oral swabs. From 2015 to 2018 we enrolled 628 children under 15 years. Children presented to health centers with TB symptoms and were examined per national guidelines, which included X-ray, TST, gastric aspirate/sputum for smear and culture. For research purposes, we collected the following sample types: stool, buccal swabs, urine, plasma, nasopharyngeal swabs.

We collected a single oral swab per child using 1) Omniswabs that were transferred to lysis medium and frozen at -80 °C until processing; or 2) FTA collection cards that were stored at +4 °C. Following DNA extraction (Qiagen), *Mtb* was amplified via IS6110 RT-PCR.

Preliminary results for 256 children show that 88 children (34%) were diagnosed with TB, of whom 24 (27%) had a culture-confirmed diagnosis and seven were also smear-positive. TB was ruled out in 186 children. Omniswabs were collected in 116 children; sensitivity was 60% [95% CI: 18.2%-92.7%] among smear positive cases and 36.4% [95% CI: 12.8-66.4] among all culture-confirmed cases. FTA cards were collected in 140 children; sensitivity was 50% [95% CI: 2.2-98.7] for the smear positive cases and 7.7% [95% CI: 0.4-32.5] among all culture-confirmed cases. Among those with clinically-diagnosed but culture-negative (unconfirmed TB), sensitivity was low: 0% for Omniswabs and 2.4% for FTA cards. Specificity was 100% with both methods. These first results on the use of oral swabs for diagnosing TB in children are promising. Adult oral swab diagnostic studies by our group and others suggest we may increase sensitivity by optimizing collection methods, such as taking tongue swabs or collecting multiple swabs per child.

DIAGNOSTIC ACCURACY OF RAPID URINE FUJIFILM SILVAMP TB LAM TESTING TO DIAGNOSE TUBERCULOSIS AMONG PEOPLE LIVING WITH HIV IN GHANA

Bjerrum, Stephanie, Ms; Broger, Tobias, Mr; Opintan, Japheth, Mr; Mitarai, Satoshi, Mr; Kenu, Ernest, Mr; Shah, Maunank, Mr; Somuncu Johansen, Isik, Ms; Denkinger, Claudia, Ms

Background: To improve tuberculosis case-detection, point-of-care tests are of priority. The novel Fujifilm SILVAMP TB LAM (FujiLAM) assay for rapid detection of mycobacterial lipoarabinomannan (LAM) in urine, has demonstrated superior sensitivity to the Alere Determine TB LAM Ag [AlereLAM] assay among inpatients with HIV, but has not yet been evaluated among outpatients with HIV.

Methods: This study evaluates and compares diagnostic accuracy of FujiLAM and AlereLAM assays for detection of tuberculosis in biobanked urine samples collected as part of the DETECT HIV-TB cohort study of adults with HIV referred for ART initiation in Ghana. Diagnostic accuracy was assessed against a microbiological and a composite reference standard. We further assessed the association of FujiLAM test positivity with mortality.

Results: Urine samples from 532 patients with HIV (462 outpatients and 70 inpatients) were evaluated. Against a microbiological reference standard, the sensitivity of FujiLAM was 74.2% (95%CI 62.0 to 84.2) compared to 53.0% (40.3 to 65.4) for AlereLAM (difference of 21.2% [13.1 to 32.5]). FujiLAM sensitivity among outpatients was 68.1% (52.9 to 80.9) and higher than for AlereLAM 44.7% (30.2 to 59.9; difference 23.4% [13.6 - 37.2]). Specificity was 89.3% (85.8 to 92.2) for FujiLAM *vs* 95.6% (93.0 to 97.4) for AlereLAM (difference –6.3 [-9.6 to -3.3]). Specificity estimates for FujiLAM increased markedly to 98.8% (96.6 - 99.8) in patients with CD4 > 100 cells per μL and when using a composite reference standard. Overall and among tuberculosis cases, FujiLAM test positivity was associated with increased cumulative risk of mortality at two months.

Conclusions: In comparison to AlereLAM, FujiLAM offers significantly increased diagnostic sensitivity. Specificity estimates for FujiLAM were lower than for

	Test	N	True positives	False positives	False negatives	True negatives	Sensitivity (95%CI)	Specificity (95%CI)	Tuberculosis prevalence
All HIV+, Microbiological reference standard	FujiLAM	450	49	41	17	343	74.2% (62.0 - 84.2)	89.3% (85.8 - 92.2)	14.7%
	AlereLAM	450	35	17	31	367	53.0% (40.3 - 65.4)	95.6% (93.0 - 97.4)	14.7%
	△Sn and △Sn*						21.2% (13.1 to 32.5)	-6.3% (-9.6 to -3.3)	
All HIV+, Composite Reference Standard	FujiLAM	450	63	27	35	325	64.3% (54.0 - 73.7)	92.3% (89.0 - 94.9)	21.8%
	AlereLAM	450	43	9	55	343	43.9% (33.9 - 54.3)	97.4% (95.2 - 98.8)	21.8%
	△Sn and △Sn*						20.4% (11.8 to 30.0)	-5.1% (-8.4 to -2.3)	

**Confidence of interval assessed by Tango, the difference considered significant if the value '0' is not included*

Table 1: Primary analyses of sensitivity and specificity and the differences between FujiLAM and AlereLAM

AlereLAM but may have been impacted by low quality of the reference standard that is prone for misclassification of severely sick individuals. FujiLAM has value as predictor of mortality.

HETERORESISTANCE AMONG PATIENTS WITH DRUG-RESISTANT TUBERCULOSIS

Berger, Christopher, Dr; Crowder, Rebecca, Ms; Allender, Christopher, Mr; Ama, Cindy, Dr; Destura, Raul, Dr; Cattamanchi, Adithya, Dr; Engelthaler, Dave, Dr; Kato-Maeda, Midori, Dr

Heteroresistance (presence of both drug-resistant and -susceptible *Mycobacterium tuberculosis* (MTB) subpopulations) is known to impact sensitivity of current phenotypic and genotypic drug susceptibility tests. We evaluated the frequency of heteroresistance in a sample of patients treated for multidrug-resistant (MDR) and pre-/extensively drug-resistant (pre-XDR/XDR) TB in the Philippines (2013-2016).

We extracted DNA from log-phase culture, and performed SMOR (Single Molecule with Overlapping Reads)-based targeted deep sequencing to quantify the proportion of mutant and wild type alleles within 15 regions of the *katG*, *inhA* promoter, *rpoB*, *gyrA*, *rrs*, *eis* promoter, *tlyA*, *gyrB*, and *gidB* genes. Heteroresistance was defined as the presence of both wild type and mutant alleles. At least 5 of 500 reads or 5 of 5000 reads showing mutant alleles was required to identify presence of resistant sub-populations at the level of 1% and 0.1%, respectively.

We included 67 MTB isolates from patients with MDR TB and 137 from patients with pre-XDR/XDR TB (analysis of 496 samples ongoing). SMOR identified a high confidence resistance-conferring mutation in 202/204 (99%) isolates resistant to isoniazid, 200/204 (98%) resistant to rifampin, 58/115 (50%) resistant to streptomycin, 68/103 (66%) resistant to fluoroquinolones (FQ), 34/40 (85%) resistant to kanamycin, 34/35 (97%) resistant to amikacin, and 34/36 (94%) resistant to capreomycin. Heteroresistance was identified in 21/136 (15%) isolates analyzed to 27 drugs, 19/27 (70%) had a resistant sub-population that comprised <1% of the total, and 10/27 (37%) reported as susceptible by culture. Heteroresistance <1% was present in 18% of FQ-resistant isolates. Heteroresistance was more common for second-line drugs (9% vs. 3%, p=0.05) and in patients with preXDR/XDR vs. MDR TB (21% vs. 9%, p=0.06).

Standard molecular tests are inadequate to identify pre-XDR and XDR TB in the Philippines. A large proportion do not have a known mutation conferring FQ resistance, and low-level heteroresistance to FQ was common.

XPERT MTB/RIF MISSES MORE THAN 50% OF RIFAMPICIN RESISTANT TB CASES IN ESWATINI: RESULTS OF THE 2ND NATIONAL ANTI-TB DRUG RESISTANCE SURVEY (2017/2018)

Sikhondze, Welile, Dr; Dlamini, Themba, Mr; Joloba, Moses, Prof; Cirillo, Daniela, Dr; Ershova, Julia, Dr; Tosas, Olga, Ms; Glaziou, Philippe, Dr; Dean, Anna, Dr; Cabibbe, Andrea, Dr

Background: The 2nd national Anti-TB drug resistance survey was undertaken in Eswatini in 2017-2018, integrating the use of whole genome sequencing (WGS). The prevalence estimates and sequencing results are presented.

Methods: This cross-sectional national survey was undertaken from 01 April – 31 December 2017 and included 100% national sampling of all public health facilities and private clinics. All 30 peripheral laboratories were included as enrolment centres for new and previously treated patients newly diagnosed with pulmonary TB based on GeneXpert MTB/RIF. Whole genome sequencing was performed on MTB positive isolates and a statistical ensemble model was developed to combine the group of patients with WGS data and the group without using a Bayesian approach. Data were analyzed using STATA15 and FASTQ.

Results: A total of 1,443 presumptive TB patients were tested by Xpert MTB/RIF and enrolled into the DRS upon diagnosis of *M. tuberculosis*. These 1,443 were cultured using the BACTEC MGIT960 of which 1015 were MTB positive and DNA extracted for sequencing with WGS data available for 72% (734 patients). The new estimates for MDR-TB prevalence is 8.6% (95%CI: 6.7-10.8%) among new cases and 17.5% (95%CI: 11.2-24.9%) among previously treated cases. However, more than half (58%) of these cases harboured the Ile491Phe mutation in the *rpoB* gene which is missed by Xpert MTB/RIF. The Ile491Phe strains showed resistant phenotypes with MIC distribution on microtiter plates above the epidemiological cut-off. While the presence of the Ile491Phe clone was already detected in the previous DRS, ongoing transmission is evident.

Conclusions: Xpert MTB/RIF remains an accurate test for the diagnosis of TB in Eswatini, but cannot be relied upon for detection of rifampicin resistance. Reassuringly, the circulation of this clone remains geographically localised. In multi-country sequencing databases which collectively contain isolates from more than 20,000 patients, less than 0.5% harboured this mutation.

Session: Prevent infection or prevent disease?

THREE-YEAR EFFICACY OF M72/AS01E VACCINE IN AFRICAN ADULTS WITH LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION

Tait, Dereck R., Dr; Hatherill, Mark, Prof; Van Der Meeren, Olivier, Dr; Ginsberg, Ann M., Dr; Van Brakel, Elana, Dr; Salaun, Bruno, Dr; Scriba, Thomas, Prof; Wilkinson, Robert J., Prof

Background: An effective tuberculosis vaccine is urgently needed. The M72/AS01$_E$ candidate vaccine (GSK), consisting of a recombinant fusion protein derived from *Mycobacterium tuberculosis* antigens (Mtb32A and Mtb39A) and the adjuvant AS01$_E$, was investigated.
Methods: This phase 2b, double-blind, placebo-controlled trial (NCT01755598) was conducted in South Africa, Kenya and Zambia to assess M72/AS01$_E$ efficacy against bacteriologically-confirmed pulmonary tuberculosis disease in HIV-seronegative adults aged 18-50 years infected with Mtb (defined by a positive IFN-gamma release assay at baseline). Participants (N=3575) were enrolled and randomized 1:1 to receive two doses of M72/AS01$_E$ or placebo one month apart. Primary analysis of M72/AS01$_E$ efficacy and reactogenicity/safety after at least 2 years of follow-up has been reported (N Engl J Med 2018;379:1621-34). The trial continued, double-blinded, until participants were followed-up for 3 years post-vaccination. We present end-of-trial results.
Results: Demographic characteristics were similar between groups. Efficacy against pulmonary tuberculosis disease bacteriologically-confirmed by polymerase chain reaction and/or culture before treatment (case definition 1) was 50% (90%CI: 12-71; p=0.04). Our final dataset does not support the hypothesis of differential vaccine efficacy by age. Efficacy using other case definitions and in a sensitivity analysis ranged between 30-68%. Throughout the study, 47 participants died: 19 in M72/AS01$_E$ group and 28 in placebo group, of which 28 (13 and 15, respectively) were due to trauma. None of the deaths were considered by investigators related to study participation.
Conclusion: The final analysis shows that efficacy of M72/AS01$_E$ against bacteriologically-confirmed pulmonary tuberculosis persists until 3 years post-vaccination in HIV-seronegative adults with latent Mtb infection, and that the vaccine has an acceptable safety/tolerability profile.
Funding: GlaxoSmithKline Biologicals SA (study sponsor) and Aeras/IAVI

IMMUNOGENICITY OF M72/AS01E VACCINE IN AFRICAN ADULTS WITH LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION

Van Der Meeren, Olivier, Dr; Tait, Dereck R., Dr; Hatherill, Mark, Prof; Ginsberg, Ann M., Dr; Van Brakel, Elana, Dr; Salaun, Bruno, Dr; Scriba, Thomas, Prof; Wilkinson, Robert J., Prof

Background: An effective tuberculosis vaccine is urgently needed. The M72/AS01$_E$ candidate vaccine (GSK) is an AS01$_E$-adjuvanted recombinant fusion protein derived from *Mycobacterium tuberculosis* (Mtb) antigens Mtb32A and Mtb39A.
Methods: We conducted a phase 2b, double-blind, placebo-controlled trial (NCT01755598) in Southern and Eastern Africa to assess M72/AS01$_E$ efficacy against bacteriologically-confirmed pulmonary tuberculosis disease in HIV-seronegative adults aged 18-50 years infected with Mtb. Participants were randomized 1:1 to receive two doses of M72/AS01$_E$ or placebo one month apart. Immunogenicity was assessed in a subgroup in South Africa (N=150) and Kenya (N=150). Serum and whole blood samples were collected on day 0, month (M)2, year (Y)1, Y2 and Y3. Humoral responses (anti-M72 antibodies) were measured by ELISA, and cell-mediated immunity (M72-specific CD4+ and CD8+ T-cells) by intracellular cytokine staining.
Results: M72/AS01$_E$'s efficacy and reactogenicity/safety until at least Y2 post-vaccination have been reported (N Engl J Med 2018;379:1621-34). Y3 efficacy is reported separately. Anti-M72 antibodies peaked at M2 in M72/AS01$_E$ vaccinees (geometric mean antibody concentration [GMC]: 547.0) and then stabilized 1 log lower at the follow-up time-points (GMC ranges: 27.0-41.5), as compared to antibodies below the assay cut-off (2.8 ELISA units/mL) at baseline and at all timepoints in the placebo vaccinees. Polyfunctional CD4+ T-cell responses were induced and maintained until 3 years after vaccination. Polypositive CD4+ T-cells peaked 2 months after M72/AS01$_E$ vaccination in Kenyan participants, while in South African participants primarily M72-specific IFN-gamma-expressing CD4+ T-cells were detected at M2. Polyfunctional responses plateaued above baseline in both countries at Y1, Y2 and Y3. No CD8+ responses could be detected.
Conclusion: M72-specific humoral and CD4+ T-cell responses persisted until 3 years after M72/AS01$_E$ vaccination in HIV-seronegative African adults with latent Mtb infection. An unexpected IFN-gamma-expressing CD4+ T-cell pattern was observed at M2 in South African participants.
Funding: GlaxoSmithKline Biologicals SA (study sponsor) and Aeras/IAVI

PREVENTION OF INFECTION VERSUS PREVENTION OF DISEASE - ESTIMATING THE POTENTIAL IMPACT OF NEW TUBERCULOSIS VACCINES

Harris, Rebecca, Dr; Sumner, Tom, Dr; Knight, Gwen, Dr; Zhang, Hui, Dr; White, Richard, Prof

Background: Thecurrent landscape of efficacy trials for new vaccines includes both infection and disease endpoints. Mathematical modelling can be used to estimate the future impact of new vaccines, across a theoretical range of efficacies and based upon the results of new clinical trials. To inform decision making, we estimated the impact of new TB vaccines in three high-burden countries using mathematical models.

Methods: TB models were calibrated to age-stratified demographic and epidemiological data from China, South Africa and India. Vaccine efficacy to prevent infection and/or disease, effective in persons *M.tb*uninfected and/or infected, andduration of protectionwere varied. Routine early-adolescent vaccination and 10-yearly mass campaigns were introduced from 2025. Median population-level TB incidence rate reduction in 2050 compared to a no-new-vaccine scenario (%IRR) was estimated.

Results: In all settings, results suggest that vaccines preventing disease in *M.tb*-infected populations would have most impact by 2050 (10-year, 70% efficacy against disease, IRR 51%, 51% and 54% in China, South Africa and India, respectively). Vaccines preventing re-infection delivered lower impact (IRR 1%, 6% and 17%). Intermediate impact was predicted for vaccines effective only in uninfected populations, if preventing only infection (IRR 21%, 32% and 50%), or disease (IRR 19%, 26%, 51%), with greater impact in higher transmission settings. Using phase IIB results, and assuming 10 years protection, predicted IRR for BCG revaccination 50% effective for preventing infection in uninfected populations was 16%, 19% and 39% for China, South Africa and India; and for M72/AS01E50% effective for preventing disease in infected populations was 37%, 32% and 41%, respectively.

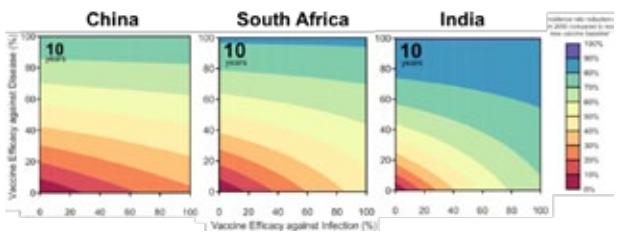


Figure 1. Median incidence rate reduction in 2050 compared to no new vaccine baseline for a pre- and post-infection vaccine with 10 years duration of protection, by percentage vaccine efficacy for prevention of infection (x-axes), and vaccine efficacy for prevention of disease (y-axis).

Conclusions: New TB vaccines could deliver substantial population-level impact. If prioritising impact by 2050, vaccine development should focus on preventing disease in *M.tb*-infected populations. Impact depended upon epidemiological context. Vaccines preventing infection or disease in uninfected populations may be useful in higher transmission settings.

EXPERIMENTAL INVESTIGATION OF A NEW TUBERCULOSIS VACCINE, BASED ON RECOMBINANT AG85, TB10 AND FLIC PROTEINS

Yeremeev, Vladimir, Prof; Shepelkova, Galina, Dr; Duhovlinov, Ilya, Dr; Gergert, Vladislav, Prof; Ergeshov, Atadzhan, Prof

Since 1924, BCG vaccine is used to protect children from the most severe forms of tuberculosis (TB). At the same time, the protective effect of BCG in adults is variable. It is known that intensity of the BCG-induced Th1 immune response decreases over time and comes to naught within 10-15 years.

Data on insufficient ability of BCG to stimulate life-long immunological memory is accumulating. In our investigation we evaluated the protective effects of several new vaccine variants based on Ag85B-TB10.4-FliC chimeric recombinant bacterial protein, and the plasmid DNA encoding Ag85A antigen.

We used an aerosol *M. tuberculosis* H37Rv infection mouse model, and compared lung and spleen CFU counts and life-span of vaccinated versus non-vaccinated C57BL/6 mice. The best vaccine variant was selected to monitor immune response (production of specific antibodies, specific protein stimulated production of IFN-gamma and proliferation in vitro) during 10 months after vaccination.

It was shown that our vaccine induced the formation of long-term immunological memory to a bacterial antigen in mice. Moreover, in the presence of glutoxim the immunological memory spectrum shifted to a “protective” type, i.e. the predominance of the cellular component of the immune response over the antibody response was stimulated.

Also we evaluated the opportunity to increase the anti-TB resistance in experimental animals by re-vaccination with our subunit vaccine preparation following primary immunization with BCG. We demonstrated that additional boost vaccination with the vaccine under study, as compared with conventional BCG vaccination, lead to further inhibition of mycobacteria dissemination from the site of infection, and significantly prolonged survival of infected animals

TRANSCRIPTOMIC RESPONSES TO PREVENTIVE THERAPY FOR LATENT TUBERCULOSIS INFECTION

Broderick, Claire, Dr; Cliff, Jacqueline M, Dr; Lee, JiSook, Dr; Clark, Taane, Prof; Moore, David AJ, Prof

Current tests for latent tuberculosis infection (LTBI) (Tuberculin skin test (TST), Interferon gamma release assay (IGRA)) demonstrate host sensitisation to *Mycobacterium tuberculosis* (*Mtb*). Neither approach demonstrates viability of infection, so they cannot discriminate between those with current viable mycobacterial infection and those who have cleared *Mtb,* in whom these tests reflect immunological memory.

We hypothesized that the differentiation of viable LTBI from immunological sensitisation without viable infection could be achieved by investigating the transcriptomic response to preventive therapy (PT). We hypothesized that IGRA-positive individuals would demonstrate binary transcriptomic responses to effective PT, reflecting the differential immunological consequences of the sterilization of viable mycobacteria in those with persisting infection, versus no *Mtb* killing in those without.

We performed transcriptomic analysis on ex vivo and on QuantiFERON-TB Gold Plus-stimulated whole blood samples from 21 IGRA-positive individuals with known recent exposure to isoniazid- and rifampicin-susceptible pulmonary tuberculosis (TB), at baseline and 2 and 13 weeks after initiating combined rifampicin/isoniazid (RH) PT. Conducting the study in a low TB transmission setting minimised reinfection risk during the study period. Healthy IGRA-negative individuals with no TB-exposure history, who received 2 weeks of RH, were included as controls.

Substantial changes in gene expression, particularly in inflammation-related genes, were observed through PT in nine IGRA-positive individuals in the QuantiFERON-stimulated samples. These changes were absent in the other IGRA-positive individuals and the healthy controls. Little change in ex vivo transcriptomes was observed.

Less than half of IGRA-positive subjects demonstrated an immunological response to RH that was clearly discernible from healthy IGRA-negative controls, supporting our hypothesis. IGRAs identify immunological sensitisation, which has been incorrectly characterised as equivalent to LTBI. This first demonstration of a transcriptomic signature of LTBI clearance challenges concepts of LTBI, questions IGRA/TST-derived estimates of LTBI burden and may accelerate evaluation of novel PT regimens.

INFECTION WITH THE BEIJING GENOTYPE OF MYCOBACTERIUM TUBERCULOSIS AND ITS INTERACTION WITH BCG VACCINE PROTECTION: A CASE CONTACT COHORT STUDY

Verrall, Ayesha, Dr; Chaidir, Lidya, Dr; Ruesen, Carolien, Ms; Apriani, Lika, Dr; Ussher, James, Dr; van Laarhoven, Arjan, Dr; Ruslami, Rovina, Prof; Huynen, Martijn, Prof; Netea, Mihai, Prof; van Ingen, Jakko, Dr; Sharples, Katrina, Dr; van Crevel, Reinout, Prof; Alisjahbana, Bachti, Dr; Hill, Philip, Prof

Background: Strains of the *Mycobacterium tuberculosis* Beijing genotype have spread across the globe. Emergence in parallel with widespread BCG vaccination has led to the suggestion that Beijing genotype could evade BCG-induced host protection. We assessed transmissions of *M. tuberculosis* Beijing and non-Beijing strains and their relationship to BCG vaccination in tuberculosis (TB) case contacts.

Methods: Indonesian household contacts of smear-positive TB cases had an Interferon Gamma Release Assay (IGRA) at enrollment and 14 weeks later. BCG vaccination was assessed by the presence of a scar. Index case lineage and genotype family were determined by whole genome sequencing. Associations between *M. tuberculosis* genotype family and IGRA conversion were assessed using a multilevel model.

Results: 36.1% (433/1201) contacts of 414 culture-positive TB cases were initially IGRA-negative and 24.9% (108/433) of these became infected as indicated by IGRA-conversion. The risk of IGRA conversion was significantly higher for contacts exposed to Beijing genotype versus other strains (adjusted RR=1.39; 95% CI 1.00-1.93; P=0.048). There was a significant interaction (p=0.01) between BCG vaccination and index case isolate genotype with respect to IGRA conversion: BCG showed strong protection against infection from other genotypes (adjusted RR 0.40; 95% CI 0.27-0.61; p<0.001), but no protection against the Beijing genotype (adjusted RR 1.02; 0.56-1.85; p=0.9) (see Table,).

Genotype	BCG vaccination	IGRA negative N=275 N (%)	IGRA positive N=108 N (%)	RR	95% CI	P
Other	No	22 (10.7)	21 (30.4)	1.00	ref	
Other	Yes	184 (89.3)	48 (69.6)	0.40	0.27,0.61	<0.001
Beijing	No	13 (18.8)	7 (17.9)	1.00	ref	
Beijing	Yes	56 (81.2)	32 (82.1)	1.02	0.56,1.85	0.9

Table. Association between BCG vaccination and IGRA at 14 weeks for TB case contacts who were interferon-gamma release assay negative at baseline, according to index case lineage.

Conclusions: In household contacts, Beijing genotype strains of *M. tuberculosis* are more likely to cause infection and, unlike other strains, are not subject to BCG

protection. New vaccines against TB need to be assessed in Asian populations where the Beijing genotype family is prevalent. Understanding how this the Beijing genotype evades BCG mediated protection may advance fundamental understanding of immunity to *M. tuberculosis*.

Session: New strategies in TB therapeutics: It's time to break the mould!

EXPERIENCE USING NEW AND REPURPOSED RIFAMPICIN-RESISTANT TB DRUGS IN FIVE PREGNANT PATIENTS

Acquah, Rebecca, Dr; Mohr-Holland, Erika, Ms; Furin, Jennifer, Dr; Hughes, Jennifer, Dr; Loveday, Marian, Dr; De Azevedo, Virginia, Dr; Mudaly, Vanessa, Dr; Reuter, Anja, Dr

Background: Tuberculosis (TB) is the leading cause of maternal mortality worldwide, and rifampicin resistant TB (RR-TB) in pregnancy is a neglected health problem. Pregnant women are excluded from clinical trials; consequentially the evidence for the use of new and repurposed RR-TB drugs in pregnancy is scarce. We aim to describe our experience of using delamanid, linezolid, and/or bedaquiline in pregnant women with RR-TB.
Design/Methods: Persons diagnosed with RR-TB and exposed to either delamanid, linezolid, and/or bedaquiline during pregnancy from January 2014 to March 2019 in Khayelitsha, South Africa were included in this retrospective file review. We report on drug exposure, pregnancy outcomes, serious adverse events (SAEs), and interim treatment outcomes.
Results: Five patients aged 18-29 years were identified (Table 1). All five had confirmed multi-drug resistant tuberculosis with no second line drug resistance and received a new drug either to substitute for an injectable agent, or to make an effective regimen with at least four effective drugs. The mean drug exposure during pregnancy was 79(range 7-163) days. There were no reported SAEs during the pregnancy or post-partum period (until discharged from TB care or the end of the study period).

Patient	1	2	3	4	5
HIV status [CD4 at beginning of TB treatment (cells/uL)]	Positive, initiated ART two weeks after diagnosis [84]	Negative	Positive, on ART at time of diagnosis [82]	Positive, on ART at time of diagnosis [94]	Negative
Drug Exposure	Delamanid (100mg BD) Bedaquiline (400mg OD then 200mg 3x week)	Linezolid (600mg OD)	Linezolid (300mg OD)	Bedaquiline (400mg OD then 200md 3xweek) Linezolid (600mg OD)	Delamanid (100mg BD) Linezolid (600mg OD) Bedaquiline (400mg OD then 200mg 3x week)
Outcome of Baby	Alive and well aged 13 months, not breastfed	Live term delivery	Live term delivery	Alive and well aged 9 weeks, breastfed	Live term delivery, breastfed
Interim RR-TB treatment Outcome of Mother	Well, month 17 of treatment	Lost from treatment (18 months), culture converted day 52	Cured	Well, month 3 of treatment	Cured

Table 1. Characteristics of pregnant mothers treated with new and repurposed RR-TB drugs as well as pregnancy outcomes for both the mother and child.

Conclusions: There is limited experience with most second-line drugs in pregnancy, with some drugs being contraindicated and others possibly unsafe based on animal studies. While more evidence would be reassuring, the experience in this small group supports improving access to new and repurposed drugs for pregnant women with RR-TB. The inclusion of pregnant women in clinical trials, as well as pregnancy drug registries is vital to ensure evidenced based safe and effective treatment options are available for mothers with RR-TB.

TRIAL OF DELPAZOLID (LCB01-0371) TO ASSESS EARLY BACTERICIDAL ACTIVITY AND EXPOSURE RESPONSE RELATIONSHIPS

Geiter, Lawrence, Dr; Shim, Tae-Sun, Prof; Alsultan, Abdullah, Prof; Shen, Xianlin, Dr; Cho, Insook, Ms; Cho, YL, Dr

Delpazolid (DZD) is a candidate oxazolidinone that may provide efficacy without the toxicity of other oxazolidinone compounds. An early bactericidal activity trial was conducted in Korea to assess the activity of DZD in TB patients. They were randomized to receive DZD 400 mg BID, 800 mg QD, 800 mg BID, HRZE or linezolid 600 mg BID for 14 days. A sixth group (DZD 1200 mg QD) was added later in the trial to further explore dosing options. Sputum was collected at baseline and 7 times during treatment for colony-forming unit counts (CFU). Blood was drawn periodically for pharmacokinetic (PK) analysis.

Interim analyses show an average daily decline in log-cfu of about 0.05, 0.03, 0.05 and 0.01 for the 400 mg BID, 800 mg QD, 800 mg BID and 1200 mg QD dosages respectively. When data collection is complete, more formal statistical analyses will be conducted to describe and adjust for various sources of variability.

Interim PK analyses was undertaken for 50 delpazolid patients (400 mg BID (n=10), 600 mg BID (n=7), 1200 mg QD (n=5), 800 mg BID (n=14), 800 mg QD (n=14)). The PK model was best described using a one compartment system with linear elimination. PK parameter estimates were Cl of 29.5 L/hr, V = 77 L and ka = 0,3 hr-1. Delpazolid has a rapid and highly variable elimination. EBA study data will be combined with PK data from the single-ascending dose, 14- and 28- day multiple ascending dose trials will be combined for a Population PK model and EBA data will also be combined for a PK/PD model.

DZD may provide a less toxic oxazolidinone treatment for TB. Analyses will allow for the estimation of key parameters to guide dose selection and enable the design of Phase 2/3 trials of regimens containing DZD

FUTURE PREVENTIVE THERAPY REGIMENS AGAINST TUBERCULOSIS: EXAMINING PERFORMANCE REQUIREMENTS IN DIFFERENT SETTINGS

Vesga, Juan, Dr; Arinaminpathy, Nimalan, Dr

Background: Treating Latent Tuberculosis Infection is an essential component of the future response to the global TB epidemic. As a result of recent and ongoing research, preventive therapy has developed from a six-month, daily regimen to a three-month, once-weekly regimen with equal efficacy. Future regimens may be still shortened, potentially with further improvements in efficacy. Here, we use dynamical transmission modelling to examine the desired performance characteristics of such future regimens.

Methods: In consultation with experts, we identified four key characteristics for assessing future regimens: (i) Duration of protection from reactivation or reinfection, (ii) Whether the regimen sterilises infection or not, (iii) Potential for inducing multi-drug-resistance, (iv) Forgiveness to non-adherence. We examined the relative importance of each of these factors, in four different epidemiological scenarios: conditions consistent with the TB epidemics in South-Africa, Kenya, Brazil and India. For each setting, we designed a mathematical model of TB transmission incorporating drug resistance and HIV status, as well as a detailed structure for the effect of preventive therapy (PT).

In each setting, regimen characteristics were sampled as random variables. The relative importance of each characteristic was summarized with partial rank correlation coefficients (PRCC) between each variable and model impact, in this case, TB cases averted.

Results: In countries with the highest TB burden (Kenya, South Africa and India), the impact was most strongly correlated with duration of protection (PRCC >0.65; p <0.001). In settings like Brazil, forgiveness to non-adherence (PRCC >0.68; p <0.001) and potential for resistance induction (PRCC < -0.58; p <0.001) become more relevant.

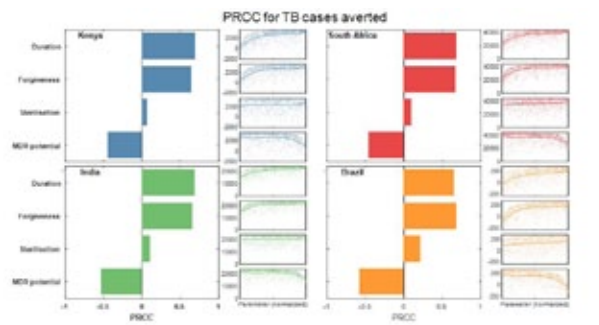


Figure 1: Partial Rank Correlation Coefficient (PRCC) of regimen characteristics vs TB cases averted: Panels show PRCCs (bars) and parameter values vs. TB cases averted (scatter plots), for the four selected countries (colour coded). PRCCs are derived from extensive parameter exploration via Latin Hypercube Sampling. Positive correlations between PT components and outcome (TB cases averted) take values from 0 to 1, with 1 reflecting a very strong positive relation, and -1 very strong negative relation. Solid lines in the scatter plots reflect the trend line obtained from polynomial regression.

Conclusions: In future, successful TB prevention may call for regimens tailored to specific settings. The duration and regimen forgiveness emerge as key factors

in high-transmission settings. Factors such as MDR potential may be more important in intermediate-burden settings while the role of sterilisation appears less important overall.

SANFETRINEM, REPURPOSING AN ORAL BETA-LACTAM WITH INTRACELLULAR ACTIVITY FOR THE TREATMENT OF TUBERCULOSIS

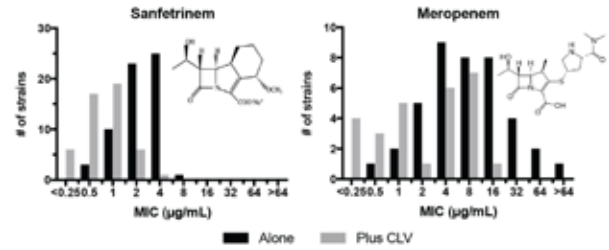
Ramon-Garcia, Santiago, Dr; Bates, Robert, Dr; González del Río, Rubén, Mr; Gamallo, Pablo, Dr; Mendoza-Losana, Alfonso, Dr; Ferrer-Bazaga, Santiago, Dr; Thompson, Charles, Prof; Barros, David, Dr

New strategies in TB therapeutics are urgently needed to cure all forms of the disease; however, developing new antimicrobials is costly and lengthy. Drug repurposing represents a rapid approach to generate new TB treatments.

Beta-lactams have an exceptional record of clinical safety. Used for decades to treat bacterial infections, they were regarded as ineffective against *Mycobacterium tuberculosis*; however, the clinical efficacy of meropenem was recently shown [PMID:27433841]. While promising, meropenem can only be administered intravenously, not practical against a disease for which oral drugs are needed.

Here, we described the discovery of the oral beta-lactam sanfetrinem cilexetil, a first-in-class tricyclic carbapenem. Sanfetrinem was identified in a screen of ca. 2,000 beta-lactams as the most active against intracellular *M. tuberculosis* H37Rv (MIC_{THP1}= 0.5 μg/mL), along with potent activity in 7H9 broth (MIC_{7H9}= 1.5 μg/mL). Time-kill assays and confocal time-lapse microscopy confirmed its intracellular and rapid bactericidal activity. To assess its potential for global implementation, sanfetrinem was tested against a panel of *M. tuberculosis* strains, including drug-susceptible and MDR/XDR clinical isolates from different geographical origins: it was more active and with a narrow spectrum of activity (MIC_{90}= 1-4 μg/mL) than the clinically active meropenem (MIC_{90}= 2-64 μg/mL), with these activities enhanced in the presence of clavulanate, although to a lesser extent in the case of sanfetrinem. Finally, mouse studies confirmed the equipotency of sanfetrinem cilexetil (oral prodrug) compared to a combination of subcutaneous meropenem and oral amoxicillin/clavulanate.

Sanfetrinem cilexetil was developed by GlaxoSmith-Kline in the 1990s and underwent phase 2 clinical trials for upper respiratory infections. Its development was stopped prior to Phase 3 primarily based on commercial considerations. Our results show that it could represent an ideal oral beta-lactam with the ability to progress rapidly into clinical implementation. A Phase 2a clinical study is planned for 2021.



Antimicrobial activity of sanfetrinem and meropenem against *M. tuberculosis*. A panel of *M. tuberculosis* drug-susceptible, MDR/XDR clinical isolates, and laboratory strains was tested alone and in the presence of clavulanic acid. Sanfetrinem (62/49) and meropenem (40/27), respectively. Chemical structures of sanfetrinem cilexetil and meropenem are depicted.

PRELIMINARY COMPARATIVE MICROBIOME ANALYSIS OF PULMONARY TUBERCULOSIS PATIENTS: METATRANSCRIPTOMICS APPROACH

Shaikh, Ambreen, Dr; Sriraman, Kalpana, Dr; Jadeja, Niti B., Dr; Oswal, Vikas, Dr; Mistry, Nerges, Dr

Background: Tuberculosis infection causes the dysbiosis of the airway microbiome leading to immune response imbalances. Furthermore, the anti-tuberculosis treatment itself may also alter the microbiome. This cross-talk between microbiome, drugs and immune responses can have an effect on disease progression and outcome. Metatranscriptomic analysis has the potential to uncover the role of a dysbiotic microbiome in tuberculosis infection. Here we describe the metatranscriptomic profiles of microbiome collected from the mask samples of pulmonary tuberculosis patients.

Methods: Microbiota released by two pulmonary tuberculosis patients (one drug sensitive: DS and one drug resistant: DR) on coughing were collected on a membrane attached to a N95 mask pre- and post-three days of anti-tuberculosis treatment. Extracted RNA was analysed using Illumina HiSeq transcriptome sequencing and MG-RAST[1] tool.

Results: The major bacterial phyla present in the patient samples were Actinobacteria, Proteobacteria followed by Firmicutes and Bacteroidetes. The five most abundant genera identified in the samples were *Propionibacterium* (28%), *Corynebacterium* (16%), *Pseudomonas* (9%), *Mycobacterium* (7%) and *Acinetobacter* (5%). Post treatment, there was a 2.2-fold decrease in abundance of Actinobacteria and a marked decrease in *Mycobacterium* and *Corynebacterium*. Functional annotations of the microbiome revealed the abundance of antibiotic resistance and toxins gene category. Most transcribed genes in this category were cobalt-zinc-cadmium resistance (23%), multidrug resistance efflux pumps (17%), resistance to fluoroquinolones (9%) and *BlaR1* (Beta lactamase regulatory protein) family disambiguation (8%). Within the genus *Mycobacterium*, a high expression for *BlaR1* family (40%) was observed. Additionally, the DR metatranscriptome showed resistance to fluoroquinolones (6%).

Conclusions: Results give for the first time, an impression of microbiome of pulmonary tuberculosis patients with additional insights into microbial gene expression and effect of anti-tuberculosis treatment. Microbial diversity dynamics may have an implication in promotion of drug resistance and development of comorbidities.

Reference:

1.Meyer et al. 2008 BMC Bioinformatics. 19;9:386

TB KNOWLEDGEBASE: INTERACTIVE APPLICATION FOR EXTRACTING KNOWLEDGE FROM THE TB LITERATURE TO INFORM TB DRUG AND VACCINE DEVELOPMENT

Azer, Karim, Dr; Michelini, Samanta, Dr; Giampiccolo, Stefano, Dr; Parolo, Silvia, Dr; Leonardelli, Lorena, Dr; Lombardo, Rosario, Dr; Kaddi, Chanchala, Dr

Background: The extensive and ever-growing body of TB literature challenges researchers to process new and inter-disciplinary knowledge to accelerate their work. As a resource for the scientific and clinical community, we present the TB Knowledgebase, an interactive web-based application that aggregates, organizes, and analyzes publicly available literature and clinical trial documentation. It employs text mining to derive associative and causal relationships among host-, bacteria-, and intervention-related terms. This tool provides a more efficient and effective way to explore the TB literature and to identify knowledge, data, and models that can inform and guide model informed drug and vaccine development.

Methods: Tuberculosis-related documents within the PubMed and ClinicalTrials.gov databases were mined to derive co-mention and relational networks [1] among terms describing TB pathophysiology, bacterial genes and proteins, host immune response, antibiotics, and vaccines. Networks were integrated with transcriptional profiles of *M. tuberculosis* [2] and previously developed systems biology networks [3, 4]. To further contextualize the results, pathway databases, public preclinical and clinical data, and mathematical models linked in the tool. An R Shiny web-application was developed to provide a user-friendly interface.

Results: Currently, the TB Knowledgebase includes more than 37,000 publications and 360 clinical trials, and integrates text mining-derived relationships with other data. Figure 1 illustrates an example use-case visualizing genes associated with bacterial response to each drug in the standard regimen (HRZE), providing insight into common and distinct mechanistic targets.

Conclusions: We present a user-friendly integrative tool to assist the TB scientific and clinical community in harnessing knowledge from the literature. It is a resource to inform many aspects of drug and vaccine development, including study design

References:

[1] Michelini et al. (2018). Microbiome, 6(1), 171.
[2] Boshoff et al. (2004). Journal of Biological Chemistry, 279(38), 40174-40184.
[3] Galagan et al. (2013). Nature, 499(7457), 17
[4] MycoPrInt: http://crdd.osdd.net/raghava/mycoprint/

Figure 1: **HRZE integrated network.** M. tuberculosis genes associated in the literature (green circles) with response to isoniazid (H, right blue triangle), ethambutol (E, left blue triangle), rifampin (R, red triangle), and pyrazinamide (Z, yellow triangle) are shown together with gene interactions derived from a transcriptional regulatory network (light blue circles) and significantly differentially expressed genes (green squares).

Session: Bacterial evolution

CHARACTERIZATION OF LIPID-DEPENDENT 'CULTURE-NEGATIVE' TUBERCULOSIS

Mesman, Annelies, Dr; Baek, Seung-Hun, Dr; Huang, Chuan-Chin, Dr; Kim, Youngmi, Dr; Lee, Eunhee, Dr; Calderon, Roger, Mr; Murray, Megan, Prof

Estimated twenty% of patients diagnosed with TB disease have sputum samples that are culture-negative on routine glycerol-rich media. *Mycobacterium tuberculosis* (*Mtb*) can use multiple carbon sources and the availability of these fuels has been shown to affect growth and phenotypic drug resistance. We identified clinical samples that did not grow in Lowenstein-Jensen (LJ) and assessed their growth in lipid-rich media.

We obtained sputum samples from TB patients in Lima, Peru before and during treatment. These samples underwent routine smear microscopy, culture (LJ), and phenotypic drug sensitivity testing and a decontaminated aliquot was stored at -80°C. We selected samples that were smear AFB+++ but culture-negative. Of these, 10/15 samples grew in lipid-rich/glycerol-poor media (containing medium and long chain fatty acids and mono-, di-, triacylglycerides extracted from BSA, Tween80 and coconut oil). Nine of ten lipid grown strains could be re-cultured in glycerol-rich 7H9 following transfer from the lipid media.

We next sought to determine whether these lipid-grown strains were drug-resistant. When we measured MICs in lipid-media, all strains had high-level resistance to isoniazid (INH, >64ug/ml), ethambutol (EMB, >16ug/ml) and streptomycin (>8-32ug/ml); resistance to INH and EMB persisted when the strains were recultured in glycerol-rich media. Whole genome sequencing detected DR-mutations in in 6/10 strains, but four strains carried no known INH mutations, and seven no known EMB mutations.

Three of the lipid-grown samples were follow-up specimens from patients who were culture-positive before treatment initiation. A comparison of whole genome sequences in the (glycerol-grown) baseline and (lipid-grown) follow-up strains demonstrated mutations in genes involved in membrane transport and lipid metabolism, including in Rv1410c (a gene associated with sensitivity to the LJ component, malachite green) and in glpK, a gene essential for glycerol utilization.

Our data suggest an association between a smear-positive, culture-negative phenotype and drug resistance, which may hamper timely diagnosis.

A FRAMESHIFT MUTATION IN GLPK GENE AND THE DRUG-RESISTANT PHENOTYPE OF MYCOBACTERIUM TUBERCULOSIS

Huang, Chuan-Chin, Dr; Contreras, Carmen, Mr;

Background: Drug-resistant (DR) tuberculosis remains an emerging challenge for global tuberculosis control. Understanding acquired resistance mechanisms may improve the clinical management of DR tuberculosis. We previously reported that frameshift mutations in homopolymeric sequences of the glpK gene are common in clinical isolates and are often associated with drug resistance. In this study, we examined whether glpK mutations are associated with the level of drug-resistance.

Method: We selected 1,031 clinical TB culture isolates from a strain archive in Lima, Peru and measured minimum inhibitory concentrations (MICs) testing for 12 anti-tuberculosis drugs. The strains were then sequenced (Illumina HighSeq) and variants were called to identify the frameshift mutations in the glpK gene. For drug-resistant isolates, we examined the association between the appearance of the the frameshift mutation and quantitative drug resistance.

Result: Among 946 strains which had both MIC and high quality sequence results available, 150 (16%) had a frameshift mutation in the homopolymeric sequence of the glpK gene. In isolates with the mutation, 99% (149 isolates) were multidrug-resistant, compared to 72% of those without the mutation. Isolates with the glpK frameshift mutation were more likely to have high-level resistance to Isoniazid (MIC > 5 mg/L; p=0.003), Rifampin (MIC > 50 mg/L; p=0.003), and Streptomycin (MIC > 100 mg/L; p=0.02) than those without the mutation.

Discussion: The frameshift mutations in glpK is associated with high level resistance to Isoniazid and Rifampin, and Streptomycin. One explanation for this observation is that under the pressure of the drugs, this mutation may provide an intermediate stage for Mtb survival before the occurrence of causal mutation against tuberculosis drugs, which usually result in a high-level DR phenotypes.

A NOVEL BLOOD-BASED TRIAGE TEST, IIMMIPRINT®-TUBERCULOSIS, TO RULE OUT ACTIVE TB: A PROSPECTIVE MULTICENTRE STUDY

Trajman, Anete, Prof; Cordeiro-Santos, Marcelo, Prof; Brito de Souza, Alexandra, Ms; Esmail, Aliasgar, Dr; Lipman, Marc, Prof; Santin, Miguel, Dr; Noguera-Julian, Antoni, Dr; Dheda, Keertan, Prof

Introduction: WHO and FIND have identified target product profiles (TPPs) for TB triage/rule-out tests, which ideally should be a point-of-care (POC) non-sputum-based test with at least 90% sensitivity and 70% specificity. ImmiPrint®-TB (ProteinLogic, Cambridge,

UK) is a blood-based rapid immunoassay utilising a TB panel with 5 biomarkers. It is a <2 hour POC assay using a table top immunosensor device.

Methods: We prospectively evaluated the accuracy and negative predictive value (NPV) of ImmiPrint®-TB in 635 participants >15 years old with suspected pulmonary TB in South Africa and Brazil. Pulmonary TB was confirmed by Xpert® and/or culture positivity in sputum (n=289).

Non-TB patients (n=346) had active TB excluded or another confirmed alternative diagnosis. ImmiPrint®-TB results were analysed according to HIV and smear status. To specifically interrogate false-positive rates, we evaluated ImmiPrint®-TB in an additional healthy control group from Brazil comprising close asymptomatic contacts of TB index-cases with normal chest X-rays (n=208), and healthy volunteers with no known history of TB exposure (n=50). Controls were also tested using Quantiferon® plus assay.

Results: In those with suspected TB, the sensitivity, specificity and NPV (95% CI) were 0.91 (0.87-0.94), 0.68 (0.63-0.73) and 0.90 (0.86-0.93), respectively. Among 104 persons living with HIV and 119 smear-negative participants with confirmed TB, sensitivity was 0.96 (0.90-0.99) and 0.84 (0.76-0.90), respectively. In the control group, ImmiPrint®-TB positivity was 24.5% (51/208) among contacts and 26.0% (13/50) among healthy volunteers (similar in Quantiferon® plus-positive and Quantiferon® plus-negative persons [22/70 (31.4%) versus 42/188 (22.3%); p=0.14]).

Conclusion: These preliminary findings suggest that ImmiPrint®-TB, a POC triage test with high NPV, is a promising community-based test for ruling out active TB, including in persons living with HIV and those who are smear-negative.

Next steps: Evaluation of ImmiPrint®-TB in larger cohorts in different community-based settings, including in those with extrapulmonary TB, presumed latent TB infection, and in children.

INFERRING TRANSMISSION FROM M. TUBERCULOSIS GENOMES: IDENTIFYING NEW APPROACHES TO IMPROVE ACCURACY AND ROBUSTNESS

Walter, Katharine, Dr; Colijn, Caroline, Dr; Cohen, Ted, Dr; Mathema, Barun, Dr; Croda, Julio, Dr; Andrews, Jason, Dr

M. tuberculosis genomic variation is frequently used to infer transmission patterns; however, approaches to measuring this variation differ substantially. While "distance thresholds" of 5 or 12 SNPs are commonly used to identify potential transmission linkages, whether different pipelines consistently assign these linkages is unclear. We investigated differences between genomic variant identification approaches and characteristics of approaches that maximize accuracy and reproducibility.

First, we collected and compared variant calls from four independent genomic epidemiology groups, using their published methods, for the same published Illumina sequence data from a clonal outbreak of 85 isolates. Second, we simulated a tuberculosis outbreak and generated sequence data *in silico*. We applied several common variant calling pipelines to simulated data and measured pipelines' performance in recovering true outbreak variation.

Finally, we investigated how variant filtering effects accuracy of phylogenetic inference using the Robinson-Foulds distance comparing reconstructed phylogenies to true phylogeny.

Variant calling pipelines from four different groups identified substantially different sets of variants in the same sequence data. Mean pairwise differences range from 3 to 52 SNPs; applying a 12 SNP threshold to variants identified by the four pipelines would lead to predictions that 0%, 8%, 97%, and 100% of isolates were epidemiologically clustered. In simulated outbreaks, pipelines incorporating neural networks or Gaussian error models enabled greater than 90% precision and recall. Phylogenetic reconstructions were sensitive to variant filters. While limited filtering improved reconstruction of the true outbreak phylogeny, increasingly stringent filters—as commonly employed—resulted in trees increasingly distant from the true tree.

We find that transmission inferences made in *M. tuberculosis* genomic epidemiology studies are strongly affected by variant calling approach, and performance varies widely. Strict variant filtering results in information loss that undermines phylogenetic reconstruction. Neural networks or statistical error models, rather than hard filters, result in greater accuracy.

GENETIC VARIATIONS OF MYCOBACTERIUM TUBERCULOSIS THAT ARE ASSOCIATED WITH TUBERCULOSIS TRANSMISSION

Huang, Chuan-Chin, Dr; Becerra, Mercedes, Prof; Lecca, Leonid, Dr; Calderon, Roger, Dr; Contreras, Carmen, Mr; Yataco, Rosa, Ms; Galea, Jerome, Dr; Zhang, Zibiao, Mr; Murray, Megan, Prof

Background: Human behavior, host immune responses, environmental factors, and Mycobacterium tuberculosis (MTB) genetic factors are the four determinants of tuberculosis transmission. Few studies have focused on the contribution of genetic variation of MTB on disease transmission. We use a cohort study to identify the shared genetic variations among TB patients that result in increased transmissions.

Methods: Between 2009 and 2012, we conducted a cohort study in Lima, Peru. We enrolled 4,500 index tuberculosis patients and their 14,044 household contacts (HHCs), measuring for the TB infection and incident secondary TB of the HHCs over a one-year follow-up.

Paired-end whole genome sequencing using the Illumina HiSeq 4000 platform was performed on the culture-positive isolates of the index tuberculosis and the incident HHCs. We first performed a genome-wide association study to identify the genetic variations associated with increased infectiousness, defined by the proportion of TB infection among <15 year old contacts at the end of follow-up. We repeated the same analyses to identify the shared genetic determinants of those index cases where at least one HHC developed TB disease at the end of follow-up.

Results: We identified index cases with variants in five genes resulted in increased transmissibility: PE_PGRS55, PE_PGRS47, PE_PGRS25, ilvB1, and ilvX. Index cases with at least one secondary case were more likely to have variants in four genes: PE_PGRS55, Rv1976c, ilvB1, and, ilvG.

Discussion: In mice model, previous studies showed that ilvB1 or PE_PGRS47 modified the virulence. The functional enrichment analyses suggest that ilvB1, ilvX, and ilvG genes are essential for acetohydroxyacid synthase or thiamine pyrophosphate binding. The detailed function of most PE_PGRS subfamily remains unclear but has been linked to both innate and immune responses after infection.

DISTINCT INTERACTIONS OF HIGH AND LOW TRANSMISSION STRAINS OF MYCOBACTERIUM TUBERCULOSIS WITH HOST ALVEOLAR MACROPHAGES SHAPES THEIR TRANSMISSION PHENOTYPE

Salgame, Padmini, Dr; Lovey, Arianne, Ms; Rodrigues, Rodrigo R., Dr; Palaci, Moises, Dr; Alland, David, Dr; Dietze, Reynaldo, Dr; Ellner, Jerrold J., Dr

Despite advances in the development of new diagnostics, vaccine candidates and drugs, tuberculosis (TB) continues to endanger global health. A major gap in knowledge is an incomplete understanding of the transmission dynamics of *Mycobacterium tuberculosis* (Mtb).

In a study of household contacts (HHC) of infectious TB cases conducted by us in Brazil, "index" cases were categorized into High (HT) and Low (LT) transmission groups based on the proportion of household contacts with a positive tuberculin skin test. Using C3HeB/FeJ mice that present with lung pathology more typical of human TB disease, we found that HT and LT strains induced distinct growth pattern and pathological disease that fit their transmission phenotype. Mice infected with LT strains exhibited significantly higher bacterial burden compared to HT strains and developed diffused inflammatory lung pathology.

In stark contrast, a significant number of mice infected with HT strains developed caseating granulomas, a lesion type with high potential to cavitate. Mechanistically, distinct interactions with alveolar macrophages and lipid droplet accumulation were found to lead to the differential trajectory in intracellular growth pattern and lung pathology.

Ongoing studies are aimed at identifying bacterial factors regulating the early distinct innate responses to develop drug targets for transmission inhibition.

TBSCIENCE2019 POSTERS:

Poster Theme: New diagnostics to reach the missing millions

APPLYING MULTI-MODALITY ARTIFICIAL INTELLIGENCE FOR SCREENING OF TUBERCULOSIS IN A TB HIGH-BURDEN LARGE RURAL REGION IN CHINA

Lure, Fleming, Dr; Jaeger, Stefan, Dr;
Cheng, Gungxun, Dr; Li, Hongjun, Dr; Lu, Pu-xuan, Dr;
Yu, Weiye, Dr; Kung, Justin, Dr; Guan, Yubao, Dr

Background: A significant shortage of physicians who can interpret radiological and pathological images from digital radiography and sputum smear in TB high-burden rural areas of China prevents the early diagnosis of TB. We deployed Multi-modality AI (MMAI) in a high-burden large rural province affected by TB, Qinhai, to assist physicians in detecting TB in radiological and pathological images. Our study investigates the efficacy of MMAI to assist physicians in detecting TB at multiple hospitals located in Qinhai.
Design / Methods: We installed a MMAI system in a central TB hospital to automatically screen for TB in radiological (DR) and pathological images received from more than 60 hospitals via secured internet connection. MMAI system classified each DR image into high-risk, low-risk, and no-TB and automatically generated heatmaps identifying abnormality. Junior physicians (~12.5 years-of-experience) reviewed these cases with MMAI support. Senior physicians (>25 years-of-experience) then reviewed results from junior physicians and MMAI to generate the final diagnosis. Finally, a Multi-Reader-Multi-Center study compared diagnoses from MMAI, junior physicians, and senior physicians from multiple hospitals to determine the effectiveness of MMAI.
Results: Within 5 months, MMAI system processed 81,836 radiographs and classified 66.3%, 6.5%, 15.6% as non-TB, high-risk, and low-risk, respectively, with heatmaps showing abnormal regions in each image. For the high-prevalence group (age>50), MMAI classified 12% and 20% of the cases as high-risk and low-risk, respectively. MMAI and junior physicians agreed 90.3% on confirmed TB and 99.6% on non-TB cases. Compared to historical data, physicians using MMAI increased the sensitivity by 23% with similar specificity.
Conclusion: This is the first reported large-scale clinical application of MMAI for TB screening in China. MMAI's performance is similar to physicians' with 12 years of experience. MMAI assisted physicians in detecting more TB cases in rural areas in a shorter time period without needing more physicians.

MOBILE VAN TB SCREENING SERVICES FOR ACTIVE TB CASE FINDING IN TWO DISTRICTS, BLANTYRE AND NSANJE IN MALAWI

Mkalira, Khwima, Ms; Mpunga, James, Dr;
Mmanga, Madalitso, Mr; Gondwe, Norton, Mr

Background: Malawi is one of the poverty-stricken countries in the world with poor access to health care among vulnerable populations with high TB Prevalence. The National TB Programme with support from global fund introduced Mobile Van TB Diagnostic Units equipped with digital X-ray machine loaded with Computer-Aided Detection for Tuberculosis (CAD4TB) software and a separate laboratory for the Gene Xpert test. (CAD4TB is used as screening tool while Gene Xpert as diagnostic tool). The aim is to provide TB screening services in highly overcrowded urban townships in order to intensify active case finding amongst vulnerable populations.
Objectives: To determine prevalence of TB among clients who used the Mobile van Diagnostic Unit services from March 2018 to May 2019 in Blantyre and Nsanje districts, Malawi.
Methods: A retrospective review of TB screening records to determine the number of individuals presumed to have TB and the number of persons diagnosed with TB.
Results: Screening was performed to 12140 using symptomatic screening and CAD4TB. Among those screened, 3101 (25.54%) were TB presumptives and a total of 243 (7.84%) clients were diagnosed with pulmonary TB. In total, 47 (19.34%) cases had bacteriological evidence of pulmonary TB using Gene X-pert and 196 (80.66%) TB cases were evaluated for pulmonary TB using Xray. Large numbers of presumptives failed to produce or submit sputum for Gene X-pert and were evaluated on radiographic findings only. These results represent a yield of 2002/100,000 population. The overall TB prevalence was 2%, Blantyre had a prevalence of 0.8% 95%CI=0.7-1.1 while Nsanje TB prevalence was 6.9%:95% CI=5.9-8.1. Prevalence rate difference was 6.1% 95% CI= 5.4-6.7%), p=0. 0001.
Conclusion: Summary results have shown that Mobile Van TB Diagnostic Units for active TB case finding have the potential to detect more TB cases among highly populated areas.

ABDOMINAL TUBERCULOSIS AMONG YOUNG ADULT DIABETES MELITUS TYPE II (PANCREAS ULTRASOUND FINDING)

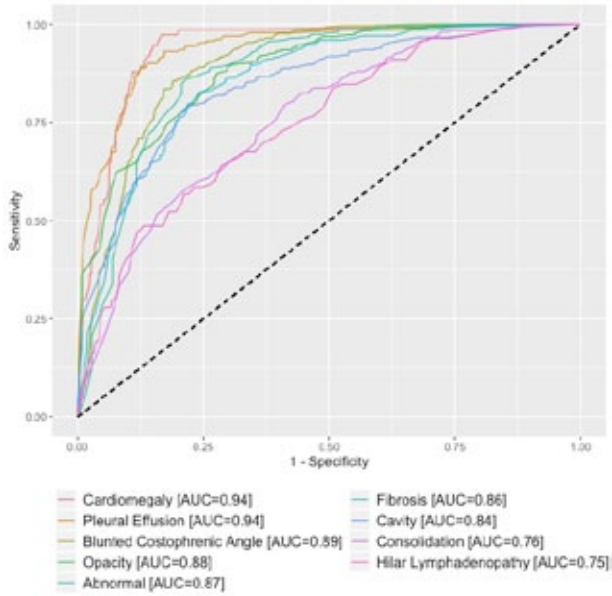
Ametembun, Maria Goretti, Dr

Objective: To describe ultrasound finding of young adult (18-35 years) diabetes melitus type II with lung and abdominal tuberculosis had ever severe epigastric pain and vomiting history suspected acute pancreatitis and complained dyspeptic syndrome for years.
Method: This descriptive study conducted at Stela Maris Hospital and Lukas Hilisimetano Government Hospital South Nias, North Sumatera from April-July 2015. Data were abstracted from medical records of diabetes melitus type II patients who were known as diabetic since 18-35 years old; with abdominal and pulmonary tuberculosis. Clinical diagnosis and ultrasound was examined with b/w ultrasound and convex probe by one certified ultrasound internal medicine specialist
Results: N=26 , 17(65,4%) female and 9(34,6%) male, with recurrent epigastric pain history , some with chronic recurrent bouts of epigastric pain radiating to the back, nausea, anorexia, abdominal distension, vomiting, chronic diarrhoea, with/ without underweight. All patients with pulmonary TB (positive X ray, negative microscopic smear sputum), peritoneal dry type and small bowel tuberculosis. Amilase and lipase were not available. Pancreas ultrasound finding in all cases were heterogeneous hyperechoic, focal/segmental/diffuse hyperechoic lesion, irregular pancreatic margin with normal or decreased pancreas size, in addition many oval/round nodular structures (patchy hyperechoic non-shadowing with an irregular hypoechoic rim) suggested tuberculoma as granuloma process of tuberculosis.
Conclusion: Ultrasound finding of pancreas among young adult diabetes mellitus type II with abdominal tuberculosis and suspected a chronic tuberculosis process of pancreatitis.

DEEP LEARNING, COMPUTER-AIDED RADIOGRAPHY READING FOR TUBERCULOSIS: A DIAGNOSTIC ACCURACY STUDY FROM A TERTIARY HOSPITAL IN INDIA

Nash, Madlen, Miss; Kadavigere, Rajagopal, Dr; Andrade, Jasbon, Dr; Amrutha Sukumar, Cynthia, Dr; Chawla, Kiran, Dr; Prasad Shenoy, Vishnu, Dr; Pai, Madhukar, Dr; Saravu, Kavitha, Dr

In general, chest radiographs (CXR) have high sensitivity and moderate specificity for active pulmonary tuberculosis (PTB) screening when interpreted by human readers. Computer-aided detection (CAD) programs have been developed to facilitate automated CXR interpretation. We conducted a retrospective case-control study to assess the diagnostic accuracy of a CAD software (*qXR*, Qure.ai, Mumbai, India) for PTB triage in a tertiary hospital in India.
The study base was individuals who presented with respiratory symptoms for which they received a CXR and underwent confirmatory microbiological testing for PTB during January 1st– December 31st, 2017. In total, 317 cases and 612 controls were included in the analysis. The area under the curve (AUC) for *qXR* for the detection of microbiologically-confirmed PTB was 0.81 (95% CI: 0.78, 0.84). Using the threshold that maximized sensitivity and specificity of *qXR* simultaneously, the software achieved a sensitivity and specificity of 71% (95% CI: 66%, 76%) and 80% (95% CI: 77%, 83%), respectively. The sensitivity and specificity of radiologists for the detection of microbiologically-confirmed PTB was 56% (95% CI: 50%, 62%) and 80% (95% CI: 77%, 83%), respectively. For detection of key PTB-related abnormalities 'pleural effusion' and 'cavity', *qXR* achieved an AUC of 0.94 (95% CI: 0.92, 0.96) and 0.84 (95% CI: 0.82, 0.87), respectively. For the other abnormalities, the AUC ranged from 0.75 to 0.94. The controls had a high prevalence of other lung diseases which can cause radiological manifestations similar to PTB (e.g., 26% had pneumonia, 15% had lung malignancy, 9% had bronchiectasis, etc.).



For triage in a high-risk setting, *qXR* demonstrated moderate sensitivity and specificity for the detection of PTB. There is likely a larger role for CAD software at the primary care level in settings where access to radiologists in limited. Larger prospective studies that can better assess heterogeneity in important subgroups are needed.

GENDER AND RR-TB TREATMENT MORTALITY: INCREASED EARLY MORTALITY AMONG WOMEN IN THE SETTING OF UNIVERSAL DRUG SUSCEPTIBILITY TESTING IN KHAYELITSHA, SOUTH AFRICA

Mohr-Holland, Erika, Mrs; Daniels, Johnny, Mr; Reuter, Anja, Dr; De Azevedo, Virginia, Dr; Kock, Yulene, Ms; Cox, Vivian, Dr; Cox, Helen, Dr

Background: Access to universal drug-susceptibility-testing (DST, Xpert MTB/RIF) has been available in South Africa since late 2011 for diagnosis of rifampicin-resistant tuberculosis (RR-TB). While universal DST improves case detection, rapid diagnosis may paradoxically increase mortality by expanding treatment access for individuals who otherwise may have died before diagnosis. We aimed to investigate the impact of universal DST on 6-month mortality during RR-TB treatment.

Methods: A retrospective cohort analysis assessing mortality among patients treated for RR-TB. Mortality data obtained from the national death registry.

Results: 1,580 patients received RR-TB treatment between 2008-2016. 807 (51%) were male, median age 34 years (interquartile range [IQR] 27-41); 1,147 (73%) HIV-positive with median CD4 count 126 cells/mm3 (IQR 49-273), 615 (39%) with no previous TB treatment, and 144 (9%) had fluoroquinolone resistance. Twenty-eight (2%) patients were excluded from the analysis of mortality as 6-month mortality status was unavailable. By 6 months, 183 (12%) had died. While there was no difference in 6-month mortality between 2008-2011 and 2012-2016 (12% in both), the overall mortality among female patients was 15% (112/762) compared to 9% (71/790) among male patients ($p<0.001$).

Mortality among males not previously treated for TB significantly decreased from 2008-2011 to 2012-2016 (12% versus 5%, $p=0.036$) while mortality among females in this group remained high (10% versus 13% respectively, $p=0.44$). Overall, female patients were more likely to have HIV and fluoroquinolone resistant RR-TB ($p<0.05$). After adjustment for year, HIV, resistance classification, and previous TB treatment, females remained with increased mortality at 6 months (adjusted OR 1.7, 95% CI 1.2-2.4).

Conclusions: Access to universal DST has highlighted a gender difference in mortality among those treated for RR-TB, with women experiencing higher early mortality on treatment. These data suggest that men have benefited more by earlier initiation of treatment due to more rapid diagnosis however, further research is needed to better understand.

ANALYZING THE IMPACT OF RAPID DIAGNOSTICS XPERT MTB/RIF IN WESTERN CAPE, SOUTH AFRICA. GAINS OR FINANCIAL BURDEN?

Swartz, Alvera, Miss

Background: Xpert MTB/RIF (GXP) was introduced in Western Cape, South Africa in 2011, in selected sites in one of 6 districts. Province wide coverage was achieved in 2012. Xpert MTB/Rif Ultra was introduced in 2017. This test replaced "smear" as primary diagnostic however the financial increase approxamiately nine-fold.

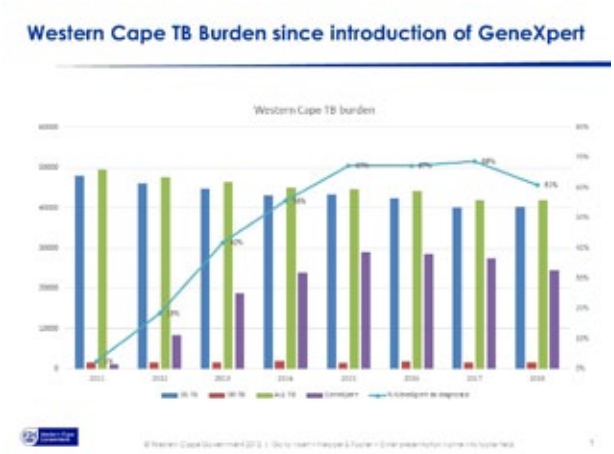
Problem Statement

While the GXP can provide results within 2 hours, the practice around treatment initiation delays remained relatively the same.

Context: GXP is a superior test and provide not only swift results but also susceptability to Rifampicin. The cost of the test should therefore be measured against the challenges faced by outdated laboratory test. As indicated in the inserted diagramme, the benefits of GXP eluded the province. Not only did we not find the numbers of TB cases as predicted, the decrease in time to treatment initiation was marginal. as far as early diagnosis of drug resistant TB, no increase numbers observed. The abstract also aim to reflect the increase in annual laboratory cost. Based on the the high grading of smear result, it is evident that the infection pool is not getting smaller, as predicted. GXP is also prone to false positives as traces of genetic material from a previous TB episode may provide false readings. An analysis of possible false positives who were treated again will also be done.

The poster will pose the following questions: (1) Is GXP finaincially viable? (2) What should changed in health practices to gain maximum benefit? (3) Why are the TB numbers not increasing as per expectations?

Conclusion: GXP and ohter genetic testing is advantageous not only in superior sentivitvity and specificity but also providing rapid drug suceptability results, however it seems not to add much to the management of and change in the epidemic in the Western Cape.



MPT64 DETECTION IN SPUTUM WITH AN ULTRASENSITIVE ENZYME-LINKED IMMUNOSORBENT ASSAY TO EVALUATE THE VIABILITY OF MYCOBACTERIUM TUBERCULOSIS

Sakashita, Kentaro, Dr; Takeuchi, Rikiya, Mr

Background: A culture examination of *Mycobacterium tuberculosis* (Mtb) is for the diagnosis of active pulmonary tuberculosis patients (PTB) and for the follow-up of treatment outcome, however, it takes several weeks to obtain the results. We hypothesized that detecting Mtb specific secreting MPT64 antigen with an ultrasensitive enzyme-linked immunosorbent assay (usELISA) can rapidly evaluate Mtb viability and is useful for the diagnosis and follow-up of PTB.
Objective: To evaluate the capacity of MPT64 usELISA for PTB diagnosis and follow-up as a proof of concept study
Methods: We included 50 PTB and 30 healthy control individuals. Each PTB patient submitted sputa on days 0 (for diagnosis), 14, and 28 after starting treatment (for follow-up), and the healthy control individuals submitted one sputum. We performed smear microscopy, Xpert MTB/RIF, culture, and MPT64 detection for all specimens. We evaluated MPT64's correlation to the smear grades, threshold of cycles (Ct) value by Xpert MTB/RIF, and time to detection (TTD) in culture positive cases.
Results: We analyzed the receiver operating characteristic (ROC) curve, and calculated the optimal cut-off, showing the highest specificity for PTB diagnosis with MPT64 usELISA. The ROC analysis of MPT64 showed the area under curve was 0.94 [95% CI: 0.90–0.99] at 0.007 (optimal cut-off). The sensitivity was 84.0% [95% CI: 70.9–92.8] and the specificity was 100% [95% CI: 91.6–100]; these values were equal to the smear and Xpert MTB/RIF on day 0. MPT64 showed a significant correlation to smear grade ($rs = 0.7681$, $p < 0.0001$), Ct value ($rs = -0.8330$, $p < 0.0001$), and TTD ($rs = -0.7746$, $p < 0.0001$).
Conclusion: This study revealed that MPT64 is comparable to Xpert MTB/RIF for detecting PTB and significantly correlated to the bacterial burden through the treatment course. MPT64 detection with usELISA will be useful for diagnosing and monitoring treatment efficacy.

MICRORNAS EXPRESSION IN POST PRIMARY TUBERCULOSIS PATIENTS' SERUM

Shepelkova, Galina, Dr; Evstifeev, Vladimir, Dr; Ergeshova, Anush, Ms; Bagirov, Mamed, Prof; Ergeshov, Atadzhan, Prof; Yeremeev, Vladimir, Prof

Introduction: Fibrotic cavitary pulmonary tuberculosis (FCT) is a chronic form characterized by the presence of a fibrous cavity, the development of fibrotic changes in the lung tissue and foci of bronchogenic dropout. Tuberculoma of the lung is a clinical form of tuberculosis (TB), combining various encapsulated caseous foci of more than 1 cm in diameter, with a long and often low-symptom course. These 2 variants of post primary TB comprise most common diagnosis at the surgery department of the CTRI.
Aim: In this study we describe serum expression pattern of 8 selected miRs in patients with different variants of post primary TB. For the first time we assessed the ability of 8 serum miRs in distinguishing fibrotic cavitary TB from tuberculoma and also their ability to serve as biomarkers of inflammation activity in TB patients.
Methods: Serum samples were collected from FCT and tuberculoma patients and TB contacts. RNA was extracted with TRIzol LS. 3 pools within each group were prepared to be analyzed by miScript miRNA PCR Array (QIAGEN) and TaqMan RT-PCR Assay.
Results: Array results revealed significant differences in miRNA expression spectra between groups under investigation. TaqMan assay verified that in patients with FCT, expression of miR-222, miR-223, miR-191 was downregulated, and expression of miR-26a was upregulated, which may reflect the inflammatory reactions accompanying this form of TB.
The expression profile of serum miRNAs in tuberculoma with degradation patients resembled that of FCT group. In silent tuberculoma group miR-191 expression was upregulated and miR-155 expression was inhibited.
Conclusions: We demonstrated significant changes of some miRNAs serum levels in patients with various forms of TB. These changes involved miRNAs from inflammatory and the fibrotic pathways. Our results form basis for differentiating post primary TB variants.

OVERVIEW OF COMMERCIAL, TARGETED GENOTYPIC DRUG SUSCEPTIBILITY TESTING ASSAYS FOR M. TUBERCULOSIS COMPLEX

Mohamed, Sagal, Dr; Hong, Seok H., Dr; Huang, Hairong, Dr; Hsueh, Po-Ren, Dr; Zimenkov, Danila V., Dr; Shin, Soyoun, Dr; Dolinger, David, Dr; Köser, Claudio U., Dr; Heysell, Scott, Dr

Background: The only realistic option to rapidly scale-up drug susceptibility testing (DST) for the *Mycobacterium tuberculosis* complex (MTBC) globally is to adopt existing and novel genotypic DST (gDST) assays. To this end, WHO has endorsed five gDST assays. However, nu-

merous additional assays are commercially available or in an advanced stage of development, but have received limited attention to date.
Design: To provide a comprehensive comparison of commercial gDST assays, the following sources of information were reviewed: i) peer-reviewed publications, ii) information from the Foundation For Innovative New Diagnostics, iii) the current Unitaid technology landscape report, and iv) assay manufacturers.
Results: 49 gDST assays are on the market, of which 39 are approved for clinical use in at least one country, and a further 13 are in advanced development. Real-time PCR is employed by 42% of assays, followed by arrays and line probe technology (by 24% and 21%, respectively). Four targeted next-generation sequencing (tNGS) assays are being designed as reflex assays and for surveillance by WHO. The number of resistance regions analysed ranges from just two mutations to 22 extended gene regions for one tNGS assay (i.e. resistance to up to 13 WHO-recommended drugs can be ruled in). Only one assay includes resistance genes for bedaquiline and none cover delamanid. Two assays interrogate mutations that do not confer resistance but are instead markers for specific MTBC lineages, which, in some settings, likely yield more systematic false-resistant results than true resistance. Six assays differentiate certain nontuberculous mycobacteria, whereas two assays differentiate some MTBC genotypes. The reporting language varies markedly between assays.
Conclusions: At least 62 commercial gDST assays will likely be available in the near future. The design flaws identified in this comparison underline that independent and systematic evaluations, while resource intensive, are crucial to ensuring high-quality gDST for patients with tuberculosis.

CELLULAR BIOMARKER ASSAY FOR DIAGNOSIS AND CONTROL OF CHILDHOOD TUBERCULOSIS

Hiza, Hellen, Ms; Hella, Jerry, Dr; Brites, Daniela, Dr; Gagneux, Sebastien, Prof; Reither, Klaus, Dr; Portevin, Damien, Dr

Every year 1 million children develop tuberculosis (TB) and 250.000 die from it. This is notably due to the lack of appropriate diagnostic tools able to indicate this serious disease in a timely manner. Current microbiological or molecular diagnostic tools aim to identify bacteria from sputum specimens, a method mainly suitable for the detection of pulmonary TB in adults. Childhood TB is characterised by low bacterial burden and a high tendency to disseminate outside the lung, rendering current diagnostic tools inappropriate. Therefore, non-sputum diagnostic tests are urgently needed.
We previously reported a proof-of-concept study using bio-archived peripheral blood mononuclear cells (PBMC) samples from Tanzanian childhood TB cohorts showing that CD27 biomarker could indicate TB disease with unprecedented sensitivity and specificity, superior to the molecular-assay Xpert MTB/RIF. As a first step to point-of-care application, we implemented a standard operating procedure with a 24h turn-around time from freshly collected whole blood to assess its diagnostic potential within an adult TB cohort with and without HIV co-infection in Tanzania. We found that an antigenic stimulation cocktail based on synthetic peptide pools delivered results with excellent reproducibility using the most basic flow cytometer configuration, available at most district level hospitals. We observed that the use of the peptide pool stimulation compared to *Mycobacterium tuberculosis* - whole cell lysate, markedly improves the CD27 biomarker's accuracy to distinguish active disease from cured TB. In addition, we found that the biomarker CD38 performed significantly better than CD27 itself and finally, that frequency-based analysis of phenotypic data would also perform better than our previously described analytical approach based on Median Fluorescence Intensity. We therefore confirmed on a large scale that the assay accuracy and format, starting with a total amount of blood of 1ml, has the potential to reliably diagnose TB in children including infants.

METHYL NICOTINATE AND METHYL PARA-ANISATE AS BREATH BIOMARKERS FOR TUBERCULOSIS DIAGNOSIS: A PILOT STUDY IN KAMPALA, UGANDA

Andama, Alfred, Mr; Crowder, Rebecca, Ms; Willis, Christina, Ms; McKinnon, Lani, Ms; Jaganath, Devan, Dr; Joloba, Moses, Prof; Cattamanchi, Adithya, Prof; Mohanty, Swomitra, Prof

Background: Non-sputum-based biomarker-based tests are a priority for tuberculosis (TB) diagnosis. Studies have identified methyl nicotinate (MN) and methyl p-anisate (MPA) as metabolic byproducts of *M. tuberculosis*. We aimed to determine if MN and MPA can be detected in the breath of TB patients and accurately discriminate between patients with and without TB.
Methods: We conducted a pilot study among adults with presumed pulmonary TB at three health centers in Kampala, Uganda to assess the diagnostic accuracy of MN and MPA. All patients underwent routine TB testing (sputum Xpert Ultra and solid/liquid culture if Xpert Ultra-negative). In addition, we collected 10-20 liters of exhaled breath into FlexFoil PLUS Breath-bags. Breath samples were adsorbed onto Tenax tubes and analyzed using gas chromatography mass spectrometry (GC/MS). Presence or absence of MN and MPA was determined using GC/MS reference standards and analyzed via extracted ion chromatograms by personnel blinded to TB status.
Results: Of the 38 patients included, 23 (61%) had confirmed TB based on positive Xpert Ultra results only; median age 31 years (IQR 22-46); 13 (34%) were female;

and 6 (16%) HIV positive. GC/MS results were inconclusive for MN in 8 (21%) patients and for MPA in 2 (5%) patients due to high background. Excluding inconclusive results, MN was detected in 14/15 patients with TB (sensitivity 93%, 95% CI 68-100%) and was not detected in 14/15 patients without TB (specificity 93%, 95% CI 68-100%). Similarly, MPA was detected in 15/22 patients with TB (sensitivity 68%, 95% CI 45-86%) and was not detected in 12/14 patients without TB (specificity 86%, 95% CI 57-98%).

Conclusions: MN is a promising breath-based biomarker that should be further evaluated for development into a TB triage or diagnostic test. Further optimization of breath collection and analysis techniques could improve performance of MN and MPA as TB biomarkers.

MFLODX® MINIMDR-TB, AN INNOVATIVE RAPID DIAGNOSTIC TEST FOR MULTIDRUG-RESISTANT TUBERCULOSIS

Mazurkiewicz, Magdalena, Dr; Molina, Bárbara, Dr; Asalapuram, Pavan, Dr; Parasa, Venkata Ramanarao, Dr; Domínguez, Jose, Dr; Hoffner, Sven, Prof; Krzywkowski, Tomasz, Dr

The occurrence of drug resistant *Mycobacterium tuberculosis*—close to 600.000 reported cases in 2017—is an increasingly recognized, global public health concern. A new approach is desired to eliminate TB, yet diagnostic practices in most high burden countries has not changed for the last 50 years. Rapid, reliable and inexpensive diagnosis of MDR/XDR-TB is urgently needed to ensure early detection of resistant cases, to maximize personalized treatment outcomes, and to restrict the transmission of drug-resistant bacteria. The multiflow diagnostics (*mfloDx*®) miniMDR-TB test, developed by EMPE Diagnostics, Sweden, combines highly specific molecular techniques (padlock probe-dependent rolling circle amplification) with signal visualization on lateral flow cassettes enabling robust detection of TB and its drug-resistance profile within 2 hours. The test was developed to detect clinically significant and most prevalent single-nucleotide mutations in MDR-TB (rpoB S531L and katG S315T1) associated with resistance to rifampicin and isoniazid, respectively. The performance of *mfloDx*® miniMDR-TB test was evaluated on 52 DNA samples (extracted from TB isolates cultured on Löwenstein-Jensen medium at IGTP, Spain) and compared with the results obtained from pyro-sequencing and GenoType MTBDRplus. Genotyping with *mfloDx*® miniMDR-TB test revealed a concordance of 90% and 96% for rpoB S531L and katG S315T1 respectively. Large scale validations of *mfloDx*® miniMDR-TB test are currently being performed in India. By successful targeting of the two most prevalent mutations responsible for antibiotic resistance in TB, the *mfloDx*®miniMDR-TB offers a rapid and inexpensive alternative to drug-susceptible testing in the field of TB diagnostics. Next generation tests, integrating additional genotypes that confer resistance to Rifampicin, Isoniazid and Fluoroquinolones are being developed for the direct use on sputum samples, enabling rapid detection of MDR/XDR-TB within 2 hours, even in resource-limited laboratories.

NEW IMMUNOLOGIC TESTS IN DIAGNOSIS OF TUBERCULOSIS INFECTION IN CHILDREN OF DIFFERENT AGE

Starshinova, Anna, Prof; Dovgaluk, Irina, Prof; Ovchinnikova, Yulia, Dr; Yablonskiy, Piotr, Prof

Introduction. Early diagnosis of TB infection in children is complicated due to poor clinical signs, minor X-ray abnormalities, and absence of bacterial excression. Potential of Mantuox 2 TE test in population with common BCG vaccination is limited due to its low diagnostic specificity. Implementation of new immunologic tests allows improvement of early diagnosis of tuberculosis in children.

Objective of the study: to compare revealing of latent tuberculosis infection (LTBI) and active tuberculosis in children with and without use of new immunologic tests (Diaskintest, T-SPOT).

Material and Methods: We analized results of examination of 1300 children (1-14 years old) in St.-Petersburg within the period 2013-2017 BCG vaccinated and with positive results of Mantuox test. We divided children into two groups: children who were examined in the period 2013-2015 without new immunologic tests (Diaskintest, T-SPOT) in screening of TB (n= 654; I group) and II group – with the use of these tests, in the period 2016-2017 (n=646). The data analysis was performed with the use of the Stata 14 software. The differences between compared groups were considered significant at p-value <0.05.

Results: In the II group LTBI was diagnosed significantly higher than in the I group (68.4% (191) vs 32.9% (127), $p<0.05$); while active TB in the II group was diagnosed significantly lower (31.5% (88) vs 67.1% (258), $p<0.01$). Number of healthy children was higher in the II group (56.8% (367) vs 41.1% (269).

Conclusion: The use of new immunologic tests in screening of TB improves early diagnosis of TB infection in children.

HEME OXYGENASE-1 AND NEOPTERIN PLASMA/SERUM LEVELS AND THEIR ROLE IN DIAGNOSING LATENT TB AND ACTIVE TB AMONG HIV/TB CO-INFECTED PATIENTS

Uwimaana, Esther, Miss; Castelnuovo, Barbara, Dr;
P Kateete, David, Dr; Joloba, Moses, Prof;
S Bagaya, Bernard, Dr

Background: TB diagnosis in the context of HIV co-infection remains challenging. Heme oxygenase 1(HO-1) and neopterin have been validated as potential biomarkers for TB diagnosis. This study was conducted to determine the levels of HO-1 and neopterin and their role in diagnosis of TB among HIV positive individuals enrolled in the Community Health and Social Network of Tuberculosis(COHSONET) study and the Kampala TB Drug Resistance Survey(KDRS)
Methods: 210 participants were enrolled in a study of diagnostic method conducted to determine the levels of HO-1 and neopterin and determine their diagnostic accuracy as biomarkers in TB diagnosis from March to May 2019. M.*tb* culture was performed on sputum culture to confirm active TB (ATB) and QuantiFERON TB gold test to confirm latent TB infection(LTB). ELISAs were performed to determine the level of HO-1 and neopterin. Analysis was done using Kruskal Wallis and Receiver Operating Characteristic curves.
Results: HO-1 levels among ATB/HIV patients, LTBI/HIV patients, and TB negative individuals were 10.7ng/ml(IQR: 7.3-12.7ng/ml), 7.5ng/ml(IQR: 5.4-14.1ng/ml) and 3.3ng/ml(IQR: 2.0-7.1ng/ml)respectively. Neopterin levels among ATB/HIV patients, LTBI/HIV patients, and TB negative individuals were 11.7ng/ml(IQR: 5.2-19.4ng/ml), 8.8ng/ml(IQR: 2.4-19.8ng/ml), and 5.9ng/ml(IQR: 3.4-10.2ng/ml) respectively. HO-1 showed sensitivity of 78.57% and specificity of 71.43% with area under the curve(AUC) of 0.833 when used to diagnose ATB. HO-1 showed AUC 0.79, sensitivity of 70% and specificity 70% when used diagnose LTB. Neopterin showed a sensitivity of 61.43% and a specificity of 74.29% with AUC 0.71 to diagnose of ATB. Neopterin as a biomarker in LTB diagnosis, showed AUC of 0.56 which was not significant.
Conclusion: HO-1 and neopterin are very good diagnostic biomarkers for ATB and LTB which could be utilized to develop cheap rapid diagnostic tools to overcome current TB diagnostic challenges.

CULTURE FREE APPROACHES FOR THE DIAGNOSTIC AND MANAGEMENT OF PATIENTS WITH DRUG RESISTANT TUBERCULOSIS: THE DIAMA PROJECT

Massou, Faridath, Dr; Affolabi, Dissou, Prof;
Diarra, Bassirou, Dr;
Semuto Ngabonziza, Jean Claude, Mr;
Supply, Philip, Dr; Nair, Chandrasekhar, Mr;
Merle, Corinne, Dr; De Jong, Bouke, Prof

Background: At this date, the Xpert MTB/Rif is the most accessible molecular test to diagnose drug resistant tuberculosis (DR-TB). However, this test can only detect resistance to rifampicin leading to presumptive diagnosis of resistance to isoniazid and maybe other drugs. Moreover, culture on monthly sputum samples is currently recommended by the World Health Organization (WHO) for follow-up of DR-TB patients under treatment. Unfortunately, culture is often not locally available and samples need to be shipped from field to culture laboratories. The associated transport delays lead to high rates of contamination and false negative culture, particularly in laboratories in low resource settings. Many gaps for the diagnosis and management of DR-TB patients still need to be addressed and the DIAMA project (DIAgnostics for Multidrug resistant tuberculosis in Africa) aims to address some of them.
Method: The Centre National de Pneumo-Phtisiologie de Cotonou, Benin leads a consortium of 11 partners in Europe, East, Central and West Africa. The DIAMA project will explore the feasibility and accuracy of:

- Diagnosing TB resistance to first and second line drugs through novel molecular assays such as Deeplex® Myc-TB, GeneXpert® 2nd line and MolBio TrueNat for 2nd line drugs by comparing them with phenotypic DST and Whole Genome Sequencing;
- Setting-up alternative culture-free approaches for the monitoring of patients' response to Rifampicin resistant treatment such as Fluorescein DiAcetate vital staining microscopy and bacterial load measurement using Xpert MTB/RIF®;

This project is funded by the European Developing Country Clinical Trial Partnership for a period of five years.
Results & Conclusion: Recruitment is ongoing in 9 African countries and to date more than 1500 patients have been included. Through this presentation, we will share the background information, the design of this project and the progress in implementation.

DEVELOPMENT OF ONE-DAY DRUG SUSCEPTIBILITY TESTING BY MONITORING MPT64 ANTIGEN SECRETED FROM MYCOBACTERIUM TUBERCULOSIS

Murase, Yoshiro, Dr; Takeuchi, Rikiya, Dr; Ohtaki, Yoshiharu, Dr; Sakashita, Kentaro, Dr; Nakaishi, Kazunari, Dr; Ito, Etsuro, Prof; Watabe, Satoshi, Dr; Mitarai, Satoshi, Prof

Background: The current anti-tuberculosis drug susceptibility testing (DST) requires more than one week, which hinders timely management of tuberculosis treatment. Alternatives, such as line probe assay and Expert MTB/RIF, do exit, but they are not universally adaptable for all TB drugs. In addition, such molecular methods sometimes lack enough sensitivity for practical use. Therefore, rapid and reliable phenotypic DST is urgently required.
Objective: To assess MPT64 antigen secreted from *M. tuberculosis* as a surrogate marker of the growth suppression by anti-TB drug and the subsequent phenotypic DST result in liquid medium
Methods: H37Rv and eight clinical *M. tuberculosis* strains were used for the assay. Fresh culture of the strains were diluted to OD_{530} of 0.002, and then exposed to seven drugs (isoniazid, rifampicin, rifabutin, streptomycin, kanamycin, levofloxacin, and ciprofloxacin) using BrothMIC MTB-I MIC plates (Kyokuto, Tokyo) for 2, 24, and 72 hours at 37 ?C. After the exposure, the concentration of MPT64 in the medium was determined by ultrasensitive ELISA (TAUNS, JAPAN). MIC result of each drug was obtained after 7 days of incubation.
Results: We found a drug concentration-dependent MPT64 secreting profile to each anti-TB drug in H37Rv. Especially to INH, a clear production of MPT64 was observed after 2 hours exposure. As to the remaining six drugs, a reduction of MPT64 was observed early in 24h and confirmed by 72h. Using clinical strains including drug-susceptible and resistant strains, we found the decreasing secretion of MPT64 were highly correlated with their MIC values.
Conclusion: MPT64 will work as a surrogate marker of conventional phenotypic anti-TB DST. This novel system potentially predicts drug resistance within 1-day.

THE ROLE OF DIGITAL CHEST RADIOGRAPHY AND GENEXPERT MTB/RIF IN COMMUNITY-WIDE ACTIVE CASE FINDING FOR TUBERCULOSIS

Nguyen, Thi Bich Phuong, Dr; Nguyen, Thu Anh, Dr; Luu, Boi Khanh, Ms; Le, Oanh Thi Tu, Ms; Nguyen, Van Son, Dr; Nguyen, Binh Hoa, Dr; Nguyen, Nhat Linh, Dr; Fox, Greg J., Prof; Nguyen, Viet Nhung, Prof; Marks, Guy B., Prof

Background: We compared the sensitivity and feasibility of sputum examination by Xpert MTB/RIF and chest radiography as screening tests for tuberculosis (TB).
Methods: We conducted a cross-sectional study in 96 sub-communes in Ca Mau, Vietnam. All men aged ≥ 15 years and women aged ≥ 46 years were eligible. Participants were visited at home and, regardless of the presence of symptoms, were invited to provide a single, spontaneously expectorated sputum specimen that was tested using Xpert MTB/RIF. Separately, participants were invited to attend a nearby location for digital chest radiography. Participants whose sputum was Xpert MTB positive or whose chest radiograph was reported as "consistent with TB" were requested to provide two further sputum specimens for culture. TB cases were defined as people with one or more sputum cultures positive for *M. tuberculosis*.The sensitivities of the two tests for detecting TB cases were compared using McNemar's test. Capture-recapture was used to estimate missed TB cases.
Results: There were 76,188 eligible participants, of whom 57,619 (75.6%) participated in sputum Xpert screening, 12,813 (16.8%) had chest radiography performed and 11,290 (14.8%) had both tests. We estimated there were 55 TB cases, of whom 20 were Xpert MTB positive (sensitivity 36.4%) and 44 had a chest radiograph reported as "consistent with TB" by one or both readers (sensitivity 80.0%, $P < 0.0001$).
Conclusions: In community-wide screening for TB, chest radiography is more sensitive than a single spontaneously expectorated sputum sample tested using Xpert MTB/RIF but has a substantially lower participation rate.

RAPID MOLECULAR ASSAY TO DIFFERENTIATE BETWEEN MYCOBACTERIUM TUBERCULOSIS COMPLEX AND NONTUBERCULOUS MYCOBACTERIA IN CLINICAL SAMPLES.

Chauhan, Varsha, Ms; Shrivastava, Kamal, Mr; Kumar, Chanchal, Mr; Singh, Anupriya, Ms; Varma-Basil, Mandira, Dr

Introduction: Nontuberculous Mycobacteria (NTM) are emerging as potential pathogens, leading to a need for identification and differentiation from *Mycobacterium tuberculosis* complex (MTBC) for better disease management. Hence, in the present study, we made an attempt to develop a real time-based assay to rapidly identify and differentiate between MTBC and NTM directly in sputum samples.
Methods: Sputum samples (n=64) of patients suspected of pulmonary tuberculosis were collected from North Delhi, India. The collected samples were subjected to AFB smear examination, culture, GeneXpert and an in-house real time PCR assay (qPCR). The qPCR targeted a genus specific gene, *hsp65*, and a species specific gene, *Rv1458c*. The sensitivity and specificity of qPCR were calculated using GeneXpert and culture as gold standards.

Results: Out of the 64 samples, 39 were smear positive and 25 were smear negative. Among the smear positive samples, 18 were culture positive; while of the smear negative samples, three were culture positive. Of the 21 positive cultures, qPCR identified MTBC in 14 samples and NTM in four samples. Line probe assay identified three of these NTM as *M. kansasii*. Considering culture as the gold standard, the sensitivity and specificity of the in-house qPCR assay were 64% and 54% respectively. On comparison with GeneXpert, the sensitivity and specificity were found to be 56% and 73% respectively.
Conclusion: The qPCR assay was found to be an economical and rapid test for the identification of MTBC in clinical specimens, though its sensitivity and specificity were lower than GeneXpert. In addition, the in-house qPCR proved to be a valuable rule in test for the presence of NTM, though, the assay needs to be evaluated on a larger number of samples.

SYSTEMATIC VALIDATION OF BLOOD TRANSCRIPTIONAL BIOMARKERS FOR ACTIVE PULMONARY TUBERCULOSIS IN A HIGH-BURDEN SETTING: A PROSPECTIVE DIAGNOSTIC ACCURACY STUDY

Turner, Carolin, Dr; Gupta, Rishi, Dr;
Roe, Jennifer, Dr; Mondal, Prasenjit, Mr;
Nyawo, Georgina, Ms; Reeve, Byron, Dr;
Theron, Grant, Prof; Noursadeghi, Mahdad, Prof

Background: The World Health Organization (WHO) has specified the urgent need for a non-sputum-based triage test to identify patients that require confirmatory testing for tuberculosis (TB). A multitude of blood transcriptional signatures have been described for TB. However, independent validation of these signatures in cohorts representative of real-world clinical scenarios in high burden settings is limited. We systematically evaluated the diagnostic accuracy of published transcriptional signatures in a clinically relevant population with high burden of TB and human immunodeficiency virus (HIV).
Methods: Symptomatic adults referred for investigation for pulmonary TB were consecutively recruited at a TB clinic in South Africa. Participants provided sputum (for Xpert and liquid culture) and peripheral blood samples (for RNA sequencing). We performed a systematic review to identify candidate transcriptional signatures for TB and directly compared their diagnostic accuracy in this real-world cohort, using a robust gold-standard of culture and/or Xpert positivity.
Results: Amongst 181 patients (median age 35 years), 44 (24%) were HIV-infected. 54 patients (30%) were diagnosed with Xpert- or culture-positive TB. Four of 25 candidate transcriptional signatures performed equivalently for discriminating TB patients from non-TB controls, with areas under the receiver operating characteristic curve of 86.8% (95% confidence interval 80.6-93.1%) to 90.6% (85.6-95.6%). Diagnostic accuracy of the four best-performing signatures (comprising 1-25 genes) was independent of HIV, previous TB, sputum smear status and TB symptom score. At a cut-off derived from the maximum Youden index, all four met or approximated the WHO minimum target product profile triage test criteria (90% sensitivity, 70% specificity), achieving negative predictive values of 89.1% (82.5-93.4%) to 94.9% (88.7-97.8%).
Conclusion: Four transcriptional signatures marginally achieve the WHO minimum diagnostic accuracy parameters required for a TB triage test. However, achieving the target price of <$2 for a triage test may be challenging for real-world translation of these biomarkers.

	Sensitivity (95% confidence interval), %	Specificity (95% confidence interval), %	Positive predictive value (95% confidence interval), %	Negative predictive value (95% confidence interval), %
BATF2	87 (75.6 - 93.6)	79.5 (71.7 - 85.6)	64.4 (52.9 - 74.4)	93.5 (87.2 - 96.8)
Kaforou25	74.1 (61.1 - 83.9)	89.8 (83.3 - 93.9)	75.5 (62.4 - 85.1)	89.1 (82.5 - 93.4)
Roe3	90.7 (80.1 - 96)	74 (65.8 - 80.9)	59.8 (48.9 - 69.7)	94.9 (88.7 - 97.8)
Sweeney3	87 (75.6 - 93.6)	85 (77.8 - 90.2)	71.2 (59.4 - 80.7)	93.9 (88 - 97)

IMPACT OF FNAC IMPLEMENTATION AT PRIMARY HEALTHCARE LEVEL TO IMPROVE DIAGNOSIS AND TREATMENT OF TUBERCULAR-LYMPHADENITIS TO IMPROVE CASE-DETECTION IN REMOTE DISTRICTS OF INDIA.

Quazi, Toufique, Dr; Khan, Kalyan, Prof;
Ramachandran, Ranjini, Dr; Sachdeva, Kuldeep, Dr;
Rade, Kiran, Dr; Mase, Sundari, Dr; Parmar, Malik, Dr

Background: Clinical-diagnosis of tubercular-lymphadenitis has poor-specificity resulting in over-diagnosis, whereas Fine-needle-aspiration-cytology (FNAC)is highly sensitive (83-94%accuracy). However, it is done mostly at tertiary-centres. Study was undertaken to determine feasibility and effectiveness of FNAC strategy implemented at DMC level for detection of tubercular-lymphadenitis including the the complication rate and accuracy of case detection. The study also looks to analyse cost-difference of FNAC performed at DMC level and that at other far-off health-facilities.
Materials and Methods: Randomized-cluster-trial with one control and one intervention-arm-DMCs. FNAC-training was given to Medical Officers, laboratory-technicians(LT)of intervention-arm-DMCs. FNAC was done in 1298 presumptive-cases of Tubercular- Lymphadenitis of which 294 included in intervention-arm and 196 in control-arm. All clinically-presumptive-tubercular-lymphadenitis cases in intervention-arm were subjected to FNAC by LTs under physician-supervision followed by smear- microscopy for presence of acid-fast-bacilli(AFB), granulomas/caseation necrosis indicating

tuberculosis infection. All FNAC slides prepared at the intervention DMCs were reviewed at Medical College irrespective of the diagnosis.Changes in indicators compared between the intervention and control groups by using paired t test, independent sample t test and Chi-square test. Statistical Analysis was done using SPSS version 14 software.

Results: Baseline population-variables showed no significant statistical difference (P values <0.05). Cervical lymph-nodes were most commonly affected (77%). No significant complication was observed during/after FNAC at DMC level. The weighted mean of the interval between advice and FNAC in the two groups was statistically significant(p-value: 0.000) leading to early detection and treatment in intervention-and significant delay in control-arm. The patient in intervention arm saved money and days as compared to control (mean:Rs311)

Conclusions and key recommendations: Implementation of FNAC-strategy at the RNTCP designated DMC level for detection of tubercular-lymphadenitis cases was found to be feasible, safe and cost-effective. Multicentric studies with similar objectives should be conducted involving different DMCs to validate the conclusions in diverse population groups and to improve TB case-detection.

Interval between clinical evaluation and Pre-Treatment FNAC

	Control (n=196_)	Intervention (n=294)	t test	p value
Mean ± SD	17.8 ± 11.2	2.0 ± 1.6	23.84	<0.001
Weighted mean	16.3	0.4		

Cost of FNAC

Means	Control (n=_196)	Intervention (n=294)	t test	p value
Mean ± SD	311.0 ± 187.4	50.0 ± 0.0	23.97	<0.001
Weighted mean	270.2	50.0		

Interval b/w FNAC advice and start of DOTS (days)

Means	Control (n=196)	Intervention (n=294)	t test	p value
Mean ± SD	21.9 ± 8.1	5.7 ± 1.5	16.49	<0.001
Weighted mean	18.3	3.4		

NOVEL ANTIGENS FOR THE DIAGNOSIS OF TUBERCULOSIS IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTION: A PILOT STUDY OF PATIENTS WITHIN THE SWISS HIV COHORT

Meier, Noemi Rebecca, Ms; Ritz, Nicole, Dr; Battegay, Manuel, Prof

Background: The diagnosis of tuberculosis in human immunodeficiency virus (HIV)-infected individuals is challenged by lower sensitivity of interferon-γ release assays (IGRA). Novel *Mycobacterium tuberculosis* antigens have become available and may improve sensitivity of IGRA in this patient group.

Methods: Confirmed tuberculosis (TB) patients and controls were selected from the Swiss HIV Cohort Study. Cryopreserved lymphocytes were used within 6 months of diagnosis and three samples in the years prior to diagnosis (TB group). One sample was taken in the years before and one at the day of or shortly after the negative IGRA results (control group). Lymphocytes were stimulated overnight with *Mycobacterium tuberculosis* antigens and cytokine production was measured. Mann-Whitney U test (MWU) was used to assess differential cytokine responses. Receiver operating characteristics (ROC) were performed for significant results of MWU.

Results: Samples from 18 individuals were included: 9 TB patients (77.8% male, median age 45 years) and 9 control patients (66.7% male, median age 51 years). Median CD4 cell count was 289/ul for the TB-group and 439/ul for the control group, with supressed viral loads in both groups (HIV-RNA of 16 and 24 copies/ml, respectively). Cytokine concentrations were generally higher in the TB-group and highest for IP-10 and TNF-α in response to *Mycobacterium tuberculosis* antigens. This reached significance for TNF-α induced by Rv2346/Rv2347c and Rv2031c and IP-10 induced by Rv2431c and Rv3614/15c at time point closest to diagnosis. ROC resulted in optimal cut-off values of 19.9 pg/ml (Rv2346/47c-TNF-α), 72.9 pg/ml (Rv2031c-TNF-α), 1.4 pg/ml (Rv2431c-IP-10) and 4.8 pg/ml (Rv3614/15c-IP-10) to differentiate between TB and controls.

Conclusion: Differential cytokine responses induced by novel antigens were measured in frozen lymphocytes. We found four novel antigen-cytokine pairs as potential candidates for improved diagnosis of TB in HIV-positive patients. These findings require now validation in a larger cohort of HIV-infected patients.

HEAD TO HEAD COMPARISON OF ANALYTICAL SENSITIVITIES OF BD MAXT MDR-TB, XPERT® MTB/RIF ULTRA AND FLUOROTYPE® MTB USING HUMAN AND ARTIFICIAL SPUTUM

Beutler, Markus, Dr; Plesnik, Sara, Ms; Mihalic, Marina, Ms; Olbrich, Laura, Dr; Schumacher, Samuel, Dr; Lindner, Michael, Dr; Grasse, Wolfgang, Dr; Hoffmann, Harald, Dr

A new generation of fully automated molecular tests for pulmonary TB has been recently launched with Xpert MTB/Rif Ultra (XP-Ultra) and BD-MAX MDR-TB (BD-MAX). However, data regarding the performance of BD-MAX and the comparability of both assays based on experiments using the same defined test matrix are scarce. For the sake of comparability, it is indispensable for such studies to use the same test matrix. Since

larger pools of human sputum are not easily obtainable and expensive to check for *Mycobacterium tuberculosis* (MTB) negativity, artificial sputum highly resembling human sputum would be a valuable alternative.
In this study, we have investigated the analytical sensitivities (LoD_{95}) of BD-MAX and XP-Ultra in comparison to the well-established FluoroType MTB (FT-MTB). We have further introduced a novel, human-sputum like, mucin-based artificial sputum (MUCAS) that was used as test matrix and compared to human sputum as well as physiological saline solution each spiked with MTB in declining culture- and qPCR-controlled concentrations.
With BD-MAX, XP-Ultra, and FT-MTB, we measured LoD_{95}^{TB} values of 2.1 cfu/ml (CI_{95}%: 0.9 - 23.3), 3.1 cfu/ml (CI_{95}%: 1.2 - 88.9), and 52.1 cfu/ml (CI_{95}%: 16.7 - 664.4) in human sputum; of 6.3 cfu/ml (CI_{95}%: 2.9 - 31.8), 1.5 cfu/ml (CI_{95}%: 0.7 - 5.0), and 30.4 cfu/ml (CI_{95}%: 17.4 - 60.7) in MUCAS; and of 2.3 cfu/ml (CI_{95}%: 1.1 - 12.0), 11.5 cfu/ml (CI_{95}%: 5.6 - 47.3), and 129.1 cfu/ml (CI_{95}%: 82.8 - 273.8) in saline solution, respectively. LoD_{95} of resistance markers were 9 to 48 times higher.
In conclusion, BD-MAX and XP-Ultra performed equally and had a significantly increased analytical sensitivity compared to the FT-MTB. MUCAS showed characteristics like human sputum while normal saline differed significantly. MUCAS would be an excellent standardized sputum-like test matrix for quality control of TB-PCR assays.

AN EXHALED-BREATH SCREENING TEST FOR THE DETECTION OF ACTIVE PULMONARY TUBERCULOSIS IN PATIENTS PRESENTING TO PRIMARY HEALTH CARE CLINICS IN CAPE TOWN, SOUTH AFRICA.

Esmail, Aliasgar, Dr; Dheda, Keertan, Prof; Dhansay, Muhammed, Dr

Introduction: GeneXpert Ultra is unsuitable for community-based mass screening and in up to one-third of patients an adequate sputum sample is unavailable. By contrast, the analysis of exhaled breath obtained by the Aeonose-TB device has the potential to provide an easy, onsite, rapid, and non-invasive diagnosis of tuberculosis. Thus, it may serve as a useful community-based triage tool (a major unmet need in the TB field).
Methods: We enrolled 1,143 participants (31% HIV-infected) with suspected TB (243 microbiologically-confirmed TB, 130 probable TB, and 770 non-TB) from primary care clinics in Cape Town, South Africa. Sputum GeneXpert MTB/RIF and/ or culture served as the reference standard. Volatile organic compounds in exhaled-breath were detected using an electronic nose containing 3 metal-oxide sensors (Aeonose™; Zutphen, The Netherlands). Data were analysed by machine learning using artificial neural networks (ANN) in a 'leave-10%-out' cross-validation training set (n=756; 189 TB and 567 non-TB) and the findings ratified in a test set (n=257)
Results: In the training set the sensitivity, specificity, PPV, NPV of Aeonose-TB (95% CI) was 81% (74-86) and 60% (55-64), 40% (35-45), and 90% (87-93), respectively. However, in HIV uninfected patients, using a ANN-derived rule-in threshold, performance characteristics were 59% (50-69), 91% (87-93), 68% (58-77), and 87% (83-90), respectively. In the same group, using an ANN-derived rule-out threshold, the performance characteristics were 90% (83-95), 59% (54-65), 43% (36-49) and 95% (91-97), respectively. Results in the validation set, and in HIV-infected persons, showed comparable performance characteristics.
Conclusion: Aeonose-TB may be useful as a triage test for tuberculosis in HIV-infected and uninfected persons as it meets the FIND/WHO minimum Target Product Profile (TPP) for a rule-out TB test. However, it may also have utility to rule in TB in sputum scarce or smear-negative persons. Further studies are now required to clarify these findings.

CLINICAL EVALUATION OF A CARTRIDGE BASED DNA EXTRACTION METHOD FOR FLUOROTYPE® MTB

Beutler, Markus, Dr; Mihalic, Marina, Ms; Plesnik, Sara, Ms; Homann, Ana, Dr; Eckart, Martin, Dr; Czurratis, Daniel, Dr; Hofmann-Thiel, Sabine, Dr; Hoffmann, Harald, Dr

Fast and reliable detection of tuberculosis (TB) is indispensable for TB treatment initiation. Alongside smear microscopy and mycobacterial culture which yield rather low sensitivity or are extensively time consuming, fast nucleic acid amplification tests (NAATs) emerged in the past years. Besides fully automated and cartridge based versions, NAATs such as FluoroType® MTB (FT-MTB, Hain Lifescience) require a separate DNA preparation step before testing. DNA used for FT-MTB is extracted from decontaminated sediment also applied for microscopy and culture. However, conducting decontamination of patient sputum samples requires a well-equipped and expensive laboratory infrastructure, which might not be affordable in high incidence countries.
We have developed a DNA extraction cartridge, which directly extracts DNA out of human sputum without previous decontamination ready for FT-MTB that can be easily run in a programmable centrifuge. The performance of cartridge based DNA extraction followed by FT-MTB (Crt-DNA FT-MTB) was compared to the conventional FT-MTB work flow including NALC-NaOH based decontamination and to Xpert® MTB/Rif (XP-MTB, Cepheid). Using spiked human sputum samples, we could show that Crt-DNA FT-MTB increased the analytical sensitivity around four times compared to the conventional FT-MTB work flow including decontamination. We have also investigated the diagnos-

tic sensitivity and specificity of Crt-DNA FT-MTB and compared to the performance of XP-MTB using clinical samples provided and characterized by GENETUP, Nepal and SYNLAB Gauting, Germany. Crt-DNA FT-MTB yielded a 100% diagnostic specificity. Compared to XP-MTB, Crt-DNA FT-MTB identified 100% of XP-MTB high and medium as well as around 80% of low and very low positive samples.
In conclusion, Crt-DNA FT-MTB has increased analytical sensitivity comparted to conventional FT-MTB and performs with a similar diagnostic sensitivity as XP-MTB. The cartridge might be an alternative for laboratories who want to perform FT-MTB but can otherwise not afford an infrastructure for decontamination and subsequent manual DNA extraction.

A DEFINED ANTIGEN SKIN TEST FOR BOVINE TUBERCULOSIS THAT CAN DIFFERENTIATE BCG-VACCINATED FROM INFECTED ANIMALS.

Srinivasan, Sreenidhi, Miss;
Subramanian, Saraswathi, Ms;
Balakrishnan, Sai Shankar, Mr; CM, Vandana, Dr;
RS, Kathiravan, Dr; Kandaswamy, Srinivasan, Dr;
Raj, Dhinakar, Dr; Veerasami, Maroudam, Dr;
Bakker, Douwe, Dr; Vordermeier, Martin, Dr;
Kapur, Vivek, Dr

It is increasingly recognized that attempts to eliminate Tuberculosis (TB) from humans without eliminating risk of spillover from cattle are likely to prove challenging. This is particularly relevant in regions where bovine TB (bTB) caused by members of the *Mycobacterium tuberculosis* complex (MTC) is endemic in cattle and human consumption of unpasteurized milk is common, posing a considerable threat for transmission of zoonotic TB.
Given the limitations of conventional tuberculin-based ante-mortem diagnostic tests for use in cattle, there is an urgent need for fit-for-purpose assays to reliably differentiate infected and vaccinated animals (DIVA) for use in vaccination-based control programs, especially in endemic settings were test-and-slaughter is not feasible.
To address this unmet need, we have developed a peptide-based defined antigen skin test (DST) for diagnosis of bTB infection in cattle comprising synthetic overlapping peptides representing *M. bovis* antigens ESAT-6, CFP10 and Rv3615c that has been found to exhibit equivalent performance compared to the comparative tuberculin test in both IFN-γ release assays (IGRAs) and skin tests in experimentally infected animals and field reactors (DOI: 10.1126/sciadv.aax4899).
Here, we evaluated the specificity of DST in 1-month to 6-month old crossbred calves (n = 30), half of which were vaccinated with BCG Danish 1331 while the rest served as controls. The DST did not induce positive skin induration responses in either vaccinated or control calves whilst 10/15 vaccinated calves presented with positive responses to bovine PPD (PPD-B), Figure 1.
Taken together, these results confirm the high specificity of the DST in both vaccinated and uninfected animals, and provide a rational framework for the implementation BCG vaccination-compatible defined antigen diagnostic assays where conventional test and cull strategies are neither feasible nor practicable.

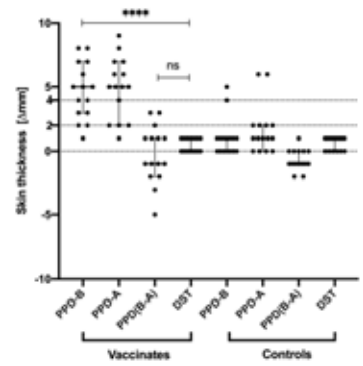


Figure 1. Skin test responses for PPD-B, PPD-A, PPD(B-A) and DST were measured at 72 hours after injection in cattle experimentally vaccinated with BCG Danish 1331 (n = 15) and naïve controls (n = 15). Results are expressed as the difference in skin thickness (in millimeters) between the pre- and post-skin test readings, with the horizontal line providing the median [±95% confidence interval (CI)]. The statistical difference between the responses was determined using analysis of variance (ANOVA) (****P < 0.0001). The solid horizontal lines at 2 and 4 mm are the cutoffs used for DST and PPDs, respectively.

TUBERCULOSIS SYMPTOMS SCREENING PRACTICES OF HEALTHCARE WORKERS IN A DISTRICT HOSPITAL IN GHANA

Der, Joyce, Miss; Grint, Daniel, Dr; Narh, Clement, Mr;
Bonsu, Frank, Dr; Grant, Alison, Prof

Background: WHO guidelines indicate health facility attendees should have a tuberculosis (TB) symptom screen and have sputum tested if symptomatic. We assessed coverage of symptom screening and sputum testing in a secondary care facility in Volta region, Ghana.
Methods: In a cross-sectional study, we enrolled adults (>=18 years) exiting outpatient clinics at a hospital reporting >=1 TB symptom (cough, fever, night sweats or weight loss). Participants completed a questionnaire on reasons for hospital visit, whether a healthcare worker (HCW) asked about cough and whether a sputum test was requested. Participants reporting cough >=2 weeks and those self-reporting to be HIV positive were asked to produce a spot sputum sample for testing with Xpert MTB/RIF.
Results: Among 2,516 hospital attendees, 653 (26.0%) were eligible; 581/653 (89.0%) were enrolled (median age 33yrs [IQR: 24.2-48.0] and 510/581 [87.8%] female). The most common symptoms were fever (348, 59.9%), chest pain (282, 48.5%) and cough (270, 46.5%). 386/581 (66.4%) participants had reported their TB-related symptom to a HCW. 157/208 (75.5%)

participants reporting cough fulfilled criteria for a sputum test, however only 31 (19.8%) were asked to give sputum. In addition, 62 (23.0%) persons did not report their cough and among them 38 (19.5%) were eligible for a sputum test.
In univariate analysis, prior TB treatment (OR: 9.15, CI: 3.17-26.34), cough duration >=2weeks (OR:4.0, CI: 1.76-9.11) and having >=3 TB (vs. 1-2) symptoms (OR: 3.62, CI: 1.73-7.59) were associated with a higher odds of being asked to do a sputum test. In multivariate analysis, cough >2=weeks (AOR: 4.01, CI: 1.60-10.05) was the strongest predictor of being asked to submit sputum. 6/189 (3.2%) sputum samples had a positive Xpert MTB/RIF result.
Conclusion: Opportunities for early identification of people with TB are likely being missed in health facilities in Ghana. Interventions to improve this are needed.

PREVALENCE OF LINEZOLID RESISTANCE AND ASSOCIATED MUTATIONS AMONGST PRE-XDR AND XDR ISOLATES REQUIRING DRUG SUSCEPTIBILITY TESTING AT THE SOUTH AFRICAN NATIONAL TB REFERENCE LABORATORY

Joseph, Lavania, Ms; Ismail, Farzana, Dr;
Ismail, Nazir Ahmed, Prof; Omar, Shaheed Vally, Dr

Background: The increasing global burden of drug-resistant tuberculosis (TB) has spurred on the need to identify alternative treatment options, including repurposing currently available antimicrobial agents such as linezolid (LZD). In July 2018, the World Health Organization (WHO) upgraded and prioritized the use of LZD in the treatment regimen for multidrug- and rifampicin-resistant TB. Literature suggests the genetic basis of resistance to LZD is mediated through mutations in the *rpl*C and *rrl* genes. We aimed to determine the prevalence of LZD resistance as part of the wider national reflex testing algorithm in South Africa and the associated genetic determinants.
Methods: This study included prospectively identified phenotypic LZD resistant *Mycobacterium tuberculosis* isolates from samples submitted to the National Tuberculosis Reference Laboratory (South Africa) for LZD phenotypic testing. These isolates were identified routinely as pre-XDR or XDR from six provinces between January 2017 and September 2018. LZD DST was performed on the MGIT 960 platform using the WHO-recommended critical concentration of 1 μg/ml. Isolates with a LZD resistant phenotype were repeat tested to confirm resistance, with purity confirmation by Ziehl-Neelsen staining. Sequencing of the associated genetic targets was performed on these isolates in a step-wise approach.
Results: Of the 2331 samples tested, 14 were phenotypically confirmed LZD resistant using the MGIT 960 platform. The crude resistance prevalence rate was 0.87% for 2017. Of these, one was pre-XDR and 13 were XDR. Sequencing revealed the presence of the Cys154Arg single nucleotide polymorphism in *rpl*C for all 14 isolates.
Conclusion: Linezolid remains an effective drug for the management of drug resistant TB in our setting due to the low prevalence of resistance. Based on our findings, the Cys154Arg mutation in *rpl*C is a suitable marker for the development of a sensitive and rapid molecular assay for the detection of linezolid resistance in South Africa.

CLINICAL PERFORMANCE OF PROTOTYPE POINT-OF-CARE TB LIPOARABINOMANNAN (LAM) TEST IN UGANDA

Connelly, John, Mr; Andama, Alfred, Mr;
Grant, Benjamin, Mr; Ball, Lex, Mr;
Ignatowicz, Lech, Mr; Hamasur, Beston, Mr;
Cattamanchi, Adithya, Dr; Somoskovi, Akos, Dr

Background: Urine-based TB lipoarabinomannan (LAM) has been used in diagnosis of active TB in people living with HIV (PLHIV), particularly individuals with CD4+ T-cell counts below 100 cells/μL. As a sputum-free diagnostic, LAM is an attractive candidate to broaden accessibility of diagnosis, particularly if sensitivity can be enhanced and dependence on HIV-status can be eliminated. We have developed a prototype point-of-care (POC) assay consisting of a simple concentration step and lateral flow assay and evaluated it urine samples of individuals with presumptive tuberculosis.
Design/Methods: Beginning in October 2018, we conducted a cross-sectional study of adults, regardless of HIV-status, presenting for evaluation of pulmonary TB at healthcare settings in Uganda. Patients able to provide sputum for GeneXpert® MTB/RIF testing were enrolled. Eligible patients submitted two sputums for solid and liquid cultures and urine for LAM testing. The cohort was enriched by enrolling consecutive patients with positive GeneXpert® results and randomly sampling patients with negative results. This study was approved by the Makerere University School of Medicine Research and Ethics Committee, the Uganda National Council for Science and Technology, and UCSF Committee on Human Research.
Results: Preliminary results (n=284) from this ongoing study indicate this prototype has 60% sensitivity (95%CI: 51-69%) and 80% specificity (95%CI: 73-86%) compared to microbiological reference standard. The prototype test also indicates similar performance regardless of HIV-status, with 67% sensitivity (95%CI: 49-81%) and 74% specificity (95%CI: 59-86%) for PLHIV (n=82) and 58% sensitivity (95%CI: 46-68%) and 83% specificity (95%CI: 75-89%) for those who do not have HIV (n=202).
Conclusions: The current prototype test demonstrates that one can eliminate the differential performance of a POC TB LAM test based on HIV-status. Though work

continues to improve both sensitivity and specificity, the current prototype may have a significant impact when used to support intensified case finding efforts.

COMPARATIVE ANALYSIS OF DETECTION AND DRUG RESISTANCE PROFILING OF MYCOBACTERIUM TUBERCULOSIS BY CONVENTIONAL AND NANOPORE SEQUENCING

Singh, D V, Dr

Whole genome or targeted sequencing offers an unprecedented opportunity to identify drug resistant tuberculosis infections and to provide insight into chains of transmission. Despite strong evidence supporting the potential utility of this approach to improve the management of tuberculosis, adoption of genomic technologies - particularly in high burden, low and middle income countries - has been limited. This has been in large part due to the high capital cost, infrastructure demands and relatively slow turnaround time of traditional sequencing technologies.

By contrast the Oxford Nanopore Technologies MinION sequencing device is handheld, low cost (as little as $1000) and provides results in real time. Being based on electronic rather than optical sensing, the device is robust and is ideally suited to use in remote and resource limited settings.

For example, the technology was used to successfully sequence the TB genome from both cultured isolate DNA and also DNA extracted directly from infected sputa as part of a research project at the Institut Pasteur in Madagascar.

To improve the ease with which genomic analysis of tuberculosis can be conducted, ONT is also developing a cloud-based analysis tool on our EPI2ME platfom that is able to identify drug resistance associated mutations from the sequencing data. Combined with the Voltrax automated library preparation device, our aim is to deliver a portable, low cost, end to end solution for the genomic analysis of tuberculosis.

SAME DAY TOOLS, INCLUDING XPERT ULTRA AND UNSTIMULATED IFN-GAMMA, FOR THE RAPID DIAGNOSIS OF PLEURAL TUBERCULOSIS - A PROSPECTIVE OBSERVATIONAL STUDY

Randall, Philippa, Dr; Meldau, Richard, Mr; Pooran, Anil, Dr; Limberis, Jason, Dr; Makambwa, Edson, Dr; Dhansay, Muhammed, Dr; Esmail, Ali, Dr; Dheda, Keertan, Prof

Introduction: The diagnosis of pleural tuberculosis (TB) is problematic. The comparative performance of newer same day tools for pleural TB including Xpert MTB/RIF Ultra (ULTRA) has, hitherto, not been comprehensively been studied.

Methods: Adenosine deaminase (ADA), Inter-Gam Ultrasensitive Rapid Immuno-suspension Assay (IRISA-TB), Xpert MTB/RIF, and ULTRA performance outcomes were evaluated in pleural fluid samples from 149 patients with suspected pleural TB. The reference standard was culture positivity (fluid, biopsy or sputum) and/or pleural biopsy histopathology (definite-TB). Those with non-TB were microbiologically test negative and were not initiated on anti-TB treatment. To determine the effect of sample concentration, 65 samples underwent pelleting by centrifugation followed by conventional Xpert MTB/RIF and ULTRA.

Results: Of the 149 patients, 49 had definite-TB, 16 probable-TB (not definite but treated for TB) and 84 non-TB. ULTRA sensitivity (95% CI) and specificity was similar to Xpert MTB/RIF [37.5% (25.3-51.2) versus 28.6% (15.9-41.2)] and [98.8% (96.5-100) versus 98.8% (96.5-100)], respectively. Centrifugation did not significantly improve ULTRA sensitivity (29.5% vs. 31.3%, respectively). Adenosine deaminase and IRISA-TB sensitivity was 84.4% (73.9 - 95.0) and 89.8% (81.3-98.3), respectively. However, IRISA-TB demonstrated significantly better specificity [96.4% vs. 87.5% (p= 0.034)], positive-predictive value [93.6% vs. 80.9 (p= 0.028)] and positive-likelihood ratio [25.1 vs. 6.8 (p= 0.032)] than ADA.

Conclusion: Xpert ULTRA has poor sensitivity for the diagnosis of pleural TB. Alternative assays (ADA and IRISA-TB) are significantly more sensitive, with IRISA-TB demonstrating a higher specificity and rule-in value compared to ADA in this high TB and HIV-endemic setting.

Theme: Prevent infection or prevent disease?

ANIMAL MODEL INDUCING INFLAMMATORY REGULATION PROCESS USING CANNABINOIDS AT THE ALVEOLAR MACROPHAGE MEMBRANE LEVEL BEFORE INITIAL REPLICATION OF M. TUBERCULOSIS, PULMONARY INFECTION

Manga, Selene, Dr

Background: For lung immune response modulation's better understanding we used cannabinoids immune modulators inducing primary TB lung infection on 32 guinea pigs to study yield of CBD
Methods: Inducing TB lung infection in case control groups,16 on each group; using permanent instillation of droplets containing AFB 106 bacilli by milliliter on droplets looking at lung parenchyma (local immune response at capillary bed, modulated by dendritic cells. Triggering the acquired immune response inducing macrophages straitening by instilling pure cannabinoid solution high distribution rate (~ 32 L/kg)in the alveolar space, sputum /smear-microscopy performed. Used bronchial washings smear.
Results: Replication in the alveolar macrophage after ingesting infected droplet containing acid-fast bacilli (AFB) was measured trough sputum /smear-microscopy. Bronchial washings smear was AFB positive in 11 guinea pigs on the control group (not instilled with cannabinoids solution) while AFB was positive on 3 guinea pigs on the case group. Total yield of CBD instillation was 40.62% (13/32); CBD instillation acts as a protector factor in 60% cases counting the BK isolated at the initial phase of primary infection.
Conclusions: High distribution rate (~ 32 L/kg) was best rate distributed quickly in the guineas pig´s lung. CBD has a protective influence on the macrophages against bacilli. We do assumed that bacilli initial replication in the alveolar macrophage have been taken up by monocytes leaving the local capillary bed, dendritic cells arriving from the airspace surface, from lymphatic capillaries at the very early carriage of bacilli out of the initial sites of implantation, into the draining lymphatic's after instilling cannabinoids the counter-balance between the macrophage attempting to kill the bacillus, bacillus taking counter-measures shows more apoptosis.

IMPLEMENTING AN ENHANCED CASE FINDING STRATEGY FOR CHILDREN AND ADOLESCENTS EXPOSED TO RIFAMPICIN-RESISTANT TUBERCULOSIS: LESSONS FROM KHAYELITSHA, SOUTH AFRICA

Mohr-Holland, Erika, Ms; Apolisi, Ivy, Ms; Reuter, Anja, Dr; Zwide, Fundiswa, Ms; De Azevedo, Virginia, Dr; Seddon, James A, Dr; Trivino-Duran, Laura, Dr; Furin, Jennifer, Dr; Isaakidis, Petros, Dr

Background and Challenges to implementation: It is estimated that 1 million household contacts are exposed to rifampicin-resistant tuberculosis (RR-TB) each year; a minority receive post-exposure care. Where done, post exposure management focuses on children < 5 years or those living with HIV.
However, older children and adolescents are also at risk of developing RR-TB. We describe an enhanced case finding strategy implemented among those 6-18 years of age exposed to RR-TB in the household in Khayelitsha, South Africa.
Intervention or response: The enhanced case finding strategy was implemented by one nurse in Khayelitsha from November 2018. The strategy entailed active case finding with symptom screening, chest X-ray, sputum testing and longitudinal follow-up over the period of a year. We describe challenges and possible solutions to the barriers encountered in the implementation of this strategy.

Number	Barriers	Possible solutions
1	Misperceptions by health care workers and guardians regarding household exposure risk in older children	-Health promotion and education focused the risk of TB among this age group
2	Multiple research and implementation stakeholders in the project setting, leading to difficult engagement and poor buy-in	-Collaboration of various stakeholders in order to streamline activities
3	Additional work-load for an already overburdened healthcare system	-Weekend mobile clinics for contact screening -Community healthcare workers to do follow-up household screenings
4	Potential exposure of healthy children to sick individuals in the healthcare facilities	-Weekend mobile clinics for contact screening
5	Logistical issues faced by families to navigate the screening and diagnostic pathways	-Community health care workers to do follow-up screenings in the contacts household
6	Children are required to miss school in order to attend the health care facility for TB screening	-School-based TB screening initiatives -Strengthen links between the Department of Health and the Department of Education

Table 1. The list of barriers encountered during the implementation of the RR-TB active case finding strategy

Results and Lessons Learnt: Barriers included:
1) Misperceptions by health care workers and guardians regarding household exposure risk in older children;
2) Multiple research and implementation stakeholders

in the project setting, leading to difficult engagement and poor buy-in of healthcare facilities;
3) Additional work-load for an already overburdened healthcare system;
4) Potential exposure of healthy children to sick individuals in the healthcare facilities;
5) Logistical issues faced by families to navigate the screening and diagnostic pathways;
6) Children are required to miss school in order to attend the health care facility for TB screening. Possible solutions to these barriers are described in Table 1.
Conclusions and key recommendations: Several challenges were encountered during implementation of the enhanced case finding strategy. Innovative models of care for contact tracing/post exposure management that consider the needs of families and health care providers need to be further explored, including school-based TB screening initiatives.

FERRET TUBERCULOSIS CO-INFECTION AND TRANSMISSION MODEL

Quinn, Fred, Prof

An animal model that helps us understand and ultimately interfere with tuberculosis (TB) transmission may be the current best path forward to slowing the spread of TB in humans and animals. Additionally, having this model also mimic co-infection dynamics of pathogens such as influenza virus will aid in identifying important contributing factors for successful transmission events.
Unlike rodents, infected larger animals including cattle and non-human primates can effectively transmit *Mycobacterium tuberculosis* and *M. bovis* bacilli to naïve hosts via the aerosol and ingestion routes; however, routine work with statistically-significant numbers of these animals is cost-prohibitive. We know that mice and Guinea pigs infected with virulent mycobacteria develop acute disease and ultimately succumb, however, this is not the variable disease response observed in humans and animals in natural settings; in high-exposure locations, TB contacts develop acute disease but remain TST-negative and free of the pathogen, remain TST-negative but culture positive, or become TST-positive but remain culture negative.
In other words, natural transmission results in variable responses. Ferrets are widely employed to study the transmissibility of influenza and other respiratory viruses, but thus far, no studies examining these transmission parameters for *M. bovis* and *M. tuberculosis* have been reported. Our team has generated exciting data demonstrating that ferrets can become infected when given intratracheal *M. tuberculosis* or *M. bovis* bacilli, and the varied disease states observed in infected humans/animals also are observed in infected ferrets.
Most importantly, natural transmission occurs when infected transmitter animals interact with naïve sentinels, and disease severity is exacerbated when co-infected with influenza virus; an epidemiological observation that until now has lacked an animal model for study.
This information will inform the TB community of the value of the ferret as an intermediate model to nonhuman primates and cattle, and provide a roadmap for examining transmission prevention.

AN ATTENUATED QUADRUPLE GENE MUTANT OF MYCOBACTERIUM TUBERCULOSIS IMPARTS PROTECTION AGAINST TUBERCULOSIS IN GUINEA PIGS

Mathur, Shubhita, Dr; Kar Bahal, Ritika, Dr; Chauhan, Priyanka, Dr; K. Tyagi, Anil, Prof

Introduction: *Mycobacterium tuberculosis*, the causative agent of human tuberculosis, is a major cause of mortality. BCG, the only licensed vaccine available for protection against tuberculosis confers highly variable protection ranging from 0%-80%. Thus, novel vaccine strains need to be evaluated for their potential as vaccine against tuberculosis. We had previously constructed a triple gene mutant of *M. tuberculosis (Mtb*Δ*mms)*, having deletions in genes encoding for phosphatases *mptpA, mptpB* and *sapM* that are involved in host-pathogen interaction. Though vaccination with *Mtb*Δ*mms* strain induced protection in the lungs of guinea pigs, the mutant strain was not able to control the hematogenous spread of the challenge strain to the spleens. Additionally, inoculation with *Mtb*Δ*mms* resulted in some pathological damage to the spleens in the early phase of infection.
Method: To overcome the pathology caused by *Mtb*Δ*mms* in the spleens of guinea pigs and also to control the dissemination of the challenge strain, *Mtb*Δ*mms* was genetically modified by disrupting *bioA* gene to generate *Mtb*Δ*mmsb* strain. Further, *in vivo* attenuation of *Mtb*Δ*mmsb* was evaluated and its protective efficacy was assessed against virulent *M. tuberculosis* challenge in guinea pigs.
Results: Our study demonstrates that *Mtb*Δ*mmsb* mutant was highly attenuated for growth and virulence in guinea pigs. Vaccination with *Mtb*Δ*mmsb* mutant generated significant protection in comparison to sham-immunized animals at 4 and 12 weeks post-infection in lungs and spleens of the infected animals.
Discussion: Our findings provide evidence that deletion of genes involved in signal transduction and biotin biosynthesis severely attenuates the pathogen and the single immunization with the auxotroph was able to provide significant protection as compared to sham-immunized animals. The protection imparted by *Mtb*Δ*mmsb* fell short in comparison to the protection observed in BCG-immunized animals. This study nevertheless indicates the importance of attenuated multiple gene deletion mutants of *M. tuberculosis* in generating protection against tuberculosis.

BIOA MUTANT OF MYCOBACTERIUM TUBERCULOSIS SHOWS SEVERE GROWTH DEFECT AND IMPARTS PROTECTION AGAINST TUBERCULOSIS IN GUINEA PIGS

Mathur, Shubhita, Dr; Kar Bahal, Ritika, Dr; Nangpal, Prachi, Dr; Singh, Swati, Dr; K. Tyagi, Anil, Prof

Introduction: *Mycobacterium tuberculosis*, the causative agent of human tuberculosis, continues to be a major cause of mortality worldwide. The BCG vaccine shows variable efficacy against adult pulmonary tuberculosis. Thus, a more efficient vaccine is required for the global control of tuberculosis. Attenuated *M. tuberculosis* strains have shown promise as potential BCG replacement vaccines. Several evidences support the essentiality of biotin biosynthesis for the *in vitro* as well as *in vivo* survival of mycobacteria.
Method: In this study, we constructed a *bioA* mutant of *M. tuberculosis* (MtbΔ*bioA*) and demonstrated its attenuation in the highly susceptible guinea pig model of tuberculosis following administration via the aerosol as well as intradermal route. Subsequently, the MtbΔ*bioA* strain was evaluated for its ability to protect against virulent *M. tuberculosis* challenge in the guinea pigs.
Results: Following aerosol infection with MtbΔ*bioA*, no bacilli were recovered from the lungs at 6 weeks post infection and from the spleen at 12 weeks post infection. Limited survival of the biotin auxotroph in the host tissue was concomitantly associated with negligible granulomatous pathology. Additionally, following the intradermal administration of MtbΔ*bioA* in guinea pigs, the bacillary numbers rapidly declined and were undetectable in the lungs by 3 weeks and in spleen by 6 weeks post inoculation. Importantly, in comparison to sham immunized animals, *Mtb*Δ*bioA* immunized animals exhibited a significant reduction of 1.5 log10 CFU and 2.4 log10 CFU in the lungs and spleens respectively.
Discussion: The study demonstrates that disruption of *bioA* renders *M. tuberculosis* severely attenuated for growth and virulence in guinea pig tissues when administered via the aerosol as well as intradermal route. Immunization with MtbΔ*bioA* conferred significant protection in guinea pigs against an aerosol challenge with virulent *M. tuberculosis*, when compared with the unvaccinated animals. The protection imparted by *Mtb*Δ*bioA* was comparable to that conferred by BCG.

ECONOMIC BURDEN AND INCIDENCE OF CATASTROPHIC EXPENDITURE OF TB DISEASES IN ETHIOPIA.

Fekadu Assebe, Lelisa, Mr

Background: Tuberculosis (TB) is a major global public health threats. The diseases is a major cause of morbidity and mortality. In the past decade, the scale up of TB treatment increased access to care. Though many countries offer ''free'' and ''decentralized'' treatment services, this strategy does not avoid the major cost burden that often expose households to catastrophic health expenditure (CHE) and impoverishment. A gap in knowledge exist, whether the existing subsidies for the disease are providing reasonable financial risk protection or not. Hence, this paper aimed to estimate the economic burden and incidence of CHE incurred by TB clients in Ethiopia.
Methods: Health facility-based cross-sectional study was employed between December 2018- July 2019. We analysed the incidence of catastrophic total cost using, as thresholds, >20% of household income. The sample size was 444. Analyses were carried out using STATA version 15.
Results: The median age of patients was 28 years (IQR 20–38) and 52% of them were female. The median family size was 4 (IQR: 3-6). Among respondents, 6% of them were co-infected with HIV. The direct cost of TB illness amount to median (IQR) US$ 28 (9.4–61.4) and constitute 32% of the total cost. The medical costs constituted only 46% of the total direct cost, while nonmedical costs accounted 54%. Patients had lost a median of US$39.9 (14.1–99.9) indirect cost. Total costs incurred amount to a median (IQR) of US$81.4 (35.9–173.8) which is equivalent to 25% of median annual individual incomes. About 49% and 51% of the total cost was spent before and after TB was diagnosed, respectively. The incidence catastrophic payment was 58.7%.
Conclusion: TB has caused a substantial economic burden and CHE for patients. Therefore, government benefit package needs to be broadened to encompass measures that reduce the substantial direct and indirect costs associated with disease.

IMMUNIZATION OF MICE WITH ETHANOL-KILLED MYCOBACTERIUM TUBERCULOSIS GENERATED MONOCLONAL ANTIBODIES AGAINST CELL WALL PEPTIDOGLYCAN

Sei, Clara J., Ms; Rikhi, Nimisha, Dr; Schuman, Richard F., Dr; Fischer, Gerald W., Dr

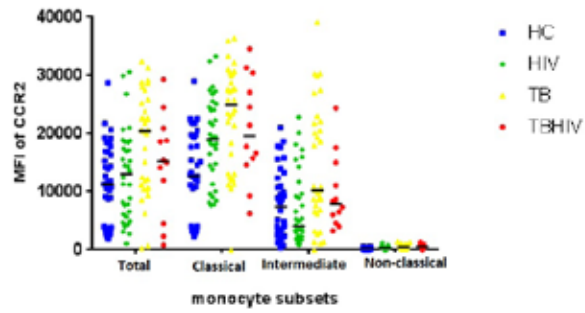
Background: Monoclonal antibodies (MABs) generated from mice immunized with ethanol-killed *Mycobacterium tuberculosis* (MTB) have previously been shown to bind to live *Mycobacterium smegmatis* (SMEG) and several strains of live MTB – susceptible, MDR and XDR, as well as enhance the opsonophagocytic killing of SMEG and MTB, using macrophage and granulocytic cell lines. In the current study we provide data showing that the anti-MTB MABs bound to cell wall Peptidoglycan (PGN). These anti-MTB-anti-PGN MABs also bound to several other live gram-positive bacteria.
Methods: BALB/c mice were immunized subcutaneously with ethanol-killed MTB (EK-MTB) and screened by ELISA for antibodies that bound to killed MTB and live SMEG using a novel Live Bacteria ELISA (LBE) assay. To

determine cell wall recognition, two anti-MTB MABs (GG9 and JG7) and an anti-LTA MAB (96-110) were analyzed for binding to a cell wall mixture and Ultrapure PGN, both from *Staphylococcus aureus*. These anti-MTB MABs were also screened on selected live Staphylococci, Bacilli, and Streptococci species in the LBE assay.
Results: EK-MTB elicited a strong humoral response in mice and two opsonophagocytic anti-MTB MABs – GG9 and JG7 were generated. These MABs @2ug/mL were shown to bind to a cell wall mixture as well as highly purified PGN (both @10ng/mL) with OD450nm of 3.0 each. The anti-MTB MABs also bound to *S. epidermidis, S. aureus, B. subtilis,* and *Group B Streptococcus.*
Conclusion: Mice immunized with EK-MTB had a robust humoral response against MTB. Ethanol may have altered the MTB capsule, exposing deeper cell wall epitopes. Anti-MTB MABs GG9 and JG7 bound to an epitope on PGN, a common bacterial cell wall component, and recognized a cell wall epitope on several other gram-positive bacteria. These data might be useful in developing strategies for MAB therapeutics and could provide new options for broadly reactive vaccines against MTB and other gram-positive bacteria.

ELEVATED EXPRESSION OF CHEMOKINE AND ADHESION RECEPTORS ON MONOCYTE SUBSETSIN IN TB AND HIV

Tamene, Wegene, Ms; Marconi, Vincent, Dr;
Abebe, Meseret, Ms; Wassie, Liya, Dr; Kassa, Desta, Dr

Background: Monocytes are an innate immune cells with wide elasticity in function. Recent studies have revealed phenotypic and functional heterogeneity of these cells. Different studies reported various impact of HIV on the normal phenotype and function of monocytes. However, few studies have characterized monocytes in detail in TB disease, in particularly in TBHIV co-infection. Therefore, this study aims to define chemokine and adhesion receptors expression on multiple monocyte subsets among patients with TB, HIV and TBHIV co-infection.
Method: We had four adult groups: TB (n=34), HIV (n=35), TBHIV (n=12) and Healthy controls (n=39) recruited from health facilities in Addis Ababa, Ethiopia. All TB and HIV patients were treatment naïve. Peripheral blood mononuclear cells were isolated and stained with a panel of flurochrome conjugated monoclonal antibodies specific for the indicated molecules, acquired on the FACSCanto flow cytometry and analyzed by Flowjo 9.4 and JMP v. 6.0.2 software. Comparison between groups was made using non-parametric Kruskal Walles test. Results considered statistically significant when p-value < 0.05.
Result: Patient groups had significantly higher intermediate (CD14+CD16+) or non-classical CD14-CD16+) monocyte subsets. There was upregulation of chemokine receptors and adhesion molecules in patients with TB and/or HIV. TB patients had significantly higher levels of CCR2, CX3CR1 and CD54, whereas patients with HIV had higher levels of CCR4 and CCR5. In general, disease specific changes for a given marker, such as CCR2, were seen in all monocyte subsets, but were most pronounced within the intermediate monocytes subset.



Conclusion: This study reveals both disease specific changes in the distribution of monocyte subsets as well as the expression of multiple markers within each subset. Future studies will be aimed to correlate monocyte phenotype with levels of multiple serum biological mediators. Such correlations may lead to mechanisms involved in and identifying immune correlates.

WHOLE BLOOD MIRNAS: SEARCH FOR BIOMARKERS OF TUBERCULOSIS INFECTION LEADING TO DISEASE DEVELOPMENT

Hijikata, Minako, Dr; Nguyen Thi Le, Hang, Dr;
Do Bang, Tam, Dr; Seto, Shintaro, Dr;
Vu Cao, Cuong, Dr; Hoang Van, Huan, Dr;
Pham Huu, Thuong, Dr; Keicho, Naoto, Dr

Background: Recently host biomarkers of tuberculosis (TB) infection leading to disease development have been widely investigated. We have hypothesized that host microRNA (miRNA) signatures in the peripheral whole blood are correlates of TB infection, and analyzed comprehensive miRNA expression profiles using massively parallel sequencing methods to find candidate miRNAs.
Methods: Healthcare workers (HCWs) in Hanoi Lung Hospital and district TB centers in Hanoi, Vietnam were enrolled and followed up (n=109). Their status of TB infection was initially assessed using interferon-gamma release assays (IGRA), and whole blood samples were collected into PAXgene Blood RNA tubes (PreAnalytiX QIAGEN/BD), and their total RNAs were extracted. Small RNA libraries were prepared from IGRA-positive (n=5) and IGRA-negative (n=7) samples, and amounts of miRNAs were analyzed using a NextSeq 500 sequencing platform (Illumina). The expression levels of the candidate miRNAs in the whole blood were also determined in the HCWs by real-time RT-PCR.
Results: Approximately 1,000 miRNA sequences, which could be categorized into 150 miRNA families, were detected, and the number of sequence reads was compared

between the groups. We extracted candidate miRNAs of which expression levels were significantly higher in the IGRA-positive group than in the IGRA-negative group after multiple comparisons adjustment. Higher expression in IGRA-positive group (n=41) than in IGRA-negative group (n=68) was further confirmed in one of the five miRNAs using real-time RT-PCR ($P = 0.0286$). Possible associations of epidemiological events during the follow up period are currently investigated.
Conclusions: The role of miRNAs as biomarkers is expanding, and we found candidates of miRNA, possible correlates of TB infection. It is necessary to validate their expression levels, and to investigate their functional roles in the host immune changes leading to TB development further.

CAN BLOOD LEUCOCYTE IMMUNOPHENOTYPING HELP EXPLAIN THE HIGH BURDEN OF EXTRA PULMONARY TUBERCULOSIS IN REGIONAL PAPUA NEW GUINEA?

Rush, Catherine, Dr; Diefenbach-Elstob, Tanya, Dr; Dowi, Robert, Mr; Pelowa, Daniel, Mr; Gula, Bisato, Ms; McBryde, Emma, Prof; Warner, Jeffrey, Dr

Background: The burden of tuberculosis in Papua New Guinea is amongst the highest in the world. We have recently reported case notification rates in the remote Balimo District, Western Province to be 729 cases per 100,000 with the majority (77%) clinically diagnosed extrapulmonary TB (EP-TB). The global prevalence of EP-TB is 15%.
Aims: As no diagnostic investigations for EP-TB are routinely available on-site, we evaluated the utility of blood leucocyte immunophenotyping by remote flow cytometry to support these EP-TB diagnoses. Furthermore as severely immunocompromised individuals have a greater risk of extrapulmonary and disseminated forms of TB, we analysed blood from uninfected and latently infected individuals, health workers and TB patients prior to and during treatment with the aim of identifying immune cell deficiencies and defects that may help explain the TB susceptibility and unusual disease pattern in this location.
Methods: Cyto-Chex-stabilised blood collected from Balimo participants (n=270) was transported for analysis in Townsville, Australia within 8 days. We used a multiparameter immunophenotyping approach with both conventional flow cytometry gating and t-distributed stochastic neighbour embedding (t-SNE) mapping algorithms to compare and visualise complex leucocyte sub-populations across TB type (LTBI, EP-TB, P-TB) and participant groups.
Results: Our conventional and t-SNE analysis revealed that immune cell profiles from participants with an EP-TB clinical diagnosis mirrored those with P-TB, supporting the EP-TB diagnosis and high EP-TB rates. For EP-TB and P-TB we observed increased frequencies of $CD16^+$ neutrophils, $CD64^+$ monocytes with depleted $CD19^+$ B cells, $CD4^+$ (and subsets) and $CD8^+$ T cells and innate lymphoid cells (NK, NKT, MAIT, ILCs) compared to walking well participants (uninfected, LTBI).
Conclusion: Immunocompromised individuals are at increased risk for EP-TB and understanding the drivers of immune compromise in TB endemic regions can be investigated by detailed characterisation of immune responses even in blood collected at very remote settings.

TIMELINESS AND PATTERN OF DRUG RESISTANCE TUBERCULOSIS: LINE PROBE ASSAY (LPA) IN NORTH-CENTRAL NIGERIA

Bimba, John, Dr; Uwaezuoke, Ndubuisi, Dr; Akinwande, Michael, Mr; Babawale, Victor, Dr; Iwakun, Mosunmola, Ms; Chijioke-Akaniro, Obioma, Dr; Lawson, Lovett, Prof

Introduction: Early detection, prompt and appropriate management of patients with Drug Resistance Tuberculosis (DR TB) is important in the fight to end TB by 2030. The use of line probe assay to report drug-resistant patterns and identify patients who can be placed on the shorter regimen can help to reduce the burden of DR TB in Nigeria.
Methodology: The data was generated from January to March 2019 at Zankli Reference Laboratory. One hundred and three (103) consecutive sputum specimens were collected from presumptive DR-TB patients in over 30 health facilities across five states in north-central Nigeria with SPSS version 24 software used for data analysis.
Results: Presumptive DR TB patients aged 21- 40 years (56.3%) are twice 41 - 60 years (28.2%). Up to 23.3% of the specimen arrived at the laboratory after a week and less than half (42.7%) within three days. The mean (SD) distance from health facilities to the Reference laboratory was 211km (113). Mycobacterium tuberculosis complex (MTBC) isolates show that 64.3% are resistant to rifampicin, whereas above 80.3% are susceptible to isoniazid and other second-line drugs. Almost 60% of the results sent to the health facility are between 4 -7 days, with 40% less than three days.
Conclusion: Rifampicin resistance is a growing problem. Hence prompt laboratory responses and appropriate drug regimen placement will go a long way in reducing TB burden in Nigeria.

T CELL SUBSETS AND CYTOKINES IN HIV+ INDIVIDUALS WITH LATENT AND ACTIVE TUBERCULOSIS

Neela, Venkata Sanjeev Kumar, Dr;
Devalraju, Kamakshi Prudhula, Ms;
Vankayalapati, Ramakrishna, Prof;
Valluri, Vijaya Lakshmi, Dr

Background and rationale: *Mycobacterium tuberculosis* (Mtb) causes almost 1.4 million deaths annually. Of the 50% of household contacts of tuberculosis (TB) patients who develop latent tuberculosis infection (LTBI), most remain well, but 10% eventually develop TB. Human immunodeficiency virus (HIV) infection increases the risk of LTBI progressing to active TB. IL-17 and IL-22 cytokines play an important role in protective immune responses against Mtb infection. Information on the production of these cytokines and the factors that regulate these cytokines in HIV+LTBI+ with or without or active TB is limited. We compared the production of these two cytokines by PBMC of HIV-LTBI+ and HIV+LTBI+ individuals in response to Mtb antigens CFP-10 and ESAT-6.

Methods: PBMCs (Peripheral Blood Mononuclear Cells) were isolated from blood (20 mL) collected from HIV- individuals and HIV+ patients with latent tuberculosis and active disease. PD1 (Programmed Death 1), ICOS (Inducible T-cell Costimulator), IL-23R and FoxP3 (Forkhead box P3) expression by CD4+ T cells was assessed by flow cytometer. Remaining PBMC were cultured with ESAT6 and CFP-10 for 96 hours. IL-17 and IL-22 levels were measured in culture supernatants by ELISA.

Results: In response to Mtb antigens CFP-10 and ESAT-6, PBMCs from HIV+ LTBI+ and HIV+ active TB patients produced low IL-17 and IL-22 and high IL-10, expressed low IL-23R, and high PD1 and expanded to more FoxP3+ cells. Active TB infection in HIV+ individuals further inhibited antigen specific IL-17 and IL-22 production compared to those with LTBI. Neutralization of PD1 restored IL-23R expression, IL-17 and IL-22 levels and lowered IL-10 production and reduced expansion of FoxP3 T cells.

Conclusion: Increased PD1 expression in HIV+LTBI+ and HIV+ active TB patients inhibits IL-17, IL-22 production and IL-23R expression in response to CFP-10 and ESAT-6.

Funding: This study is supported by ICMR-NIH (No: 5/8/3(13)/2009-ECD-I (A)).

THE CAPTURE AND VISUALIZATION OF LIVE MYCOBACTERIUM TUBERCULOSIS BACILLI FROM TUBERCULOSIS-PATIENT BIO-AEROSOLS.

Dinkele, Ryan, Mr; Gessner, Sophia, Dr;
Morrow, Carl, Dr; Kamariza, Mireille, Dr;
Bertozzi, Carolyn, Prof; Mizrahi, Valerie, Prof;
Kamholz, Andrew, Dr; Bryden, Wayne, Dr;
Call, Chuck, Dr; Wood, Robin, Prof;
Warner, Digby, Prof

Mycobacterium tuberculosis (Mtb) is the causative agent of tuberculosis (TB) and the leading killer due to an infectious disease worldwide. For almost seventy years, TB control efforts have been predicated on chemotherapeutic intervention in active disease, an approach increasingly undermined by the propagation of drug-resistant Mtb strains. Consequently, there is renewed interest in alternative approaches to reduce the TB burden. Given its importance in maintaining elevated TB prevalence rates, disrupting Mtb transmission represents a potentially tractable strategy for disease control; however, this demands a greater understanding of the factors influencing the successful transmission of Mtb. To address this challenge, we utilized advanced, high-efficiency sampling technologies that allows biosafe, non-invasive capture and isolation of patient derived biological and particulate matter – including Mtb bacilli. Here, we detail the use of live-cell fluorescence microscopy of these bioaerosol samples to enable quantitative detection, visualization, and characterization of Mtb bacilli released by confirmed TB patients in a clinical setting. Applying the fluorogenic probe, DMN-trehalose (DMN-tre), we demonstrate the capacity to differentiate between mycobacterial growth states and discriminate Mtb from corynebacteria - a major constituent of the aerosol microbiome with capacity for trehalose incorporation. Finally, applying this capture and detection protocol in a small pilot study, we identified Mtb in ~75% of diagnostically confirmed TB cases. This represents a significant improvement on previous work utilizing animal infection and cough sampling to estimate transmission events and supports the utility of this platform for research aimed at identifying critical points for intervention to interrupt Mtb transmission.

DEFECTIVE MONOCYTE SIGNALING PATHWAY IN HIV+ INDIVIDUALS WITH LATENT TUBERCULOSIS INFECTION

DEVALRAJU, KAMAKSHI PRUDHULA, Miss;
Neela, Venkata Sanjeevkumar, Dr;
Vankayalapati, Ramakrishna, Prof;
Valluri, Vijaya Lakshmi, Dr

Background and rationale: HIV infection markedly increases the likelihood of latent tuberculosis infection (LTBI) progressing to active tuberculosis (TB). We determined TLR2, MyD88 and IRAK4 expression and cytokine production by CD14+ monocytes obtained from peripheral blood mononuclear cells (PBMCs) of HIV-LTBI+, HIV+LTBI+ individuals, HIV+TB+, HIV-TB+ patients and pleural fluids of TB patients with and without HIV infection.
Methods: Freshly isolated monocytes from HIV- and HIV+ individuals with and without LTBI were cultured in the presence or absence of γ-irradiated Mtb. IL-1β, TNF-α, and IL-10 levels in the culture supernatants and the expression of signalling molecules involved in these cytokines production was determined.
Experimental plan. To identify TLR2 expression by freshly isolated PBMCs, flowcytometry was performed. CD14 cells were isolated by immunomagnetic selection and cultured with γ-irradiated Mtb. After 48h, culture supernatants were collected to measure cytokine and chemokine levels by multiplex. RNA was collected to perform Real time PCR.
Results: We found significantly higher percentages of CD14+TLR2+ cells in PBMCs of HIV+LTBI+ patients compared to HIV-LTBI+ individuals. γ-irradiated Mtb was unable to induce MyD88, IRAK4 expression and IL-1β, MCP-1, IP-10 production in HIV+LTBI+ patients. Pleural fluids from HIV+TB+ patients had low IL-1β, MCP-1, IP-10 and high IL-10, TNF-α production. γ-irradiated Mtb stimulated CD14+ cells from HIV+TB+ patients had low IL-1β, MCP-1, IP-10 production and MyD88, IRAK4 and similar NF-kB expression compared to those from of HIV-TB+ patients.
Conclusions: Our results suggest defective expression of MyD88, IRAK4 but not NF-kB inhibit IL-1β, MCP-1 and IP-10 production by CD14+ cells of HIV+ individuals with LTBI and active TB disease. Stimulation with TLR2 agonist is unable to induce the MyD88 and IRAK4 expression and IL-1β, MCP-1, IP-10 production.
Funding: This project is supported by ICMR-NIH (No: 5/8/3(13)/2009-ECD-I (A)).

HOW MIGHT NOVEL VACCINES FOR PREVENTION OF TUBERCULOSIS DISEASE IMPACT MULTIDRUG RESISTANT TUBERCULOSIS BURDEN? A MATHEMATICAL MODELLING BASED ANALYSIS OF EPIDEMIOLOGIC AND HEALTH ECONOMIC IMPACT

Weerasuriya, Chathika, Mr; Harris, Rebecca, Dr;
Bozanni, Fiammetta, Ms; Gomez, Gabriela, Dr;
White, Richard, Prof

Background: We model the potential impact of novel prevention of disease vaccines on MDR-TB burden in China and India and identify vaccine characteristics likely to contribute most towards achieving the 2030 UN SDG and 2050 WHO End TB targets.
Methods: We constructed an age-stratified, deterministic, compartmental dynamic transmission model of TB, including treatment history, drug resistance and vaccination strata. We fitted "baseline" (no new vaccine) scenarios to historic epidemiological data and projected (MDR-)TB epidemiology until 2050 in China and India, with and without scaled-up future programmatic MDR-TB management.
Within these baseline scenarios we simulated TB vaccination from 2027, with (1) efficacy pre-infection, post-infection or pre- and post-infection, (2) 5-years to lifelong duration of protection, (3) and 30-90% prevention of disease efficacy. We simulated routine vaccination of 9-year olds, with 10-yearly adult mass campaigns. We then compared MDR-TB incidence and mortality between future scenarios with- and without vaccination.
We estimated economic costs from a health service perspective to calculate incremental cost-effectiveness ratios as incremental costs per disability-adjusted life year averted and budget impact of vaccination.
Results and Conclusions: Prevention of disease vaccination will likely contribute towards reducing MDR-TB burden, even alongside scaled-up programmatic management. In China, such scale up altered the primarily transmission-driven MDR-TB epidemic towards a mixed transmission-reactivation driven epidemic, improving the effectiveness of post-infection vaccines relative to pre-infection vaccines. Analyses for India and vaccine cost-effectiveness and budget impact analysis in China are underway.
We present the first dynamic model of TB which includes both vaccines and MDR-TB, whose results are important for informing decisions in vaccine development, and programmatic considerations in efforts to end TB.

SCREENING OF HEALTH CARE WORKERS IN KYRGYZ TB-HOSPITALS WITH QUANTIFERON-TB GOLD PLUS -- SURPRISINGLY HIGH LTBI RATES AMONG STAFF OF LABS AND DRUG RESISTANT TB

Hoffmann, Harald, Dr; Kadyrov, Abdylat, Prof; Umetalieva, Nagira, Ms; Iskakova, Altyn, Ms; Vogel, Monica, Ms; Kalmambetova, Gulmira, Ms; Ahmedov, Sevim, Dr; Kosimova, Dilorom, Ms

Health Care Workers (HCW) in TB facilities of high-incidence countries belong to the populations with highest risk of TB-infection. In high-resistance countries like Kyrgyzstan where approximately 30% of TB patients have MDR-TB, HCW are exposed to the particular danger of drug-resistant forms of TB.

We investigated the individual risk of HCW to be infected and identified factors associated with risk of TB infection. In 2019, the Kyrgyz NTP screened staff of four hospitals with the WHO endorsed QuantiFERON-TB providing higher specificity than the TST in Kyrgyzstan where >90% of the population is BCG vaccinated. A positive QuantiFERON without TB specific symptoms or radiological findings was considered probable latent TB infection (LBI). In the peripheral hospitals of Kemin, Kara-Balta and Karakol, LTBI was less frequent (38-39%) than in the Republican TB Center (54%). Hospital staff with lowest risk of LTBI were administration and technical workers (15-30%), while laboratory staff (68%) and attending doctors (63%) had the highest risk. Resident doctors, nurses and cleaners had LTBI rates around 50%. PDR-TB- and smear-negative TB-departments were the clinical wards with highest, pediatric wards with the lowest LTBI rates among HCW. Sequential testing in the hospital of Karakol, the smear-positive and the MDR-TB departments of the NTC over several months revealed that the risk to convert from negative to positive (considered as newly acquired LTBI) was highest in the MDR-TB department.

In the smear-negative TB department, 12% more HCW had LTBI than in the smear-positive TB department. In clinical departments, negligence to use respirators and other WHO recommended protection gear were identified as strong risk factor for LTBI. The infectious potential of smear-negative TB seems to be largely underestimated. Work in older premises seems to bear lower risk of LTBI potentially due to constant air convection through leaky windows.

Poster Theme: New strategies in TB therapeutics: It's time to break the mould!

FNDR-20081- A NOVEL PRE-CLINICAL CANDIDATE FOR TREATMENT OF TB/MDR TUBERCULOSIS

Kaur, Parvinder, Dr; Potluri, Vijay, Dr; Ahuja, Vijay Kamal, Mr; Naveenkumar, C N, Dr; Shruthi, T G, Mx; Shivarudraiah, Prasad, Dr; Eswaran, Sumesh, Dr; Shandil, Radha Krishan, Dr; Narayanan, Shridhar, Dr

There is an urgent medical need to develop novel-tuberculocidal drugs to combat MDR or XDR-TB. We report a novel, first in class lead candidate, FNDR-20081, with MIC of 2 μg/ml on sensitive, SDR (Isoniazidr, Rifampicinr, Ethambutolr and Streptomycinr), and MDR-TB isolates (0.5-16μg/ml) of *Mycobacterium tuberculosis* (Mtb). In-vitro combination studies of FNDR-20081 with first line drugs (Isoniazid, Rifampicin and Ethambutol) and second line drugs (Amikacin, Capreomycin, Kanamycin, D-cycloserine and Fluoroquinolones) exhibited no antagonism; suggesting its fitment into the combination-regimens.

FNDR-20081 is mycobactericidal in in-vitro killing kinetic assays, with exposure dependent killing of replicating Mtb (Emax=2.1 log10 cfu/ml). It is also bactericidal on non-replicating Mtb (Low pH =1.2 log10 cfu/ml, Nutrient starvation=0.7 log10 cfu/ml), and in THP-1 human macrophages (Emax=1.24 log10 cfu/ml).

FNDR-20081 is metabolically stable with no CYP liability (IC50 >25μM), and no HepG2 cytotoxicity (>100 μM). It is orally bioavailable, with plasma exposures above MIC (Cmax of 7.443 and 3.182 μg/ml, and AUClast 11.861 and 8.252 h*μg/ml) at 0 and 28 day post infection respectively. In in-vivo efficacy studies, FNDR-20081 exhibited a statistically significant 0.6 log10cfu reduction ($p<0.05$) in lungs of Mtb infected mice at 100 mg/kg dose.

In summary, FNDR-20081 is a novel first in class compound with a potential to develop new combination regimens for the treatment of MDR TB.

ALL ORAL SHORT-COURSE REGIMENS FOR THE TREATMENT OF RR-TB: EARLY EXPERIENCES FROM KHAYELITSHA, SOUTH AFRICA

Reuter, Anja, Dr; Mohr-Holland, Erika, Ms; Acquah, Rebecca, Dr; Cox, Helen, Dr; Cox, Vivian, Dr; De Azevedo, Virginia, Dr; Mudaly, Vanessa, Dr; Hughes, Jennifer, Dr; López, Paola, Dr; Furin, Jennifer, Dr

Background: South Africa's national department of health - supported by stakeholders, a clinical advisory committee, and a national surveillance system - recently became the first country to implement an all-oral short course regimen (SCR, 9-11 month regimen starting with Linezolid – Bedaquiline - Clofazimine – Ethambutol – Pyrazinamide – Levofloxacin – high-dose Isoniazid) for rifampicin-resistant tuberculosis (RR-TB).
Methods: This retrospective cohort study included all persons initiated on RR-TB treatment between November 2018 and March 2019 in Khayelitsha. Exclusion criteria for the SCR included haemoglobin <8 g/dL, extensive or extra-pulmonary disease, suspected or demonstrated second-line drug resistance, and previous exposure to second-line agents for >1 month. We describe characteristics of patients who received the SCR as well as exclusion criteria.
Results: Overall, 34 patients were started on treatment for RR-TB; 18 (53%) on the SCR. Of those on the SCR, 10 (56%) were males, median age 31 years (interquartile range [IQR] 24-38), 7 (39%) had previous exposure to first-line TB drugs, and 10 (56%) were HIV-infected with a median baseline CD4 count of 46 copies/mm3 (IQR 5 – 100). All 18 had rifampicin-resistance detected on GeneXpert; molecular line probe assay found 5 (28%) to have rifampicin mono-resistant TB and 10 (56%) multi-drug resistant TB without second line resistance. The median baseline haemoglobin was 10.8 g/dl (IQR: 9.9-12.1). Of the 16 (47%) excluded from the SCR: 2 (13%) had extra-pulmonary TB; 4 (25%) prior exposure to second line drugs; 3 (5%) RR-TB with fluoroquinolone and/or injectable resistance and 3 (5%) a baseline haemoglobin <8g/dL.
Conclusion: Over half of patients were eligible for the SCR. Early reporting on the eligibility for the regimen can be used to guide other programmes considering all-oral SCR in their settings.

RESPONDING TO THE SUBSTANCE USE CHALLENGE IN RIFAMPICIN-RESISTANT TUBERCULOSIS: PRELIMINARY OUTCOMES OF A PRIMARY HEALTH CARE SUBSTANCE USE MANAGEMENT MODEL IN KHAYELITSHA, SOUTH AFRICA

Reuter, Anja, Dr; Mohr, Erika, Ms; Rodriguez, Erickmar, Ms; De Azevedo, Virginia, Ms; Domingo, Abdul Kader, Dr; Isaakidis, Petros, Dr; Snyman, Leigh, Ms; Vermeulen, Marcia, Ms; Weich, Lize, Dr; Trivino-Duran, Laura, Dr

Background: Substance use (SU) is associated with poor rifampicin-resistant tuberculosis (RR-TB) treatment outcomes. In 2017, Medicines Sans Frontieres and department of health integrated screening, brief intervention and referral to treatment (SBIRT) into the RR-TB treatment programme. Here we describe early experiences of the use of the SBIRT.
Methods: This was an observational cohort of patients with RR-TB who were screened for SU between October 2017-March 2019 in Khayelitsha, South Africa. Screening was conducted using the ASSIST or the AUDIT. Patients who scored moderate or high-risk were referred to a SU support group; those with moderate or high-risk alcohol use and considered eligible by a clinician, were offered naltrexone. Here we describe the number screened, risk category, and number started on naltrexone.
Results: Overall, 102 RR-TB patients were screened for SU, 48 (47%) were females and the median age at RR-TB diagnosis was 37 years (interquartile range [IQR] 31-45); 79 (77%) were HIV co-infected. Ninety two (90%) patients reported SU, with 37/92 (40%) using more than one substance; 65/92 (71%) scored moderate or high-risk for at least one substance. Overall patients reported using the following: 86/92 (93%) alcohol, 40/92 (43%) tobacco, 11/92 (12%) cannabis, 4/92 (4%) mandrax, 3/92 (3%) methamphetamines, and 1/92 (1%) cocaine. Twenty two (35%) of the 65 moderate or high-risk patients attended a support group at least once.
Of the 86 patients that reported alcohol use, 35 (41%), 16 (18%), and 35 (41%) scored low, moderate, and high-risk, respectively. Of the 51 patients that scored moderate or high-risk, 48 (94%) received a brief intervention, 34/48 (71%) were offered naltrexone and 17/34 (50%) initiated naltrexone.
Conclusions: Moderate and high-risk SU was common among the RR-TB patients screened; alcohol was the most common substance reported. Integrating SBIRT, pharmacotherapy and support groups into primary health RR-TB care could be beneficial.

MULTIDRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS STRAINS IN SAUDI ARABIA: MYTH, REALITY AND WORLDWIDE IMPACT.

AL-Hajoj Al-Nakhli, Sahal, Prof

Several studies documented that Saudi Arabia is suffering from high level of Multidrug resistant *Mycobacterium tuberculosis* complex (MDR-MTBC) strains. Some of these studies even reported 44% MDR-TB rate, other studies showed variation of MDR-TB within different cities.

However, as per our nationwide prospective study, guided by the World Health Organization, we found that the country is not suffering from high level of drug resistance. We consider this finding as the first reality, as all previous studies were small, retrospective, fragmented, not guided and not nationwide. The second reality is that the country is suffering from an ongoing transmission. This is evidenced by high cluster rates obtained upon genotyping more than 4000 isolates. This ongoing transmission is caused by unmatched huge clade diversity. Thereby, cross-border transmission of MDR-MTBC strains might be particularly fostered by high immigration influx and mobility dynamics.

In an exploratory study, we investigated 71 MDR-MTBC strains collected from provincial mycobacteria referral laboratories in Saudi Arabia and compared demographic and clinical parameters to a convenient cohort of non- MDR-TB patients using whole genome sequencing approach. This guided us to third reality which indicates that the country is suffering from persistence of MDR-MTBC strains. It is worth mentioning that some patients are re-infected with MDR-MTBC strains. Persistence of MDR-MTB strains may lead to the development of extensively drug resistant strains. 22•5% of enrolled isolates were already predicted to be fully resistant to all five first-line drugs and (7•0%) exhibited fluoroquinolone resistance conferring mutations.

Last but not least, our accumulated data showed that the nature of an ongoing transmission is admixing. This is totally opposite to the picture in Europe and elsewhere. Optimized TB molecular surveillance, diagnosis, and patient management are urgently needed to contain MDR-MTBC transmission and development of additional drug resistances.

ADVERSE REACTIONS IN TREATMENT OF MDR/XDR TB PATIENTS WITH VIRAL HEPATITIS

Testov, Vadim, Dr; Vaniev, Eduard, Dr; Lovacheva, Olga, Prof; Glebov, Konstantin, Dr; Samoilova, Anastasia, Dr; Russkikh, Anastasia, Dr; Burmistrova, Irina, Dr; Vasilyeva, Irina, Prof

Objective: To compare frequency and timing of adverse drug reactions (ADR) in MDR/XDR TB cases with presence/absence of viral hepatitis (VH).

Methods: Frequency and type of ADR were studied in MDR/XDR TB patients with concomitant VH treated from 2011 to 2016 with the following anti-TB drugs: Lfx 43%, Mfx 47%, Cm 45%, Am 39%, Cs 96%, Z 73%, Pto 55%, PAS 62%, E 18%, Lzd 60%, Bq 63%. 111 cases with MDR/XDR TB and concomitant VH (group 1) were examined: 12 cases with VHB (10.8%), 92 - VHC (82.9%), 7 - VH "B+C" (6.3%). 143 cases with MDR/XDR TB without VH (group 2) were examined.

Results: ADR were observed: 94/111 in group 1 - 84.7% [95% CI 77,43 - 90,75] and 82/143 in group 2 - 57.3% [95% CI 49,17 - 65,31] ($p < 0,05$). Gastrointestinal ADR in both groups were 58/94 - 61.7% and 45/82 - 54.9%, respectively. Hepatotoxic ADR ranked second in group 1 (50/94 - 53.2%) and allergic ADR (19/82 -23.2%) in group 2. In the 3rd and following places in group 1 were: arthralgia (25/94 - 26.6%), hematological changes occurred in 24/94 - 25.5%, allergic reactions to TB drugs - 19/94 - 20.2%, neurotoxic (18/94 - 19.2%), cardiotoxic (18/94 - 19.2%), nephrotoxic (15/94 - 16.0%). In group 2: neurotoxic (18/82 - 22,0%), hematological (16/82 -19,5%), cardiotoxic (15/82 - 18,3%), hepatotoxic (14/82 - 17,1%), nephrotoxic (13/82 - 15,9%), arthropathy (12/82 - 14.6%). Endocrine and visual impairment ADR in both groups were less than 2.5%.

Conclusion: MDR/XDR TB patients both with and without associated VH had the same ADR, but the frequency of occurrence was different. The most frequent ADR in cases with VH were gastrointestinal, hepatotoxicity and arthralgia, without VH - gastrointestinal, allergic and neurotoxic.

SMEAR-BASED MONITORING OF FIRST-LINE TUBERCULOSIS TREATMENT IN MALI: CHALLENGES WITH EARLY IDENTIFICATION OF INITIAL RIFAMPICIN RESISTANCE AND TRUE TREATMENT FAILURE

Diarra, Bassirou, Dr; Decroo, Tom, Dr; Somboro, Amadou, Dr; Murphy, Robert, Prof; Siddiqui, Sophia, Dr; Doumbia, Seydou, Prof; Diallo, Souleymane, Prof; de Jong, Bouke, Prof

Introduction: Non-conversion on auramine sputum smear microscopy (AR) shows lack of treatment response, possibly caused by initial rifampicin resistance (RR). However, dead bacteria still stain positive and may be detected in sputum. Fluorescein di-acetate sputum smear microscopy (FDA) shows live mycobacteria only. Therefore, we studied the potential of 2-month (2M) FDA as screening tool for the identification of initial RR and describe FDA results among patients with a positive auramine smear at 5M or 18M, after one year of post-treatment follow-up.

Methods: Between 2015 and 2018, we prospectively enrolled adults with new smear-positive pulmonary tuberculosis (PTB) from five local reference centers in

Bamako. After baseline screening, sputum samples were collected at 1M, 2M, 5M, and 18 M. A posteriori we tested for RR, by sequencing the rpoB gene.
Results: Of the 1,359 total patients enrolled, 1,019 (75%) had an isolate successfully tested for rpoB. Twenty -six (2.6%; 95%CI: 1.7-3.7) had mutations conferring RR. Most of the rpoB mutations were located at the codons Asp435Val (42.4%) and Ser450Leu (34.7%).
Among patients with initial RR, 72.2% (13/18) had a negative 2M FDA. Viability on FDA at 2M was not associated with initial RR (p=0.2). Among patients with a positive 5M and 18M AR, 63.9% (76/119) and 61.5% (8/13) tested FDA negative, respectively.
Among patients with a positive 5M culture, 78.6% (11/14) had a negative 5M FDA. The positive and negative predictive value of 5M FDA for culture-based failure was 20.0% and 94.7%, respectively.
Conclusion: RR mutations found in Mali are those identified by frequently used rapid molecular tests. FDA did not identify the majority of patients with initial RR or culture-confirmed treatment failure.
However, the high proportion of FDA negative results among patients with AR-positive / culture-negative failure or relapse suggests that further research is needed to explore how FDA can be used best to identify true failure and relapse.
Key words: FDA, RR, 2-month, rpoB, Bamako.

GENOME-WIDE SEQUENCING USING BIOLOGICAL CHIPS IN CHILDREN AND ADOLESCENTS WITH TUBERCULOSIS

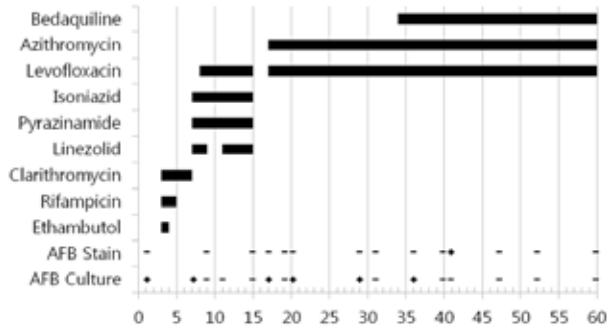
Kazakov, Alexey, Mr; Mozhokina, Galina, Ms; Smerdin, Sergey, Prof; Aksenova, Valentina, Prof; Klevno, Nadezda, Dr; Krasnenko, Anna, Ms; Plotnikov, Nikolay, Mr

A lot of data has been accumulated in the scientific literature on the effect of the patient's genome on the course and development of various diseases, as well as on the tolerability and efficacy of various drugs, including antituberculosis ones.
Research objective: is to conduct a genome-wide analysis using DNA-chips and to identify genetic variants that determine the risk of hepatotoxic reactions to TB drugs.
The study involved 5-14 years children. Whole blood sampling was taken, then it was frozen at -20-700C and delivered to the laboratory for genetic testing. DNA isolation was performed using the QIAamp DNA Blood Mini Kit (Qiagen). Quality control of the obtained DNA was conducted using agarose gel electrophoresis, the concentration was measured with a Qubit 3.0 device. DNA genotyping was performed on Infinium Global Screening Array-24 chips.
Sample preparation and HiScan (Illumina) scanning were performed according to the Infinium HTS Assay Guide protocol. In total, at least 635,562 mitochondrial and autosomal markers were studied for each sample. Markers were collected from 31 databases, including NHGRI-EBI GWAS catalog, PharmGKB, RefSeq and others.
In the studied group of patients, no AA alleles were found in SNP rs1799931 together with AA and AG alleles in SNP rs1799930, as well as TT or CT alleles in SNP rs1041983, determining the activity of the enzyme NAT2. This allows to predict a low probability of occurrence of hepatotoxic reactions to TB drugs in these patients. Also a database of the patient's genome has been created.

A SUCCESSFUL BEDAQUILINE SALVAGE THERAPY ON MYCOBACTERIUM INTRACELLULARE LUNG DISEASE

Chung, Chiwook, Dr; Joh, Joonsung, Dr

Macrolide, rifampicin and ethambutol are recommended as first line therapy for *Mycobacterium avium* complex (MAC) lung disease. However, in case of treatment failure, there are few options for salvage therapy.
An 86-aged man was diagnosed as *Mycobacterium Intracellulare (M. Intracellulare)* lung disease in April, 2018. Clarithromycin 500mg, rifampicin 600mg and ethambutol 400mg were prescribed but due to severe adverse effects, medication had to be changed. On week 17, he was prescribed azithromycin 250mg and levofloxacin 250mg. But despite four months of therapy, there was no sputum culture negative conversion and his symptoms were aggravated. On week 34, bedaquiline 200mg daily was added, and after two weeks bedaquiline was reduced 200mg three times a week. After administering bedaquiline, sputum culture was converted negative 40 days later and then five consecutive negative cultures were achieved. Also his symptoms and radiologic findings were improved. After six months of medication including bedaquiline, he stopped all medication and remained stable state.
In 2015, Philley et al. reported the result of bedaquiline salvage therapy for ten nontuberculous mycobacterium patients. Their treatment failure may be concurrent use of rifampicin, because it induces CYP 450 system and lowers serum bedaquiline concentration. Bedaquiline without rifampicin may be key factor to favorable outcome and clofazimine can be recommended as alternative for rifampicin. Bedaquiline and clarithromycin combination had antagonistic interaction for *M. Intracellulare* and clarithromycin with levofloxacin caused unfavorable clinical results for MAC lung disease. Additionally, adding moxifloxacin to bedaquiline could increase the risk of QT interval prolongation because moxifloxacin is relatively ranked high among fluoroquinolones regarding cardiac toxicity. Therefore, we prescribed azithromycin and levofloxacin with bedaquiline. As far as we know, this is the first successful treatment of *M. Intracellulare* lung disease using bedaquiline.



ANTIMICROBIAL POTENTIAL OF METABOLITES FROM MANGROVE ACTINOBACTERIA AGAINST TUBERCULOSIS (TB) SURROGATE MYCOBACTERIA

Adanan, Norshamiera, Miss; Shuib, Shuhaida, Dr; Mohd Hanafiah, Khayriyyah, Dr

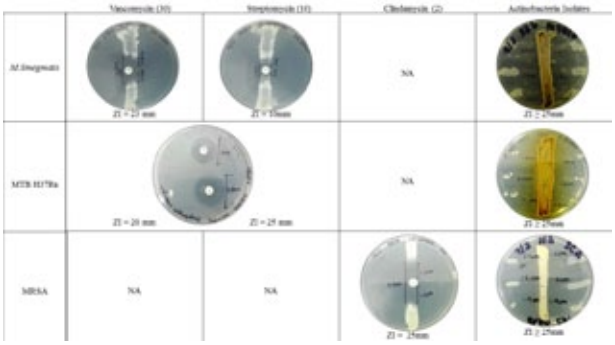
Majority of antibiotics derive from Actinobacteria, including the discovery of the first tuberculosis cure, Streptomycin from Streptomyces *sp.* Harsh environments such as mangroves may harbor new Actinobacteria with antimicrobial potential.

Thus, this study aims to evaluate the antimicrobial potential of actinobacteria isolated from Malaysian mangrove ecosystem against slow- and fast-growing Mycobacterium tuberculosis (MTB) surrogate mycobacteria (MTB H37Ra, *M.smegmatis*) and *Methicillin-resistant Staphylococcus aureus* (MRSA).

Sediment and water from crab holes, rhizosphere roots, undisturbed and disturbed areas were collected and pretreated using the dry heat at 100°C method. Actinobacteria isolated from sediment were cultured on selective starch casein agar supplemented with 80 µlg/mL cycloheximide while water samples were cultured without pretreatment. 31 isolates were successfully cultured, with most isolates from sediment samples (n=25) and majority from rhizosphere roots (n=12).

The antimicrobial activity of isolates were evaluated using the cross-streak method after an initial incubation period of 5 days followed by further incubation periods of 2 days, 10 days, and 1 day for *M.smegmatis,* MTB H37Ra, and MRSA. respectively. The zone of inhibition (ZI) of positive controls (without Actinobacteria inoculation), negative controls (with commercial antibiotic discs Vancomycin (V30), Streptomycin (S10) and Clindamycin (DA2)) and test plates were measured and recorded.

In total, 17 isolates were active against at least one of the test organisms. Among them, four isolates showed activity against only one test organisms, 12 isolates showed activity against two test organisms and only one isolate from a water sample of Site B (Rhizosphere roots), WB b, exhibited antimicrobial activity against all three test microorganisms and showed the strongest inhibition effect against *M.smegmatis* (ZI≥25mm), MRSA (ZI=18.5mm), and MTB H37Ra (ZI=18mm) compared to standard antibiotics used as controls which showed ZI ≤ 25 respectively. In conclusion, Mangrove Actinobacteria may be a significant source of new antibiotics against tuberculosis warranting further investigation.



CLINICAL CHARACTERISTICS, SECOND LINE DRUG SUSCEPTIBILITY RESULTS AND TREATMENT OUTCOME AMONG PATIENTS WITH MULTIDRUG -RESISTANT TUBERCULOSIS

Mishra, Richa, Prof; Kesarwani, Vasudha, Dr; Nath, Alok, Dr

Background: Molecular methods such as Xpert MTB/RIF assay and Line probe assay version2 have been game changers in improving the diagnosis as well as treatment of MDR-TB patients. Recently, the World Health Organisation and guidelines for the programmatic management of drug-resistant tuberculosis (PMDT) in India has included a recommendation on the use of the shorter MDR-TB regimen under specific conditions.

Methods: We performed a retrospective study from March 2017 to June 2019 at a tertiary care centre in Northern India to assess the clinical characteristics , second line drug susceptibility results, current treatment regimen and outcome on 44 patients of MDR-TB. Patient details were retrieved either through the Hospital Information System (HIS) or case files. The Xpert MTB/RIF assay and version 2.0 Line probe assay for second line DST testing was performed on samples or culture.

Results: Out of 44 cases, 34 cases were of pulmonary TB and 10 were extra-pulmonary. 26 were male and 18 were female. Thirty patients gave a prior history of TB treatment. Second line DST results were as follows: 29.9 % cases (n=13) were sensitive to both FQs as well as SLID, 56.8% patients (n=25) were resistant to FLQ and sensitive to SLID (Pre-XDR) while 13.3% (n=6) were resistant to both (XDR-TB).Conventional MDR TB Regimen was initiated in 35 patients and shorter MDR TB Regimen in 9 patients. Four patients died,6 were completely cured while 3 failed treatment. The remaining 31 patients are continuing treatment.

Conclusion: The majority of our patients were resistant to FQs and were therefore put on conventional regimen. The shorter MDR treatment as endorsed by WHO/PMDT is not feasible for a TB endemic setting like India.

PREVALENCE OF ADVERSE DRUG REACTIONS TO CO-TRIMOXAZOLE AMONG TB/HIV CO-INFECTED PATIENTS ATTENDING CARE AT MULAGO NATIONAL REFERRAL HOSPITAL, ART CLINIC

Abila, Derrick Bary, Mr

Background: Tuberculosis (TB) has been managed by antibiotics which are ranking among the most prescribed medication at the global level. In sub-Saharan Africa, cotrimoxazole is being used as a standard-of-care for prophylaxis against TB in HIV/AIDS patients which signify an increased risk of cotrimoxazole-linked adverse drug reactions (ADRs). In Uganda, TB infection is also the major cause of death among people with HIV/AIDS. Co-trimoxazole preventive therapy increased from 25% in 2005 to 90% in 2010. This study assessed the prevalence of ADRs to co-trimoxazole among TB/HIV co-infected patients attending care at Mulago National Referral Hospital, Uganda

Methods: A retrospective study involving a review of records of TB/HIV co-infected patients (aged 18 years and above) seeking care at the ART clinic of Mulago National Referral Hospital. The data extraction tools included the Schumock and Thornton preventability scale and Naranjo's algorithm scale of causality. Data were analyzed using STATA15.

Results: A total of 100 were included in the study. Majority of the patients (68.13%) were female with a mean age of 34.16±10.43 years. Chronic pulmonary disease was the most common co-morbidity with 95.63% HIV positive. Majority of patients (68.1%) reported that they had ever experienced an adverse reaction to co-trimoxazole and with 77.8% having taken it before hospitalization. Some patients (79.1%) had ADRs before hospitalization with 64% causing hospitalization and nausea (37.5%) was the most common presentation. From the Naranjo's algorithm scale of causality, 54.1% of nausea cases were definite while Schumock and Thornton preventability scale 75.9% were not preventable.

Conclusion: The prevalence of ADR from co-trimoxazole was high. The most common ADR caused by administration co-trimoxazole were nausea fever and cough. Physicians need to prescribe co-trimoxazole and be able to manage the adverse events that develop.

USING AN OPTIMAL DESIGN APPROACH TO EFFICIENTLY DESIGN A PKPD STUDY OF MULTIPLE ANTI-TB DRUGS REGIMENS: EXPERIENCE FROM THE PRACTECAL-PKPD STUDY

Nyang'wa, Bern-Thomas, Dr; Moore, David, Prof; Davies, Gerraint, Prof; Kloprogge, Frank, Dr

Introduction: Understanding the pharmacokinetics and pharmacodynamics of drugs in a regimen is critical, especially in Tuberculosis treatment shortening studies. The PRACTECAL-PKPD is investigating the relationship between patients' exposure to drugs in the TB-PRACTECAL trial and their treatment outcomes.

Methods: Identification of prior information

We conducted a systematic literature search in Medline, Embase and Pubmed databases and relevant conferences to identify published population pharmacokinetic models for linezolid, pretomanid, bedaquiline, clofazimine and moxifloxacin. Where more than one model was published, the following criteria listed hierarchically was used to choose the most suitable model: study population (healthy subjects, non-TB, TB or MDR-TB patients), original PK study sample size, and a critical appraisal of the publications including whether the authors reported enough parameters to allow for parameterisation of the model.

Identification and definition of constraints

The overriding constraints were drugs, doses and dosing intervals in TB-PRACTECAL. Study nurses' availability, pharmacokinetics study experience and working hours, laboratory opening hours, access to centrifuges and freezers, availability and competence of staff. Collecting samples only on days when patients were meant to come in for other laboratory samples collection and keeping hospitalisation to a minimum.

Sampling schedule optimisation

Using PopED R-package we firstly conducted a simultaneous sampling schedule optimisation for Pretomanid and Linezolid only.

Design evaluation

The optimised sampling schedule was evaluated for each drug using stochastic simulation and estimation in NONMEM. This step and the previous ones were iterative until acceptable residual standard errors (RSEs) for clearance were obtained. The final optimised design was for 240 patients sampled at Day 0 (0, 2, 23hrs), Week 8 (0, 6.5, 23hrs), troughs at weeks 12, 16, 20, 24, 32 and 72. The evaluated RSEs for clearance were:

Drug	Simulated clearance (ml/min)	mean re-estimated clearance (ml/min)	RSE re-estimated
linezolid	1.86	1.96	16.6%
pretomanid	7.71	4.16	2.02%
bedaquiline	2.78	2.84	6.08%
clofazimine	10	11.2	6.32%
moxifloxacin	10.6	12.6	1.47%(prior)

Conclusion: An efficient sampling schedule for multiple anti-TB drugs with varying pharmacokinetic profiles can be identified while also considering operational constraints.

APPLICATION OF MACHINE LEARNING FOR PHENOTYPIC PREDICTION OF DRUG-RESISTANT TUBERCULOSIS FROM WHOLE GENOME SEQUENCING DATA

Mapiye, Darlington, Dr

The World Health Organisation (WHO) aims to end the tuberculosis epidemic by 2035. However, to attain this goal, effective diagnostic tools that elucidate the diagnose drug susceptibility are required. The application of whole genome sequencing (WGS) as a tool for the diagnosis and clinical management of tuberculosis promises to circumvent the long lead times and the limited scope of conventional phenotypic drug susceptibility testing and targeted sequencing techniques. However, to achieve this target, novel methods which harness the power of deep learning and the large volumes of data generated from WGS are required to effectively identify these emerging mutations. Critically, WGS data will also provide information beyond just drug susceptibility to include information such as strain lineage, which could be used to intervene in outbreaks, however, such opportunities are relatively unexplored.

We propose the application of Machine Learning methods to WGS data, in conjunction with already-collected routine clinical and microbiological meta-data across three conceptual domains: the identification and prediction of novel drug-resistant mutations, the identification of mycobacterial genetic biomarkers that predict TB treatment outcomes, the emergence of new strains and the types of patients or facilities they are associated with. The Machine learning models will be used to develop a classification system that can distinguish between drug sensitive (DS), multidrug (MDR) and extensively drug (XDR) resistant TB. The Machine learning models will be built using novel alignment free algorithms.

As routine WGS of TB patients is fast approaching in TB endemic countries, this approach promises to revolutionize the way we do non-conventional DST and optimize therapeutic pathways of TB patients.

POOR INTRA-FACILITY REFERRAL LINKAGES: A MISSED OPPORTUNITY FOR TUBERCULOSIS CASE DETECTION AND TREATMENT IN NORTH-CENTRAL, NIGERIA

Anejo Okopi, Joseph, Dr; Audu, Onyemocho, Dr; Ogiri, Samuel, Dr; Shember-agela, Igbabu, Dr; Ijachi, Ochola, Dr

Background: Despite the scale up of quality-assured Tuberculosis diagnostic and treatment strategies over the years, 34% of the cases still remain undetected globally; Nigeria is ranked third in the world and first in Africa of all undiagnosed cases. We aimed to assess the effect of poor two way intra-facility referral system in relation to tuberculosis case detection rate in Benue State University Teaching Hospital in North-central Nigeria.

Methods: A 27-months retrospective review of all presumptive Pulmonary TB cases sent to DOTS Centre of the hospital for sputum microscopy/Gene-Xpert was carried out to assess the source of referrals and what happened to the results after the investigations. Chi-square test was used for test of association between the intra-facility referral system and the case detection rate.

Results: There were 918 presumptive TB cases with males to females ratio (M:F) of 1:1.3. The mean age of patients was 41.0.0 ±18.4 years. Majority (59.8%) of the referrals were from general outpatient department of the hospital. Positive sputum result constitutes 145(15.8%), of which 69(7.5%) of the patients collected their result and 76(8.3%) did not collect their results. Among the patients with negative results, 554(60.3%) collected their results and 295(23.9%) did not collect their results. Poor follow-up between the facilities from where the test was requested for and the DOTS center where the investigation was conducted was the main reason for not retrieving the results. The relationship between the missed positive cases (8.3%) and poor intra-facility referral linkages within the hospital was statistically significant (p=0.000).

Conclusion: Poor intra-facility referral linkage is a missed opportunity for effective tuberculosis case detection rate in BSUTH. Therefore, engagement of all relevant health care providers on efficient two way referral system should be encouraged in all health facilities to ensuring adequate TB case notification and prompt treatment.

CAUSAL METHOD TO ESTIMATE THE EFFECTS OF PREVIOUS TUBERCULOSIS TREATMENT IN MULTIDRUG-RESISTANT TUBERCULOSIS IN SUDAN: CASE CONTROL STUDY.

Elduma, Adel, Dr

Introduction: Robust estimator is required to overcome the problem in case control by implementing marginal statistical parameters are required such targeted maximum likelihood estimation (TMLE). We used a LTMLE as a double robust methodology which estimates the causal quantity of outcome regression in addition to censoring mechanism.

The aim of this study is to estimate the causal association between previous tuberculosis treatment history and the occurrence of MDR-TB using Targeted Maximum Likelihood estimation in Sudan. Method: Data for this study were obtained from a case control study of the risk factors associated with MDR-TB in Sudan. The study population consists of Multidrug resistant tuberculosis patients and tuberculosis patients who were sus-

ceptible to anti-tuberculosis drugs. A total number of 29 hospitals or health facilities were sampled to select cases. Taking previous TB treatment was considered as an exposure variable, the outcome variable was MDR-TB patents as cases and whose susceptible to the first line anti-tuberculosis drugs as control, and the for possible confounders variable. Targeted maximum likelihood estimation (ltmle) was used for the estimation of the parameters. ltmle R -- Package was for the statistical analysis.

Results: The analysis retuned the summary result as follow: The additive treatment effect parameter estimate was (0.18948, 95% CI; 0.16135, 0.21761) with SE 0.014353, and p. value (2e-16). the estimated Risk ratio was (16.083, 95% CI; 12.932, 20.001) with SE equal 0.014353 and p. value (2e-16). The estimated Odds ratio was (19.902, 95% CI; 15.601, 25.389) with SE equal 0.12424 and p. value (2e-16).

Conclusion: In this study the analysis showed that there was causal association between the history of previous treatment and the occurrence of the MDR-TB in Sudan. The result of this study indicated that treatment effect and risk ratio can be calculated in case control study design using double robust methods.

ANTIOXIDANT SUPPLEMENTATION TO IMPROVE OXIDATIVE STRESS AND OUTCOME OF CHEMOTHERAPY IN PATIENTS OF SMEAR POSITIVE PTB

Munje, Radha, Prof

Pilot-Initial screening of PTB patients showed increased oxidative stress in newly diagnosed PTB patients than healthy volunteers Which persisted at end of 6 month and correlated with residual changes in chest X-ray

Hypothesis: Supplementation of antioxidants along with antitubercular drugs may decrease oxidative stress and improve outcome of chemotherapy.

Method: Randomised controlled trial (RCT) was conducted in 100 newly diagnosed sputum positive PTB patients of both sexes in control & study groups (each 50) (Recommended 37 in each group).

Both groups received ATT regime as per DOTS while study group received supplementation of 2 months vit p2& vit C as antioxidants in thereupatic doses.

Sputum conversion and radiological response was studied in both groups.

Results: LOP levels as measure of oxidative stress in both group were similar at the time of diagnosis (control =11.69=+3.47, study group 12.69+3.09 MDA nmol/g of Hb) In study group LOP levels significantly reduced to 8.38+1.82 as compared to and in control group further significant rise was observed (21.31+8.04)sputum was negative at 15 days in 50% patients of study group and 14%in control group. At the end of intensive phase it was 100%in study group and 86%in control group.

At end of 6 months Radiological improvement was seen in 100% patients in study group and 80% in control group with less residual lesions in study group as compared to control group.

As early sputum conversion reduces transmission of disease in community and less residual radiological lesion would in turn decrease post TB complications.

Inference-Supplementation with antioxidants in thereupatic doses along with ATT can be recommended for better outcome

A larger study with more no of sample size as well as longer follow up for relapse is recommended.

DEVELOPMENT AND CHARACTERIZATION OF METERED DOSE INHALER (MDI) FORMULATIONS FOR DRUG SENSITIVE AND MDR TUBERCULOSIS.

Saini, Vinay, Dr; Pando, Rogelio Hernande, Dr; Srivastava, Rohit, Prof

Present investigations were aimed to identify few APIs (not disclosed due to IP having good activity against H37rv, MDR and XDR TB) to target MDR TB bacteria into the alveoli of the lungs. Before developing aerosol formulations, we performed preformualtion studies of selected APIs and in vitro anti TB activities against H37rv and MDR TB bacteria.

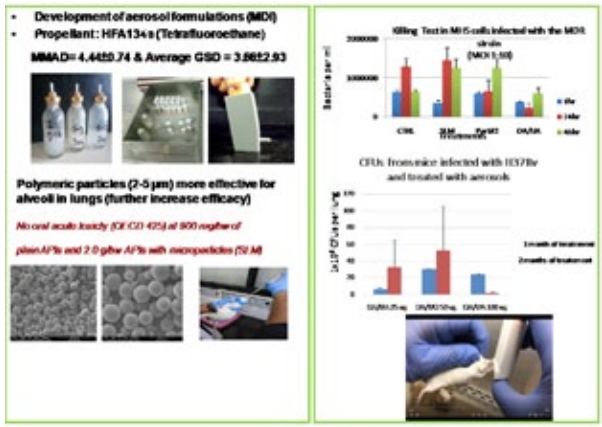
Oral inhalation toxicity studies of selected APIs were performed in Holtzman (OECD 25) and no toxicity was observed at the dose of 900 mg/kg body weight. Pharmacokinetic studies were also performed and biological half-life was ~5.87 hr-5.59 hr.

We found good anti TB activities in alevelor macorphase cell lines infected with H37rv and MDR TB bacteria. Metered dose inhaler formulations (Aerosol) were developed and characterized for their particel size, release studies and preclinical studies against H37rv. Mean median aerodynamic particle diameter (MMAD) was 4.44±0.74 μm with geometric standard deviation of 3.66±2.93.

During preclinical studies, we optimized the dose of aerosol for treating mice infected with H37rv. 3-D Model of Inhaler pump was developed using Using 3-D printer (Software : CATIA V5).

Further, we have developed solid lipid microparticles (SLM) of 2.84±0.67 micron to increase efficacy and reducing dose of the developed formualtions against MDR TB bacteria. Inhalation toxicty studies, Pharm acokinectic,pharmacodynamic studies and preclinical studies against MDR TB are going on.

Based on current results, we hope that these formulations may work as an adjunct therapy to control drug resistance bacteria in conjuction with primary and secondary TB antibiotics.



Funding agency: India Health Fund (TATA TRUST-2.8 Cr)

PHARMACODYNAMIC DRUG-DRUG INTERACTIONS OF THE ISONIAZID-RIFAMPICIN BACKBONE FOR TREATMENT OF DRUG SENSITIVE TUBERCULOSIS.

Kloprogge, Frank, Dr; Ortiz Canseco, Julio, Dr; Sadouki, Zahra, Ms; Phee, Lynette, Dr; McHugh, Timothy, Prof

Background: The isoniazid-rifampicin drug combination has been the treatment backbone for drug sensitive tuberculosis since the 1960's. Isoniazid has a potent sterilising effect in sputum that diminishes over the course of the treatment. Rifampicin also has a potent sterilising effect in sputum but it does not diminish over the course of treatment. However, rifampicin, at current standard dosing of 10 mg/kg O.D., does not compensate for the diminishing sterilising effect of isoniazid in combination treatment. In light of recent efforts to address this by escalating rifampicin dosages up to 40 mg/kg O.D. we aimed to obtain a holistic understanding of the isoniazid-rifampicin pharmacodynamic drug-drug interactions *in vitro*.

Methods: Ten *in-vitro* incubation experiments were conducted in duplicate using *Mycobacterium tuberculosis* H_{37}Rv in OADC supplemented 7H9 liquid culture. Each experiment comprised a drug exposure phase (one week), a regrowth phase (two weeks) and a second drug exposure phase (one week). Cultures were exposed to 0, 0.25, 1, and 8 X MIC for isoniazid, rifampicin, or isoniazid and rifampicin in combination in both drug exposure phases. Experiments were sampled on 24 hourly basis and bacterial load quantified.

Results: Overall, anti-tubercular effects for isoniazid and rifampicin experiments tends to be more potent during the first drug exposure phase compared to the second drug exposure phase. This resulted in stabilisation or regrowth of the bacterial load with increasing drug exposures.

Conclusions: The findings demonstrate that a temporary under-exposure or absence of drug results in altered susceptibility and increased risk of emergent resistance. This is an important consideration for clinical dosing regimens where trough-levels may have dropped to sub-therapeutic concentrations for significant periods of time.

LONG-TERM IMPACT OF ADOPTION OF BEDAQUILINE-CONTAINING REGIMENS ON DRUG-RESISTANT TUBERCULOSIS BURDEN IN CHINA

Agnarson, Abela Mpobela, Ms; XiaoChun, Wang, Mr; Potluri, Ravi, Mr; Bhandari, Hitesh, Mr; Dhir, Amit, Mr; Kambili, Chrispin, Dr; Metz, Laurent, Dr

Purpose: To assess the impact of broad adoption of bedaquiline-containing regimens on the drug-resistant tuberculosis (DR-TB) burden in China, following the 2018 update of the World Health Organization (WHO) guidelines that has prioritized the use of bedaquiline in DR-TB treatment regimens.

Methodology: A state-transition model that allows movement and interaction between susceptible, latent and active TB disease states, and differentiates between drug-sensitive (DS) and DR-TB patients was developed. Model inputs were sourced from published literature or were derived to calibrate the model with metrics published by WHO. Future infrastructural changes were built in to estimate the baseline forecast through 2040, without the introduction of bedaquiline.

More widespread utilization of bedaquiline-containing regimens (85% peak share) was then modeled in two scenarios differing in the treatment success rate of the regimens, 61% (per clinical trial), and 80% (in observational studies), as compared to 44% success rate with standard-of-care treatment.

Results: In the baseline scenario without bedaquiline, the model predicts annual incidence of DR-TB to increase by 6-8% in each five-year period from 2020 to 2040, while with the adoption of bedaquiline-based regimens, the incidence increases by only 1-3% in the 61% success rate scenario, and actually declines by 1-6% in the 80% success rate scenario. Similar impacts of bedaquiline adoption are seen on DR-TB prevalence (4-5% increase in baseline, 0-7% decline in scenario 1 and 4-19% decline in scenario 2) and mortality (5-7% increase in baseline, 0-16% decline in scenario 1 and 6-40% decline in scenario 2).

Conclusion: Increased adoption of bedaquiline-containing regimens for DR-TB treatment will significantly reduce DR-TB burden in China, and thus negate the currently projected increase in burden. The results of our study could be beneficial to public health policy and decision-making.

	Incidence	Incidence	Incidence	Prevalence	Prevalence	Prevalence	Mortality	Mortality	Mortality
	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate
Change over 2020-2025 period	8%	1%	-6%	5%	-7%	-19%	7%	-16%	-40%
Change over 2035-2040 period	6%	3%	-1%	4%	0%	-4%	5%	0%	-6%
Change over 2020-2040 period	30%	8%	-12%	19%	-12%	-38%	26%	-21%	-60%

EVALUATION OF MARKERS OF CLINICAL IMPROVEMENT AMONG HIV INFECTED ADULTS TREATED FOR TUBERCULOSIS IN JOS, NORTH-CENTRAL NIGERIA: A RESTROSPECTIVE COHORT STUDY

Anejo Okopi, Joseph, Dr; Samuel, James, Mr; Ojeh, Victor, Mr; Isa, Yetunde, Ms; Akanbi, Maxwell, Dr; Ibrahim, London, Mr; Agbaji, Oche, Prof

Background: Clinical improvement remains an important determinant of tuberculosis treatment outcome especially among TB/HIV co-infected adults due to high morbidity and mortality rates associated with the infection.
Aim: We determined the proportion of patients who demonstrated significant clinical improvement after completing TB chemotherapy, as well as predictors of treatment outcome.
Methods: We retrospectively evaluated data of 612 HIV+ patients aged ? 18 years co-infected with pulmonary tuberculosis (PTB) who were enrolled for treatment between January 2009 and December 2013 at the HIV clinic of the Jos University Teaching Hospital, Nigeria. TB was defined as sputum positive by smear microscopy, Chest X-ray suggestive of PTB, and clinician diagnosed TB (clinical diagnosis). Patients diagnosed with TB were initiated on chemotherapy and followed-up for 8 months. Logistic regression was done to determine factors associated with treatment outcome.
Results: The median (IQR) age was 35 (30, 41) years and 64.5% were female. 85.1% (521)completed treatment. 9.5% (58) died, 25 (4.1%) patients defaulted and 1.3% (8) transferred out. 94.6% (493) of those who completed treatment achieved cure. Median baselineLog viralload of the cured group significantly declined from 4.20 (2.30, 5.01) to 2.30 (2.30, 3.00) ($p<0.001$). Similarly, median baseline BMI and CD4 increased from 19.68 (17.50, 22.50) kg/m2to 21.83 (19.42, 24.17) kg/m2 ($p<0.001$), and 161.0 (78.0, 321.0) to 253.00 (116.5, 406.5) cell/mlm3($p<0.001$) respectively.
However, in the failed treatment group, there was no significant difference between the pre- and post-treatment median levels of BMI, CD4 and viral load ($p>0.05$). In analysis adjusted for age, sex, baseline BMI, CD4 and viral load, male gender independently predicted successful treatment outcome (aOR=3.00; 95%CI 1.06-8.77; $P<0.05$).
Conclusion: the proportion of patients that achieved cure following completion of treatment was high. The male gender was associated with positive treatment outcome.

LONG-TERM IMPACT OF ADOPTION OF BEDAQUILINE REGIMENS ON DRUG-RESISTANT TUBERCULOSIS BURDEN IN INDONESIA

Agnarson, Abela Mpobela, Ms; Chiou, Chiun-Fang, Dr; Insani, Uray Camila, Ms; Mansjur, Henny, Ms; Potluri, Ravi, Mr; Dhir, Amit, Mr; Kambili, Chrispin, Dr; Metz, Laurent, Dr

Purpose: The World Health Organization (WHO) has recently prioritized the use of bedaquiline in DR-TB treatment regimens. We evaluate the potential impact of broad adoption of bedaquiline-containing regimens on the incidence, prevalence, and mortality burden of drug-resistant tuberculosis (DR-TB) in Indonesia.
Methodology: We used a state-transition model that features susceptible, latent and active TB disease states, and differentiates between drug-sensitive (DS) and DR-TB patients. Inputs were populated from published literature, or where unavailable, derived by calibrating key epidemiological metrics in the model for 2015-2017 with WHO published data. Anticipated infrastructural changes relating to TB diagnosis and treatment were built in for the baseline forecast through 2040.
Assuming universal use of the longer DR-TB regimens, the model was then used to analyze two scenarios centered on broad adoption of bedaquiline-containing regimens (95% peak share), with differing treatment success rates – 61% (per bedaquiline's clinical trial) in one scenario, and 80% (per observational studies) in the other, as compared to 44% success rate with standard-of-care treatment.

	Incidence	Incidence	Incidence	Prevalence	Prevalence	Prevalence	Mortality	Mortality	Mortality
	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate	No bedaquiline	Bedaquiline use; 61% success rate	Bedaquiline use; 80% success rate
Change over 2020-2025 period	-2.7%	-3.3%	-4.0%	-9.7%	-12.6%	-15.8%	-14.7%	-21.9%	-30.0%
Change over 2035-2040 period	-0.8%	-1.2%	-1.5%	-4.1%	-5.0%	-6.1%	-6.6%	-9.5%	-14.8%
Change over 2020-2040 period	-4.9%	-6.8%	-8.6%	-25.4%	-32.2%	-39.3%	-39.3%	-54.1%	-70.0%

Results: The model estimates annual incidence of DR-TB to decline by 0.8-2.7% in each five-year period from 2020 to 2040 in the baseline scenario without bedaquiline. With the adoption of bedaquiline-based regimens, the incidence declines by 1.2-3.3% in the 61% success rate scenario, and by 1.5-4.0% in the 80% success rate scenario. A similar pattern is observed for DR-TB prevalence (4.1-9.7% decline in baseline, 5.0-12.6% decline in 61% success rate scenario and 6.1-15.8% decline in 80% success rate scenario) and mortality (6.6-14.7% decline in baseline, and 9.5-21.9% decline and 14.8-30.0% decline respectively in the two scenarios).

Conclusion: The adoption of bedaquiline-containing regimens in Indonesia as recommended by WHO has the potential to reduce its DR-TB burden on the back of the regimen's superior treatment success rate, and the attendant lowering of disease transmission.

PHARMACOGENETIC ANALYSIS OF DRUG METABOLISM POLYMORPHISMS FROM SALIVA OF PATIENTS TREATED FOR TUBERCULOSIS IN EAST AFRICA

Operario, Darwin, Dr; Masiphephethu, Maano, Ms; Gratz, Jean, Ms; Peloquin, Charles, Prof; Mduma, Estomih, Mr; Mpagama, Stellah, Dr; Heysell, Scott, Dr

Pharmacokinetic/pharmacodynamic (PK/PD) variability is common and increasingly understood as a contributor to tuberculosis (TB) treatment outcomes. Achieving PK/PD targets is important to the individual patient. Plasma concentrations should be sufficiently high for bactericidal activity, and ideally the prevention of acquired resistance, while avoiding concentration-related adverse effects. Rapid microbiological clearance of *M.tb* decreases transmission. Even with proper weight-based dosing, individual PK variability persists. At the population level, observed trends in PK variability suggest shared mechanistic predictors.

Early studies of the pharmacogenetics of drug absorption, distribution, metabolism, and excretion, or "ADME" targets, have found clinically relevant associations between gene polymorphisms and anti-TB drug PK. However, few data are from East Africa. Therefore, we collected saliva samples from adult and pediatric patients in Tanzania within an existing prospective cohort study of PK/PD and outcomes. We extracted DNA to determine genotypes at eight loci thought to influence the PK of rifampin, isoniazid, pyrazinamide, and fluoroquinolones. These loci include c.388, c.463, and c.521 in SLCO1B1, c.341, c.590, and c.803 in NAT2, P341L in SLC22A1, and c.3435 in ABCB1. We utilized a custom-designed qPCR plate which employed duplex testing at each locus. This testing was performed on-site at the Kilimanjaro Clinical Research Institute in Tanzania.

Our initial findings indicated some genotype distributions were similar to those found in South African populations while others differed significantly from previous studies. Preliminary studies comparing the ABCB1 c.3435 genotype and levofloxacin PK indicated that adult patients with the CT genotype had a higher overall median Cmax and AUC0-24 values during their first evaluation visits, versus adults with the CC genotype.

In summary, we developed a field-deployable qPCR assay capable of assessing genotypes influencing the most clinically relevant anti-TB drugs and furthering current understanding of ADME targets. Importantly, this test can be scaled for use in other regional laboratories.

ANALYZING RV3083 OF MYCOBACTERIUM TUBERCULOSIS AS A POTENTIAL DRUG TARGET

Kaur, Dashleen, Ms; Aggarwal, Vithika, Ms; Shashank, Mr; Saraka, Amandeepa, Ms; Sharma, Monika, Dr; Sharma, Sadhna, Dr

The cell wall of *Mycobacterium tuberculosis* makes many antibiotics ineffective. Mycolic acids is an important property of the bacterial cell wall. These impact persistence as well as the virulence of the bacterium, thus providing us with a source to discover potential drug targets. MymA operon seems to play an important role in cell envelope formation. By inhibiting the first gene of the operon, Rv3083, synthesis of mycolic acid will be affected as a result of disruption of the operon. Thus, Rv3083 serves as a potential drug target. In this study, we studied the interaction of this target with 177 ligands from GSK library to understand the mechanism of inhibition. Rv3083 protein 3D structure was extracted us-

ing Phyre Software. Using AutoDock4.2.6, 177 inhibitors from GSK library were docked on the active site of Rv3083. These inhibitors are known to inhibit the bacterium. After docking, energy scores for interaction between each inhibitor and the protein target were retrieved from the command prompt. Isoniazid (INH), a potent drug against tuberculosis, gave an energy score of -9.8. Based upon the energy scores, 20 inhibitors were shortlisted with highest energy scores. The top 20 energy scores fell in the range of -11.6 to -9.5 Kcal/mol. Inhibitor no. 1 exhibited the highest energy score of -11.6 Kcal/mol. However, when a set of repeats were performed, the energy score reduced by 1.3 units. In contrast, the energy score went as low as -5.7 for some inhibitors. Inhibitors no. 1 and 37 have turned up with the best possible energy scores out of the listed 177 inhibitors.
This study suggests that 20 inhibitors with highest energy scores are suitable to be tested as potential drugs against the disease since they showed the most stable interactions with the potential drug target Rv3083.

THE POSSIBLE HEALTH IMPACT OF EFFECTIVE HOST-DIRECTED THERAPY FOR TB

Menzies, Nicolas, Prof; Wallis, Robert, Dr

Motivation: Tuberculosis disease (TB) can cause significant lung injury, with additional impairment associated with delayed diagnosis and multiple disease episodes. Impaired lung function (in terms of reduced FEV1) is a strong predictor of mortality, cardiovascular disease, and respiratory hospitalization. With TB therapy there can be modest improvement in lung function but patients will typically experience ongoing impairment following treatment. Adjunctive host-directed therapy (HDT) can protect lung function during TB treatment, and lead to greater recovery of TB-associated lung damage.
Methods: We examined the possible health benefits of HDT regimens for patient diagnosed with RIF-resistant TB in low- and middle-income countries, as compared to current treatment regimens. We created a microsimulation model to project individual TB treatment outcomes (the trajectory of lifetime lung function, life expectancy, disability-adjusted life years (DALYs)), for different combination of patient demographics, pre-treatment lung function, and country setting. We combined incremental outcomes (HDTs vs current care) with projections of patient volume for all low- and middle-income countries over the period 2020-2030, to estimate the total possible health benefits.
Results: As compared to current TB regimens for RIF-resistant TB, HDT regimens could produce greater recovery of lung function during TB treatment. Assuming that published results relating reduced FEV1 to elevated mortality can be applied to the consequences of TB treatment, effective HDT regimens could result in major improvements in post-treatment survival, with up to 1.5 year gains in life expectancy, and 2.0 DALYs averted per person. The magnitude of survival gains differed by HDT regimen effectiveness, pre-treatment lung function, age, and country setting.
Conclusions: Estimates of the population-level impact of TB policy change typically ignore the consequences of TB and TB treatment for future lung function. Effective HDT therapy could protect lung function during TB treatment and produce substantial individual and population-level health improvements.

EVALUATION OF MOXIFLOXACIN AND LEVOFLOXACIN BY MGIT960 DRUG SUSCEPTIBILITY TESTING FOR MANAGEMENT OF RETREATMENT CASES OF TUBERCULOSIS- A COMPARATIVE STUDY

Bhalla, Manpreet, Dr

Background: Newer generation of fluoroquinolones i.e.Moxifloxacin and levofloxacin are successfully introduced for tuberculosis treatment. Although, these fluoroquionolones are very active against *M. tuberculosis*,misuse or wrong concentrationof an antibiotic may lead to resistance of low level to high or pre-XDR to XDR-TB.Genotype MTBDRsl assay is a rapid diagnostic tool to detect the mutations associated with baseline second line drugs, but it cannot differentiate one fluoroquionolone from the other. Furthermore it cannot make a decision to select high or low dose of fluoroquionolones for treatment of tuberculosis patients. Therefore in vitro susceptibility testing is required to guide the clinician to take a decision for proper management of drug resistant patients.
Methods: In the present study 1550 strains were subjected to susceptibility testing to moxifloxacin and levofloxacin drug. The cross resistance between moxifloxacin and levofloxacin was analysed. The susceptibility was tested using their critical concentration i.e levofloxacin (1.5µg/ml), and moxifloxacin (0.5 and 2µg/ml).
Results: The results of susceptibility testing of the panel of strains used for determination of levofloxacin and moxifloxacin revealed that, out of 1550 M. tuberculosis strains, 146 (9.4%) were resistant to levo (1.5µg /ml) and moxi both concentrations (0.5µg /ml, 2.0 µg /ml) and 611 (39.4%) strains were resistant to levo (1.5µg /ml) and moxi (0.5µg /ml). The resistance to levofloxacin alone was higher (3.6%) than that reported to moxifloxacin (1.5%) using critical concentrations i.e 1.5µg /ml and 0.5µg /ml respectively.
Conclusion: Our results demonstrated that despite cross-resistance between these two fluoroquinolones, moxifloxacin is comparatively more effective even when used in lower concentration. More studies are needed using different concentrations of fluoroquinolone in various categories of patients to evaluate treatment outcomes for management of tuberculosis patients.

FEASIBILITY OF ONCE-A-DAY DOSING OF DELAMANID BASED ON PK/PD ANALYSIS

Mallikaarjun, Suresh, Dr; Hariguchi, Norimitsu, Mr; Sasaki, Tomohiro, Dr; Matsumoto, Makoto, Dr; Geiter, Larry, Dr; Hafkin, Jeffrey, Dr; Wang, Xiaofeng, Dr; Liu, Yongge, Dr

Delamanid is approved in several countries for the treatment of multi-drug resistant tuberculosis (MDR-TB) at a dose of 100mg twice-a-day (BID). A pharmacokinetics/pharmacodynamics (PK/PD) analysis was performed in accordance with the European Medicines Agency 2016 guideline on the use of PK/PD in the development of antimicrobial medicinal products to evaluate the feasibility of 200mg once-a-day (QD) dosing.

To determine the delamanid PK parameter best correlated with effect, a PK/PD analysis, using colony forming unit (CFU) from ICR mice infected with *M. tuberculosis* Kurono and PK data from uninfected mice, was performed. The results indicated that CFU reduction was best correlated with AUC/MIC. Next, PK/PD analyses were performed using sputum bacterial load reductions from two early bactericidal activity trials in drug susceptible TB patients. Delamanid AUC/MIC and log10CFU reduction data were modeled using a nonlinear mixed effects approach.

An inhibitory sigmoid Emax model with random effect on Imax provided the best fit to the data. The clinical PD target (cPDT), defined as EC80, i.e. the AUC/MIC achieving 80% of maximum efficacy (Emax), determined to be 171.

Using the cPDT of 171, the probability of target attainment (PTA) following the currently approved 100mg BID dose, was determined in two trials, -204 and -213, using individual baseline delamanid MIC values (dMIC) and steady-state AUC (AUCss) values. The PTAs were 100% and 97.6% in trials -204 and -213, respectively. Using data from Trial 213 (100mg BID for 8 weeks + 200mg QD for 16 weeks), the PTA for 200mg QD was calculated to be 95.4%, using dMIC and AUCss for 200mg QD (estimated by population PK analysis).

In conclusion, the PTA of the 200mg QD is close to that of the currently approved dose of 100mg BID in MDR-TB, indicating that once-a-day regimen for delamanid is likely feasible, based on PK/PD analyses.

OUTCOMES OF PULMONARY REHABILITATION IN FOUR COUNTRIES ON THREE CONTINENTS

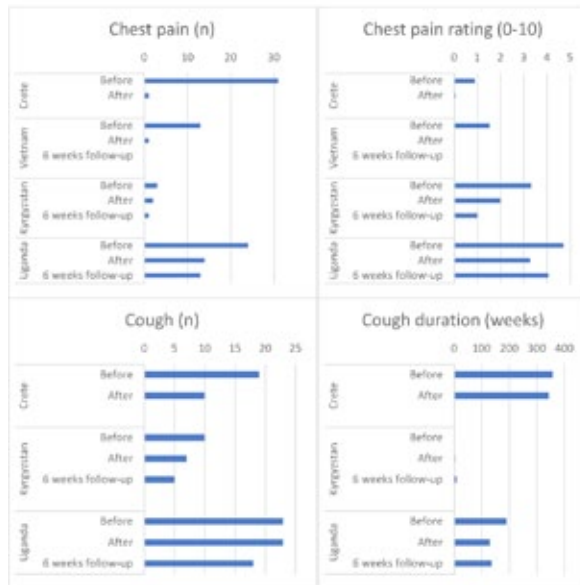
van Kampen, Sanne, Dr; Jones, Rupert, Dr; Katagira, Winceslaus, Dr; Kirenga, Bruce, Dr; Pham, An Le, Dr; Anastasaki, Marilena, Ms; Sooronbaev, Talant, Prof; Singh, Sally, Prof

Introduction: Pulmonary rehabilitation (PR) is an evidence-based non-pharmaceutical intervention for people with chronic lung diseases with potential benefit in post-TB lung disorders (PTBLD). In the FRESH AIR research programme, implementation studies of PR were undertaken in Greece, Kyrgyzstan, Uganda and Vietnam.

Methods: A six week twice-weekly PR program was co-designed with local physiotherapists, doctors and nurses. The program consisted of education and exercise sessions including strength and endurance based on walking. Inclusion criteria were a confirmed diagnosis of a chronic lung disease, MRC dyspnoea scale >=2 and no important co-morbidities. In addition to conventional PR outcomes of exercise capacity and quality of life, we recorded changes in symptoms including cough, chest pains and haemoptysis.

Results: 116 patients completed the programme: 31 in Greece; 17 in Kyrgyzstan; 44 in Uganda; and 24 in Vietnam. The median age was 60 years (49, 69 IQR), 51% female, 10% current smokers, 31% had PTBLD, 34% COPD, and others had asthma, bronchiectasis etc. Clinically important improvements were seen in exercise capacity, breathlessness and quality of life (reported elsewhere). The number of participants reporting chest pains reduced considerably after PR for both COPD (from 59% to 8%) and PTBLD patients (from 53% to 29%). Cough reduced among COPD (from 62% to 38%) but not among PTBLD patients (from 47% to 53%). Reported duration of cough as well as average chest pain rating scores reduced as shown in Figure 1. Haemoptysis was only present in PTBLD and fell from 19% to 6%.

Figure 1. Chest pain and cough reported among participants of pulmonary rehabilitation programmes in Greece, Vietnam, Kyrgyzstan and Uganda.



Conclusions: In this implementation study, chest pains and cough were very prevalent in both patients with COPD and PTBLD. Besides the improvements in conventional PR outcomes, major improvements were seen in chest pains and haemoptysis after PR.

NUTRITION STATUS AMONG TB/HIV CO-INFECTED PATIENTS ATTENDING KAPKATET COUNTY HOSPITAL, KERICHO COUNTY KENYA

Sambu, Cheruiyot, Dr

Background: Despite national progress on increased acess to care and treatment of patients with tuberculosis TB/HIV still remain a major cause of mortality in undernourished patients. 60% of TB/HIV co-infected patients in Kapkatet hospital are undernourished. Undernutrition lowers immunity leading to more complications. Currently nutrition supplements supporting TB/HIV patients target only severe acute malnutrition with body mass index less than 16 kg/m^2 leaving out others.
All the relapse TB cases were undernourished and 50% missed admission criteria for nutrition supplements. This study aimed to evaluate Nutrition status of TB/HIV co-infected attending Kapkatet hospital.
Methods: Prospective study was done on patients who attended TB/HIV clinic for care and treatment from January 2018 to December 2018. Body mass index (BMI) was the main anthropometric assessment done to establish nutrition status and data analysis done using STATA.
Results: Under nutrition ith BMI <18.5 kg/m2 was 60% (n=112) among them 80% were male. only 15% were severely malnousished with BMI <16 while the rest had BMI between 16 and 18.5 classified as moderate acute malnutrition.There was a positive corelation between nutrition status and gender (p=0.005) whereby all severe acute malnutrition cases were Males.
Conclusion and recommendations: Structured nutrition assessment, nutrition diagnosis and nutrition intervention is critical in adressing malnutrition in TB/HIV co-infected patients. there is need to support all undernourished with BMI <18.5 kg/m2 with regular and timely supply of nutrition supplements and more emphasis should be put on male clients in terms of nutrition counselling and supplementation.

EVALUATION OF TREATMENT PROGRESS IN TUBERCULOSIS PATIENTS BASED ON THEIR SERUM METABOLITE PROFILES

Antti, Henrik, Prof; Prat, Cristina, Dr;
Dovga, Natalia, Ms; Jonsson, Pär, Dr;
Nikolayevskaya, Elena, Dr; Zinchenko, Oksana, Dr;
Dominguez, Jose, Dr; Rzhepishevska, Olena, Dr

Background: Drug-resistant TB is a global challenge. Treatment of drug-resistant TB takes up to 2 years and the tools to measure the progress of treatment are limited. Here, we evaluate an approach to monitor treatment progress through metabolite signatures from serum of TB patients under treatment. We identified and used metabolites - markers of TB severity for evaluation of the treatment progress. Our hypothesis has been that when treatment scheme is successful, the signatures of the disease would decrease.
Methods: serum samples were collected from 64 Ukrainian patients. Patients with drug resistant and drug sensitive TB where included. Of these patients 22- had TB classified as a severe case; 17 - medium severity, 19-mild TB. Samples were collected before treatment start and after 1 month of treatment. Serum samples were analyzed with gas chromatography/mass spectrometry (GC-MS). Spectra were identified through comparison to a metabolite library.
Clinical evaluation of patients was done by chest X ray/tomography, acid-fast bacilli in sputum 2 month after treatment start (clinical practice in Ukraine). Orthogonal partial least squares discriminant analysis (OPLS-DA) and principal component analysis (PCA) were employed to discover and validate the metabolite markers.
Results and Conclusions: OPLS-DA modelling revealed 13 metabolites characteristic of mild or severe TB. Among those metabolites tryptophan has previously been shown to be involved in host defense mechanism and methyl histidine is a biomarker for tissue breakdown. Samples from medium severity cases where used to validate the 13 metabolite panel for evaluation of treatment success after the first month of treatment.
Valid model for separation of samples with good and poor treatment progress has been developed. Hence, treatment evaluation by metabolite panel can be done one month earlier than traditional evaluation by conventional clinical methods. Further validation of the results is needed with larger cohort of TB patients.

CHARACTERISATION OF PYRAZINAMIDE MINIMUM INHIBITORY CONCENTRATIONS AND PNCA SEQUENCING AMONGST RIFAMPICIN-RESISTANT TUBERCULOSIS ISOLATES IN KWAZULU-NATAL, SOUTH AFRICA

Millard, James, Dr; Nimmo, Camus, Dr;
Chetty, Kandaseelan, Mr; Mthabela, Ntombifuthi, Ms;
Brien, Kayleen, Ms; Naidoo, Taryn, Ms;
Moodley, Sashen, Mr; Karim, Farina, Ms;
Pym, Alexander, Dr; Davies, Geraint, Prof

Background: Pyrazinamide (PZA) is a key drug in tuberculosis (TB) therapy, allowing drug-susceptible TB treatment to be reduced to six months and forming part of most current and trial regimens for multidrug-resistant TB (MDR-TB). This is despite one-third to two-thirds of MDR-TB isolates being resistant to PZA.
Alongside recent evidence that minimum inhibitory concentrations (MIC) of TB drugs predict outcomes even amongst sensitive isolates, the distribution of PZA MICs in MDR-TB is likely to be of clinical importance. Most PZA-resistant isolates demonstrate mutations in

the *pncA* gene and given difficulties in PZA resistance testing, sequencing technologies may offer an alternative to phenotypic testing.

Methods: Patients with at least rifampicin resistant TB were recruited in KwaZulu-Natal, South Africa as part of a pharmacokinetic study. Baseline positive sputum samples were evaluated with phenotypic drug susceptibility testing, PZA MICs and whole-genome sequencing.

Results: Forty-two isolates were characterised, 50% (21/42) of which were resistant and 50% sensitive (21/42) to PZA at a concentration of 100μg/ml. Most (76.2%, 16/21) resistant isolates demonstrated high-level resistance (MIC ³1000μg/ml), of these 93.8% (15/16) had a non-synonymous *pncA* mutation. Several (23.8%, 5/21) resistant isolates demonstrated lower-level resistance (MIC 120-200μg/ml), of these only 40% (2/5, both with an MIC of 200μg/ml) had a *pncA* mutation. Amongst sensitive isolates, MICs were distributed throughout the range and none had a *pncA* mutation.

Discussion: The prevalence of PZA resistance was similar to other MDR-TB cohorts and underscores the importance of more fully understanding the role of PZA in MDR-TB therapy. The MIC range for isolates without a *pncA* mutation was broadly distributed and extended above the usual resistance threshold. The clinical implications of this merit further pharmacokinetic / pharmacodynamic study. Mutations in the *pncA* gene predicted the vast majority of isolates with an MIC ?200μg/ml and suggest that this should prompt PZA discontinuation.

Pyrazinamide minimum inhibitory concentration (MIC)*	Frequency of MIC	Frequency of non-synonymous pncA mutations at MIC	pncA mutation
<10	4/42 (9.5%)	0/4 (0%)	n/a
20	3/42 (7.1%)	0/3 (0%)	n/a
40	9/42 (21.4%)	0/9 (0%)	n/a
60	3/42 (7.1%)	0/3 (0%)	n/a
80	2/42 (4.8%)	0/2 (0%)	n/a
120	1/42 (2.4%)	0/1 (0%)	n/a
160	1/42 (2.4%)	0/1 (0%)	n/a
200	3/42 (7.1%)	2/3 (66.6%)	175T>C, 452T>C
1000	2/42 (4.8%)	1/2 (50%)	175T>C
1200	1/42 (2.4%)	1/1 (100%)	22G>A
1400	1/42 (2.4%)	1/1 (100%)	100T>G
≥1600	12/42 (28.6%)	12/12 (100%)	100T>G (x2), 173T>C (x2), 204G>T, 289G>T (x2), 290G>A, 452T>C, 456dup (x3)

*Table: Frequency of pyrazinamide minimum inhibitory concentrations (MIC) and associated non-synonymous pncA mutations in a cohort of 42 patients with rifampicin-resistant tuberculosis. *MICs tested in BACTEC MGIT at the following concentrations; 10,20 ,40,60,80,100,120,160,200,300,400,500,600,700,800,100 0,1200,1400 and 1600μg/ml.*

MINOR GROOVE BINDERS AS NOVEL ANTI-MYCOBACTERIAL AGENTS AND THE EFFECT OF USING NON-IONIC SURFACTANT VESICLES AS A DRUG DELIVERY SYSTEMS FOR PATHOGEN-DIRECTED DRUG THERAPY FOR

Hlaka, Lerato, Ms; Rosslee, Michael, Mr; Ozturk, Mumin, Dr; Kumar, Santosh, Dr; Parihar, Suraj, Dr; Brombacher, Frank, Prof; Khalaf,, Abedawn, Dr; Karter, Katherine, Prof; Scott, Fraser, Dr; Suckling, Colin, Prof

Minor groove binders (MGBs) have previously revealed promising antimicrobial activity against various infectious agents; however, they have not yet been screened against Mtb. We have evaluated the role of MGBs as antimycobacterial compounds against Mtb and further investigated the use of non-ionic surfactant vesicles (NIVs) as a drug delivery system on the improvement of delivery and efficacy of MGB compounds to Mtb *in vitro* and *in vivo*.MGB compounds were screened for mycobactericidal activity using an H37Rv-GFP microplate assay yielding a hitlist of MIC99 concentrations of 0.39 uM and 1.56 uM. Of the 168 compounds screened, 17 hits were identified of which 2, MGB-362 and MGB-364 displayed intracellular mycobactericidal activity against Mtb HN878 at an MIC50 of 4.09 and 4.19 uM, respectively, whilst being non-toxic. Subsequent formulation in NIVs increased intracellular mycobacterial activityof drug compounds. Treatment with MGB 364 or MGB-NIV 364 formulation did not cause DNA damage as displayed by low expression of ?-H2Ax compared to H2O2 and DMSO. Therapeutic treatment with MGB and MGB-NIV via a weekly intranasal dose of 0.5mg/kg in HN878 infected C57BL/6 mice showed a reduction in Mtb CFU burden in MGB; MGB-NIV together with an increase in lung pro-inflammatory/type 1 cytokine profile, suggesting that treatment with MGBs enhances protection against Mtb *in vivo*. Therefore, MGBs show potential as a novel class of drug/chemicals in the future of anti-TB therapy. Furthermore, the ability of NIVs to better deliver entrapped MGB compounds to an intracellular Mtb and *in vivo* provides hope for a novel TB therapy.

IL-4I1 REGULATES MACROPHAGE MEDIATED IMMUNE RESPONSES TO ACUTE MYCOBACTERIUM TUBERCULOSIS INFECTION

Hlaka, Lerato, Ms; Ozturk, Mumin, Dr; Chia, Julius, Mr; Brombacher, Frank, Prof

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*) is the leading infectious disease epidemic that claims over 1.6 million lives, while 10 million fell ill in 2017. Understanding the complex host-pathogen interaction may help find new drug targets for TB therapy. This interaction may then lead to host-directed therapies (HDT) for TB. IL-4i1 was among the candidate genes that were upregulated in IL-4/IL-13 alternatively activated macrophages during *Mtb* infection in our genome-wide CAGE transcriptional analysis. IL-4i1 is a secreted L-amino oxidase which converts Phenylalanine into phenylpyruvate releasing toxic products ammonia and hydrogen peroxide. The enzymatic activity was previously reported to in turn cause immunosuppression of effector T-cells by directly inhibiting polarization, proliferation and function of T-cells. These data suggested that IL-4i1 is involved in immune-regulatory mechanisms and may be implicated in immune evasion mechanisms by *Mtb*. To determine the functional role of IL-4i1 during *Mtb* infection, IL-4i1-deficient mice and wild-type (WT) littermate controls were infected with *Mtb* H37Rv and hyper-virulent HN878 *Mtb* strain. IL-4i1 deficient mice were highly resistant to both strains at 21 days post-infection and at 12 days post-infection during HN878 *Mtb* infection. Resistance to *Mtb* infection was denoted by a significant reduction of bacterial loads, reduced inflammation, reduced tissue iNOS expression, and reduced recruitment of interstitial macrophages, in IL-4i1-/- mice compared to WT. Pro-inflammatory cytokines were reduced, however not significant. Interestingly there was a significant increase in nitric oxide production in infected IL-4i1-/-tissues. At 12 days post-infection, IL-4i1-/- showed increased in M1-like macrophages that correlated with increased pro-inflammatory cytokines and chemokines when compared to WT. These data suggested that IL-4i1 regulates macrophage-mediated inflammatory responses during acute *Mtb* infection, thus showing potential as an immunomodulatory target for TB HDT therapy.

A SMART APPROACH TO REVERSING DRUG RESISTANCE IN TB AND DEPLOYING THE HIDDEN POTENTIAL OF CURRENT TB DRUGS

Lociuro, Sergio, Dr; Gitzinger, Marc,Dr; Kemmer, Christian, Dr; Bourotte, Marilyne, Dr; Trebosc, Vincent, Dr; Dale, Glenn, Dr; Pieren, Michel, Dr; Baulard, Alain, Dr; Deprez, Benoît, Prof; Willand, Nicolas, Prof; Ballell, Lluis, Dr; Mendoza, Alfonso, Dr; Jimenez, Elena, Dr; Martinez, M. Santos, Dr; Barros, David, Dr; Porras, Esther, Dr; Perez-Herran, Esther, Dr; Rullas, Joaquin, Dr; Gresham, Stephanie, Dr; Remuinan, Modes, Dr

How much potential is hidden in existing prodrugs that have been used for several decades? In previous reports we have shown that Small Molecules Aborting Resistance (SMARt) can reverse the innate resistance to the TB prodrug ethionamide (ETH) by interfering with the transcriptional regulator EthR (2009) and to acquired resistance by activating cryptic bioactivation pathways such as EthR2/EthA2 published in 2017. Further optimization and investigation into the mode of action links our clinical candidates to an additional bioactivation path for the prodrug ETH (VirS/MymA operon). We present two molecules with a good resistance profile, a very high potency in vitro and in vivo, and excellent PK and safety, meeting in both cases clinical candidate requirements. These molecules are currently in preclinical toxicology studies. Murine efficacy data and time kill curves give first insights to the true potential of the old TB prodrug ETH for future treatment regimens. Combining the two essential features of the SMARt-ETH combination: i) overcoming ETH resistance and no cross resistance with isoniazid (INH) in clinical TB isolates and ii) the ability to potentiate ethionamide efficacy at lower clinical doses of the drug, hint at the possibility to replace isoniazid in future TB drug regimens as the fast CFU reducing agent.

OPTIMIZING THE SHORTER REGIMEN FOR MULTIDRUG-RESISTANT TUBERCULOSIS PATIENTS WITH MOLECULAR DRUG SENSITIVITY TESTING: FEWER, SHORTER, BETTER

Li, Yang, Dr; Sun, Feng, Dr; Zhang, Wenhong, Prof

Background: Treatment of multidrug-resistant tuberculosis (MDR-TB) remains challenging, with lengthy treatment durations and complex drug regimens. Introducing drug susceptibility testing are proven to guide treatment decisions and improve treatment outcomes.
Methods: A multi-center, prospective singer-arm study was launched in twelve hospitals located in six provinces (Zhejiang, Jiangsu, Sichuan, Xinjiang, Henan, Chongqing) in China. Patients aged between 18 to 65 years with active laboratory-confirmed pulmonary MDR-TB were

screened. Among them, patients with pyrazinamide sensistivity were eligible for inclusion and received the shorter regimen of 12-month regimen that included 6 months of pyrazinamide, amikacin, moxifloxacin, prothionamide, and clarithromycin or cycloserine if cycloserine was available when they initiated their treatment, followed by 6 months of pyrazinamide, moxifloxacin, prothionamide, and clarithromycin or cycloserine.
Results: A total of 51 patients were enrolled. 42 (82.4%) patients were treated successfully. Of the seven patients with treatment failure, four discontinued treatment due to intractable adverse drug reactions, two did not have culture conversion within the intensive phase, and one achieved subsequent reversion. Two patients were lost to follow up. After exclusion of fluroquinolone- and amikacin-resistant tuberculosis patient, the treatment success rate reached 86.2%.
Conclusion: Introducing molecular susceptibility testing to pyrazinamide could select MDR-TB patients who could be treated successfully with the 12-month regimen of five drugs.

Poster Theme: Bacterial evolution

THE GENETIC PROFILE OF DRUG RESISTANCE AND TB HISTORY

Huang, Chuan-Chin, Dr; Calderon, Roger, Dr; Mercedes, Becerra, Prof; Lecca, Leonid, Dr; Contreras, Carmen, Mr; Yataco, Rosa, Ms; Galea, Jerome, Dr; Zhang, Zibiao, Mr; Murray, Megan, Prof

Background: In clinical tuberculosis (TB) settings, it is important to distinguish between primary drug resistance and acquired drug resistance, as the former suggests the need for better transmission control, while the latter indicates poor patient compliance. The most frequently used indicator of primary or acquired resistance is a patient's history of tuberculosis. However, it is still unknown whether the genetic profiles of clinical isolates reflect the two different mechanisms. In this study, we evaluate whether the genetic profiles of drug-resistance TB clinical isolates vary by the patient's history of tuberculosis, conditional on the resistance phenotypes.
Methods: We conducted a cohort study in Lima, Peru. Over a 36-month enrollment period, we enrolled 4,500 incident tuberculosis patients. Culture-positive isolates of the patients underwent drug sensitivity tests and paired-end whole genome sequencing. We first identified the single nucleotide polymorphism (snps) of the well-known resistance-causal-genes of the five first-line drugs in our study cohort (isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin). We then evaluated whether the prevalence of these drug-resistant-associated snps varied by the patients' history of tuberculosis.
Results: We identified four resistance-associated-snps which were more prevalent in patients with TB history than in those without it, indicating that these snps were associated with acquired resistance. We also identified one resistance-associated-snp that only appeared in patients without TB history.
Discussion: We demonstrated that the genetic profiles of resistance varied by the patients' history of tuberculosis. Our findings provide fundamental information for future exploration of the differential mechanisms involved in acquired resistance and transmitted resistance.

POTENTIALLY MISSED DRUG-RESISTANT MUTATIONS AMONGST DR-TB PERSONS LIVING IN CHENNAI, INDIA

Sembulingam, Tamilzhalagan, Dr;
Shanmugam, Sivakumar, Dr; Sakthi, Suba, Dr;
Surie, Diya, Dr; Selvaraju, Sriram, Dr;
Tripathy, Srikanth Prasad, Dr;
Sachdeva, Kuldeep Singh, Dr; Moonan, Patrick K, Dr;
Hall, Patricia J, Dr; Ranganathan, Uma Devi, Dr

Background: Laboratory detection of drug-resistant (DR) *M. tuberculosis* is a major challenge. Despite the availability of commercial drug susceptibility testing (DST) assays, persons with DRTB can be missed or misclassified. In particular, there are challenges establishing biologically-relevant drug concentrations for phenotypic DST, detecting low levels of mutation-associated resistance, and detecting resistance-associated mutations not included in WHO-recommended molecular diagnostics.
Methods: All viable *M. tuberculosis* isolates stored from patients that received line probe assay (LPA)-based DST and multidrug-resistant TB treatment in Chennai from 2013–2016 underwent solid culture, DNA extraction, whole genome sequencing (WGS), and MGIT DST (14 drugs). An in-house WGS pipeline was used for mutation identification and resistance prediction – averaging 80X depth of genome coverage. We assessed discordance between LPA, WGS and MGIT DST results.
Results: A total of 166 isolates were included. Seventeen (12%) of 137 isoniazid-resistant isolates were detected by MGIT. WGS mutations in *kat*G (n=11), *ahp*C (n=2) and *inh*A (n=4) were originally undetected by LPA — the most commonly used test for isoniazid resistance in India. Among these 17, 2 (12%) were isoniazid mono-resistant. Fifteen (10%) of 146 rifampicin-resistant isolates with *rpo*B mutations (L430P/R, L452P, D435Y, and H445S/L) were associated with low-level resistance and missed by MGIT using the WHO-recommended minimal inhibitory concentration (MIC:1µg/ml). One-third of clinical isolates, (54/166) harboring low-level resistance-associated mutations for ethambutol were susceptible by MGIT (MIC:5µg/ml).
Conclusion: WGS improved our ability to detect drug-resistant TB, not otherwise detected by other methods. Expanded MICs for rifampicin and ethambutol should be considered to complement WGS results for low-level resistance detection. Given the substantial proportion of isoniazid resistance undetected by LPA, testing for all known mutations – amongst persons presumed to have DR – would best inform patient classification and treatment.

DIAGNOSIS OF ZOONOTIC MYCOBACTERIUM AFRICANUM TRANSMISSION BETWEEN HUMAN AND CATTLE: A CASE REPORT

Abubakar, Bello, Dr

Tuberculosis is one of the most important infectious diseases of Humans and cattle in Nigeria and Africa. This study aimed at reporting a case of human to cattle transmission of zoonotic *Mycobacterium africanum* based on culture, SD Bioline TB Ag MPT64 and multiplex PCR known as Genotype MTBC.
A cattle herd was tested for *Mycobacterium* infection using single caudal fold intradermal tuberculin test and a bull reacted positively, but showed no gross TB pathological lesions after slaughter. The cattle rearer was also diagnosed with active pulmonary TB in the hospital. The cattle rearer's sputum and the bull's bronchial as well as retropharyngeal and mediasternal lymph nodes were obtained, processed and cultured. The isolates were analysed using SD Bioline TB Ag MPT64 as well as Genotype MTBC. The results revealed that both the rearer's sputum as well as the bull's lymph nodes yielded *Mycobacterium africanum* which is primarily a human pathogen and rarely been isolated from cattle.
The report highlight the importance of *Mycobacterium africanum* and it zoonotic public health implications between humans and cattle transmission. Measures for control are also been suggested.

ASSOCIATION OF MYCOBACTERIUM AFRICANUM INFECTION WITH SLOWER DISEASE PROGRESSION AND LOW BODY MASS INDEX COMPARED TO MYCOBACTERIUM TUBERCULOSIS IN MALIAN PATIENTS WITH TUBERCULOSIS

Diarra, Bassirou, Dr; Baya, Bocar, Dr; Diabate, Seydou, Dr;
Kone, Bourahima, Mr; Maiga, Mamoudou, Dr;
Diakite, Mahamadou, Prof; Doumbia, Seydou, Prof;
Diallo, Souleymane, Prof

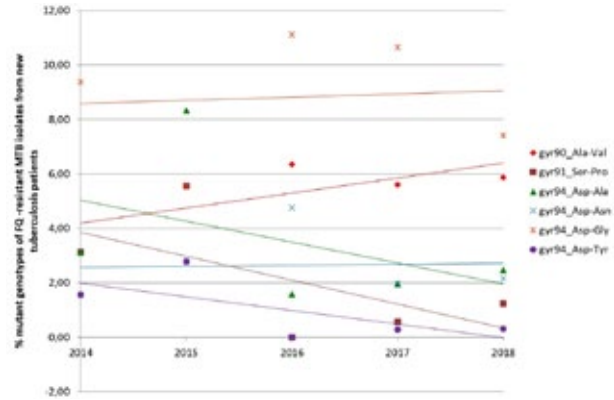
Introduction: Tuberculosis (TB) remains a critical public health issue in resource-limited settings but also globally because of migration. M. africanum (MAF) or Lineage (L) 6 is known to endemically cause up to 40-50% of all pulmonary TB in West Africa. The aim of this study was to compare MAF with M. tuberculosis senso stricto (MTB) (L4) with regard to time from symptom onset to TB diagnosis, and clinical and radiological characteristics.
Methods: We conducted a cross sectional study to enroll new TB patients and naïve to treatment in Bamako. Seventy-seven (77) consecutive, newly diagnosed patients with pulmonary TB and naive to treatment were enrolled. Sputum cultures were used to make the diagnosis and spoligotyping was used to identify the mycobacterial strain.

Results: MAF infection was more common in female [25% vs. 10.0% for MTB (OR =2.9)], and in patients ≥ 30 years [57.1% vs. 36.7% (OR = 2.3)]. More MAF- than MTB-infected patients had a history of prior TB contact [32.1% vs. 14.3% (OR= 2.8)].
The mean duration between symptom (e.g., cough) onset and TB diagnosis was 111 days (~3.7 months) for MAF and 72 days (~2.4 months) for MTB lineage-4 (p= 0.007). In a multivariate regression, weight loss (BMI < 18.5 kg/m2) and cough duration (> 4 months) were strongly associated with MAF infection [OR= 5.20 (1.49-18.26), p= 0.010 and 4.74 (1.2-18.58), p= 0.02], respectively.
Conclusion: Our data show that MAF infection was significantly associated with lower BMI and a longer time between symptom onset and TB diagnosis compared to MTB. While a larger cohort study is needed, our data support the concept that MAF infection may have slower disease progression and less severe cough symptoms compared to MTB, and could explain partially why MAF is endemic in our West African region.
Keywords: M.africanum; M. tuberculosis, Disease progression, Bamako, Mali

EVOLUTION OF SPREAD OF M. TUBERCULOSIS WITH DIFFERENT GENETIC DETERMINANTS OF RESISTANCE TO FLUOROQUINOLONES (BASED ON THE POPULATION IN RUSSIA FOR THE PERIOD OF 2014-2018)

Ergeshov, Atadzhan, Prof; Andreevskaya, Sofya, Dr; Smirnova, Tatiana, Dr; Larionova, Elena, Dr; Chernousova, Larisa, Prof

Fluoroquinolones (FQ) is the main group of drugs used for MDR-TB treatment. Therefore, further evolution of MBT with multidrug resistance will be targeted on the development of resistance to FQ. The objective is to study the evolution of the modern population of MBT in the Russian Federation in terms of accumulation of genetic determinants of FQ resistance.
Materials and **Methods:** The study was focused on the MBT isolates from 2,429 patients with MDR-TB treated at the Central TB Research Institute in 2014-2018. The genotypic resistance to FQ was identified by the presence of mutations in the gyrA gene with the use of biochips "TB-BIOCHIP-2" (BIOCHIP-IMB, Russia) and allele-specific real-time PCR in "AMPLITUBE-FQ-RV" (Syntol, Russia).
Results: The study showed that of 2,429 MDR-TB patients, MBT with the wild type gyrA was isolated in 1,747 (72%) patients, and with mutations in gyrA - in 682 (28%) patients. The frequency of the main MBT mutations in gyrA in new cases is presented in the graph. It shows that MBT with three mutant genotypes (gyrA91_Ser-Pro, gyrA94_Asp-Ala and gyrA94_Asp-Tyr) have a negative trend of distribution in the population and with genotypes gyrA94_Asp-Asn, gyrA94_Asp-Gly and, especially, gyrA90_Ala-Val - a positive trend of distribution.
Conclusion: According to the study results, mutations associated with resistance to FQ, ambiguously affect the ability of MBT to spread in the population. The positive trend in accumulation of mutations gyrA94_Asp-Asn, gyrA94_Asp-Gly and gyrA90_Ala-Val in the modern population of MBT suggests that these mutations do not have a negative impact on the fitness of mycobacteria and provide evolutionary success to the MBT strains with resistance to FQ.
The study is performed within the topic of research project # 0515-2019-0015 "Development of anti-TB drugs resistance in mycobacteria and somatic cells".



GENOME TB EPIDEMIOLOGY FROM NATIONAL PREVALENCE SURVEY IN MONGOLIA

Tumenbayar, Oyuntuya, Dr; Murase, Yoshiro, Dr; Narmandakh, Erdenegerel, Dr; Erkhembayar, Baasansuren, Dr; Borolzoi, Tsetsegtuya, Dr; Boldoo, Tsolmon, Dr; Dambaa, Naranzul, Dr; Aono, Akio, Dr; Morishige, Yuta, Dr; Chikamatsu, Kinuyo, Dr; Burneebaatar, Buyankhishig, Dr; Mitarai, Satoshi, Prof

Background: WGS of MTB is an attractive method for the confirmation of genetically identical strains and accurate detection of clinically relevant mutations/indels for AMR predictions. Mongolia has conducted national TB prevalence survey in 2014-2015. TB prevalence rate was much higher (560/100,000) than the estimation by the WHO for 2013. The NTRL and RIT have been conducting the molecular analysis of MTB isolates collected from this survey to examine TB transmission and analyse DR-TB clusters using WGS.
Methods: The MTB isolates were confirmed as pure culture, and the genome DNA was extracted using Isoplant (Fujifilim Wako, Japan). The DNA library was prepared using Nextera XT DNA library preparation kit (Ilumina), and subjected to MiSeq sequencer (Ilumina). MTBseq program was used for the SNV analysis. For the

tree construction, we employed the programme FastTree version 2 (Price, Dehal & Arkin, 2010) in the double precision built with a general time reversible substitution model, 1,000 resamples, and Gamma20 likelihood optimization. EvolView was used to visualize the phylogenetic tree.
Results: We analysed a total of 216 MTB isolates (54% from Ulaanbaatar), of which 22 (10.2%) were MDR-TB. The isolates in PVS were mainly composed of lineage 2 (75.0%), especially East-Asian Beijing, and 54 (25.0%) of lineage 4 (Euro-American LAM and others). A total of 26 clusters (?12 SNVs) was identified (cluster size, 2-13). The clustering rate was 48%, and two MDR-TB clusters (size 5 and 6) were identified. No specific strain was predominant in the country, but approximately half of the strains were considered new transmissions.
Conclusion: TB isolates from the PVS indicated the predominance of lineage 2 in the community. The high clustering rate suggests recent transmissions are common in Ulaanbaatar. Infection control and prophylaxis will be a key to reduce TB.

POPULATION-BASED MOLECULAR EPIDEMIOLOGICAL STUDY IDENTIFIES TRANSMISSION HOTSPOT AND A HIGH RATE OF RELAPSE AMONG RECURRING TB CASES IN ACCRA, GHANA

Asare, Prince, Mr; Otchere, Isaac, Dr; Bedeley, Edmund, Mr; Brites, Daniela, Dr; Asante-Poku, Adwoa, Dr; Gagneux, Sebastien, Prof; Yeboah-Manu, Dorothy, Prof

The understanding of risk factors that aid transmission is useful for TB control. Accordingly, a population-based molecular epidemiological study was conducted to determine the transmission pattern and dynamics of *Mycobacterium tuberculosis* complex (MTBC) strains in Ghana. Isolates from consecutively sampled TB patients between July 2012 and December 2015 were confirmed as members of the MTBC by standard genotyping techniques and combined with demographic and clinical data for risk factor assessment. We used SaTScan and ArcMap analyses to identify and map significantly clustered MTBC lineages/sub-lineages. Whole-genome sequencing (WGS) analysis was performed to resolve traditional genotype clusters following which phylogenetic analysis was then used to assess strain relatedness. Among 2,551 isolates genotyped for Spatio-temporal analysis, 2,019 (79.1%), 516 (20.2%) and 16 (0.6%) were identified as *M. tuberculosis* sensu stricto (MTBss), *M. africanum* (MAF) and *M. bovis* respectively. MAF lineages were found to persist at approximately 20% over an 8-year period. Whereas the Cameroon sub-lineage was associated with Southern Ghana, the Beijing, Ghana and animal genotypes were significantly ($p<0.05$) associated with Northern Ghana. We estimated the recent transmission rate of 24.7% using WGS and confirmed the existence of reduced recent transmission of MAF compared to MTBss L4. WGS confirmed a widespread of a Cameroon sub-lineage clone mainly from the Ablekuma sub-district (transmission hotspot) and more importantly, identified a recent transmission cluster associated with isoniazid resistance belonging to the Ghana sub-lineage. Risk factor analysis using logistic regression modeling identified younger individuals (age <30 years) and male gender as significant risk factors for recent TB transmission. Recurrent TB was attributed to inadequate treatment (relapse of the same strain) in 75.0% (27/36) of participants with 25.0% (9/36) attributed to re-infection. For the first time in Ghana using WGS, we confirm high recent TB transmission within the population-driven largely by MTBss sub-lineages Cameroon and Ghana.

NEED TO CONSIDER ZOONOTIC TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS TO CURB TUBERCULOSIS THROUGH ONE HEALTH STEWARDSHIP

Das, Samir, Dr; Vise, Esther, Dr; Garg, Akshay, Dr; Mawlong, Michael, Dr; Shakuntala, Ingudum, Dr; Sanjukta, Rajkumari, Dr; Bharat Prasad, Chendu, Dr; Sen, Arnab, Dr

The devastating morbidity from tuberculosis (TB) in human should garner stronger participation from the public, policy makers and researchers alike. While human TB remains endemic to a country like India, with *Mycobacterium tuberculosis* as the main causative agent, around 7% bovines are positive for tuberculin test, caused by *M.bovis*. Additionally, the seemingly harmless nontuberculous mycobacteria (NTM) presents clinical dilemma while managing TB cases in the endemic regions and surpasses pulmonary TB cases in developed countries. The diagnosis of tuberculosis mainly rests on sputum smear microscopy for most of the human population that does not differentiate these three entities which requires different treatment regimen. In our study of different mycobacterial flora from bovine milk (n=200), one *M.tuberculosis* and 23 NTM were obtained. Our representative human study (n=119) from targeted TB patients isolated 21 *M.tuberculosis* and two NTM. In a collaborative approach with medical, veterinary and other research institutions, detection of mycobacterial infections in human and animals through isolation and advanced instrumentation were attained, there by bolstering the attendance of such cases in the region. In India, TB diagnosis in bovine population is usually limited to tuberculin testing which presents its own inadequacies. Segregation policy is followed in most parts of the country but culling is not practiced. While the country has a nation-wide TB control program in place, several patients runs the risk of being misdiagnosed as *M.tuberculosis* at the initial stage and

as drug resistant-TB during follow-ups. Identification of the mycobacterial entity in TB cases at least up to the complex level is crucial for the right treatment outcome. Our observations cements the need for differential diagnosis and an urgent action to improve TB diagnostics. There is also a requirement to combat zoonotic tuberculosis in mission mode and holistic One Health approach to eradicate the TB burden.

COMPARISON OF TUBERCULOSIS (TB) YIELD AND RISK FACTORS AMONG HOUSEHOLD CONTACTS OF PERSONS WITH DRUG-RESISTANT AND DRUG-SUSCEPTIBLE TB IN SOUTH AFRICA

Velen, Kavindhran, Dr; Podewils, Laura, Dr; Shah, Sarita, Dr; Churchyard, Gavin, Prof; Charalambous, Salome, Prof; Reichler, Mary, Dr

Household contact tracing (HHCT) remains a key TB case-finding approach, however variability in TB yield among HHCs and low uptake from national TB programmes has limited its impact globally. Little evidence exists around transmissibility, specifically whether drug-resistant TB (DR-TB) strains are more transmissible than drug-susceptible-TB (DS-TB). As part of a multi-country study, we analyzed the South African cohort and compared yield among HHCs of DR-TB and DS-TB index patients and identified factors associated with co-prevalent TB.

We enrolled adult index cases with smear-positive and Xpert-positive rifampicin-resistant (RIF-R)-TB diagnosed from August 2013-July 2015 in Bojanala, South Africa. For each RIF-R case, we matched two non-RIF-R patients on age, location and date of diagnosis. HHCs were symptom screened and sputa were collected from persons with >1 symptom; specimens were tested using smear microscopy, Xpert and MGIT liquid culture.

We enrolled 73 RIF-R-TB and 145 non-RIF-R-TB index cases and 619 HHCs. We identified 47 new TB patients among 619 HHCs; TB yield was similar for HHCs of RIF-R compared to non-RIF-R-TB index patients (8.0 vs 7.4%). HHC aged 35-44 years [vs. <15 years; adjusted Risk Ratio (RRadj)=2.8, 95% confidence interval (CI) 1.2-6.3] and prior TB disease [vs. no prior TB; RRadj=4.3 (95%CI 2.3-8.1)] had increased risk of TB disease. Only 8/47 (17%) new TB patients had DR-TB; 4 were from RIF-R index patients (2 isoniazid-monoresistant, 2 RIF-R) and 4 were from non-RIF R index patients (1 multidrug-resistant-TB, 3 RIF-R).

HHCT demonstrated a continued ability to identify undiagnosed TB and remains a critical intervention for realizing the goal of TB elimination. Although sample size was small, we observed no differences in TB yield between DR-TB and DS-TB index households. The resistance profile of TB among HHCs was discordant with their index patients, which raises questions regarding potential community sources of TB transmission among HHCs.

GENETIC COMPOSITION AND EVOLUTION OF THE PREVALENT MYCOBACTERIUM TUBERCULOSIS LINEAGES 2 AND 4 IN THE CHINESE AND ZHEJIANG POPULATION

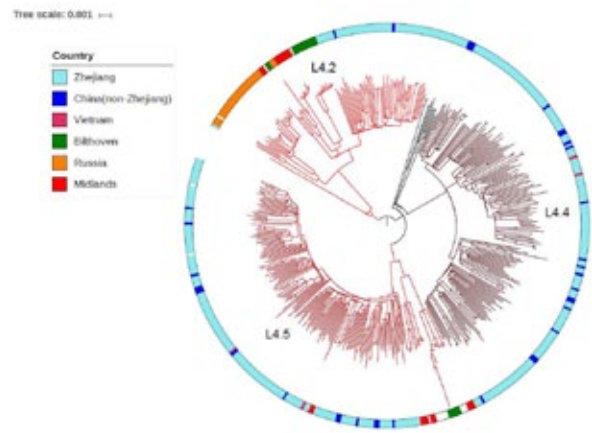
Wang, Yue, Mr; Fu, Lijuan, Ms; Wang, Weibing, Dr

Background: The causative agent of tuberculosis (TB) comprises seven human-adapted lineages. Human movements and host genetics are crucial to TB dissemination. Detailed lineage distribution in Zhejiang Province are unknown.

Objective: To find how different sub-lineages transmitted and distributed within China and Zhejiang, to reconstruct the phylogenomic history of TB epidemic to understand the intersection of phylogeny, geography and demography, and to explore the common genetic characteristics that contributed to wide transmission.

Methods: We analyzed the whole-genome-sequencing (WGS) information of a countrywide collection of 1,154 isolates and provincial collection of 1,296 isolates, constructed the best-scoring maximum likelihood phylogenetic tree, conducted Bayesian evolutionary analysis to compute the most recent common ancestors of lineage 2 and lineage 4, and assessed the antigenic diversity in human T cell epitopes by calculating pairwise dN/dS ratios.

Results: Of the 1296 Zhejiang isolates, 964 (74.38%) belonged to the lineage 2 [L2.1 (10.17%), L2.2 (32.57%), L2.3 (57.26%)], 332 (25.62%) belonged to the lineage 4 [L4.2 (18.07%), L4.4 (38.56%) and L4.5 (43.37%)]. The distributions of sub-lineages varied in 5 geographic regions (East, West, South, North, and Middle) of Zhejiang Province. L2.2 is the most ancient sub-lineage in Zhejiang, appearing 6,897 years ago (95% HDI: 6,513-7,298). L4.4 is the most modern sub-lineage, appearing 2,217 years ago (95% HDI: 1,864-2,581). The dN/dS ratio of epitope and non-epitope regions in lineage 2 strains was significantly (P<0.001) more conserved than in lineage 4.



Conclusions: The spatiotemporal distribution characteristics of lineage 2 and lineage 4 strains are changing. An increase in the frequency of lineage 4 may arise from successful transmission over last 20 years. The recent

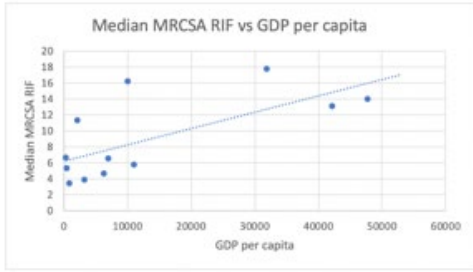
common ancestors and transmission routes of sub-lineages are related to the humans entering China and Zhejiang. Diversity in T cell epitopes might be beneficial for MTB to escape immunization and to spread.

PHYLOGENETIC ANALYSIS OF GLOBALLY REPRESENTATIVE MYOBACTERIUM TUBERCULOSIS WHOLE GENOME SEQUENCES IDENTIFIES GEOGRAPHICALLY DISTINCT PATTERNS OF DRUG RESISTANCE EVOLUTION

Ektefaie, Yasha, Mr; Dixit, Avika, Dr; Freschi, Luca, Dr; Farhat, Maha, Prof

Background: Mycobacterium tuberculosis (MTB) whole genome sequencing (WGS) data can provide insights into temporal and geographic trends in resistance acquisition and inform public health interventions.
Methods: We curated a set of 10,299 clinical MTB isolates with sequencing and culture based drug susceptibility data spanning 20 countries. We constructed geographic and lineage specific MTB phylogenies and used Bayesian molecular dating to infer the most-recent-common-susceptible-ancestor age for 4,869 instances of resistance acquisition to 10 drugs. We assessed the geographic distribution of diagnostically relevant resistance mutations including those detectable by commercial molecular diagnostics (CMDs).
Findings: Independent resistance acquisition events were lower than the total number of dated resistance isolates across 15 countries suggesting ongoing transmission of drug resistance. Ancestral age distributions supported the presence of old resistance, >20 years prior to isolation, in the majority of countries. Dating also suggested a globally consistent order of resistance acquisition of isoniazid then rifamycins then ethambutol and lastly pyrazinamide and second line drugs, but resistance age varied by country. We found a direct correlation between country wealth and resistance ancestral age (R2 = 0.47, p-value = 0.014). Amplification of fluoroquinolone (FLQ) or second-line injectable (SLI) resistance among (multidrug-resistant) MDR isolates was found to be very recent (median ancestral age 3.8 years IQR 1.8-10.9 prior to sample collection). Using culture based tests as the gold standard, we estimated that CMDs would miss 42% of FLQ resistance and 29% of (isoniazid) INH resistance. WGS is estimated to miss 31% and 7% of resistance respectively.
Interpretation: Our results highlight that both resistance transmission and amplification are contributing to disease burden globally, but are variable by country. The observation that wealthier nations are more likely to have old resistance suggests that programmatic improvements can reduce resistance amplification, but that fit resistant strains can circulate for decades subsequently.

Median Rifamycin (RIF) most-recent-common-susceptible-ancestor (MRCSA) date vs Gross Domestic Product (GDP) per capita for 12 countries. (R^2 = 0.47, F-test P-value (1 DF) =0.014).



TIME TO SPUTUM CULTURE CONVERSION AMONG MULTI-DRUG-RESISTANT PATIENTS REFERRED TO THE UGANDA NATIONAL/ SUPRANATIONAL TUBERCULOSIS REFERENCE LABORATORY BETWEEN JUNE 2017 AND DECEMBER 2018

Mujuni, Dennis, Mr

Drug-resistant tuberculosis (DR-TB), especially multi-drug-resistant tuberculosis (MDR-TB), is a serious medical and societal problem in Sub-Saharan Africa due to the co-epidemic of human immunodeficiency virus infection and TB. In Uganda, no nationwide studies have been conducted yet to demonstrate the time to sputum culture conversion among MDR-TB patients. Prognosis interventions at the Uganda National Tuberculosis Reference Laboratory (NTRL) are based on anecdotal observation of peculiar island positives.
As the first attempt in-country, a retrospective review and analysis was conducted on a collection of DR-TB patient data profiles contained in the Laboratory Information Systems for patients referred to the NTRL between June 2017 and December 2018. Kaplan-Meier survival analysis across different patients' variables with use of the Fisher's exact test and Log-rank tests. The significance level was set at 5%, and a P value of ?0.05 was considered statistically significant.
Overall, 554 cultures were identified as MDR-TB and 506 (91.3%) tested positive at baseline (month 0), upon retrieval from the database. On comparing the numbers that were converted in relation to time, the differences in the time taken to convert were statistically significant with age. The sputum cultures of patients aged <20, 20-35, and >65 years took 1 month to convert from positive to negative compared to those from patients aged 36-65 years who took 2 months. Comparison amongst states was statistically significant, with Liberia having a longer time to sputum culture conversion (2 months) than all the rest at 1 month. The gender of the patients did not have statistical significance when related to the time to sputum culture conversion.
The time to sputum culture conversion among MDR-TB patients referred to the Uganda NTRL was found

to be within 2 months for most patients and is in agreement with similar studies conducted elsewhere, barring a few outliers.

ENERGY METABOLISM IN THE MYCOBACTERIUM TUBERCULOSIS COMPLEX: THE CASE OF EVOLUTIONARY CONVERGENCE IN THE ELECTRON TRANSPORT CHAIN AND CENTRAL CARBON METABOLIC PATHWAY

Ofori-Anyinam, Boatema, Dr; Rigouts, Leen, Dr; Antonio, Martin, Dr; de Jong, Bouke, Dr; Gehre, Florian, Dr; Meehan, Conor, Dr

With no new drugs in over 40 years of Tuberculosis (TB) drug research, the discovery of an ATP synthase inhibitor, Bedaquiline, and other promising compounds, all targeting energy metabolism, renewed research interest in mycobacterial energy generating pathways.

Our research shows the conservation of genes encoding crucial enzymes in the energy generating pathways of *Mycobacterium tuberculosis* complex (MTBc) but also reveals that in certain genes, convergent evolution has occurred, potentially contributing to niche adaptation and phenotypic similarities.

We compared the whole genome sequences of clinical isolates collected within the framework of the INTERRUPTB transmission blocking study in The Gambia between 2013-2017 and from a study by the West African Node of Excellence for TB, AIDS and Malaria (WANETAM) network to build capacity in mycobacterial work and resistance detection. In our analysis, we compared 205 *M. tuberculosis* (MTB) strains belonging to the four most isolated MTB lineages in The Gambia, Lineages (L) 1-4, 289 of the two *M. africanum* (MAF) lineages, L5 and L6 and 6 MAF L5 from Nigeria. Bioinformatics and phylogenetic analyses were done using custom scripts, to find genes in which convergent evolution had occurred.

We found the same nonsynonymous mutation or different nonsynonymous mutations in the same gene in some MTB and MAF lineages. Convergence occurred at the level of glucose, glycerol and pyruvate metabolism, acetyl-CoA metabolism and the Tricarboxylic Acid Cycle and in the respiratory chain, in Fumarate reductase and the Succinate and NADH dehydrogenases. Convergence occurred mostly between MTB L1, MTB L3, MAF L5 and L6. Notably, these lineages reportedly grow slower than the wide-spread and more transmissible MTB L4, have reduced transmission and produce cytokine induction patterns suggestive of immune evasion. Therefore, our findings may provide some insights into the evolutionary determinants influencing the transmission fitness of these lineages.

THE GENETIC SPATIAL ANALYSIS OF MYCOBACTERIUM TUBERCULOSIS IN TUBERCULOSIS HOT AND COLD SPOTS OF GUANGXI, CHINA

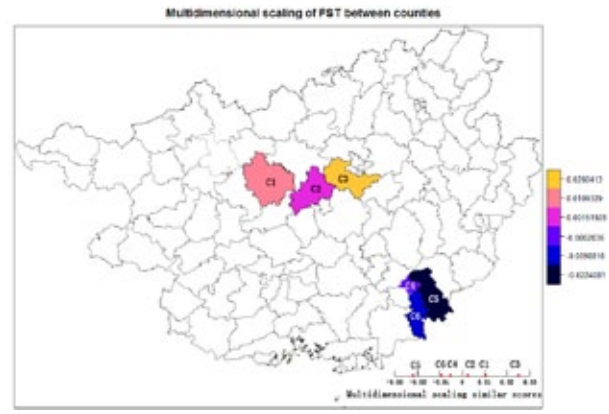
Cui, Zhezhe, Dr; Lin, Dingwen, Mr; Chongsuvivatwong, Virasakdi, Prof; Palittapongarnpim, Prasit, Prof; Chaiprasert, Angkana, Prof

Background: Diversity of genotypes of *Mycobacterium tuberculosis* (Mtb) has been rarely analysed against the differential in TB incidence.

Objective: This study aimed to identify the differences of polymorphisms between tuberculosis hot and cold spot areas in Guangxi Zhuang Autonomous Region of China.

Methods: The Cold and hot the spot areas had been pre-identified from 5 years TB incidence from the surveillance database. Sputum specimens from newly notified TB cases in these two areas during January and June 2018 were cultured. Whole genome sequencing analysis was carried out with 147 isolates from the hot spot and 144 from the cold spot areas. SNPs of each isolate compared to the H37Rv strain were called and used for lineage and sublineage identification as wells for calculation of pairwise SNP differences between every pair of isolates. Analysis of Molecular Variance (AMOVA) across counties of the same hot or spot area and between the two areas was performed.

Results: The predominate Mtb strain is sublineage 2.2 (Beijing family strain) accounting for 57.7% followed by Lineage 4 (39.3%), and the percentages of sublineage 2.2 are significantly higher in hot spots. The median of SNPs distance in cold spots is greater than that in hot spots (897 vs 746, Rank-sum test $p < 0.001$). Through the MDS dimension reduction, the genomic population structures in three hot spot counties are significantly different from those three cold spot counties (T-test $p = 0.05$).



Conclusion: Mtb genotype distribution is associated with TB incidence. Hot spot area in Guangxi is associated with Beijing family strain TB predomination. Narrower genotype diversity in the hot area may indicate unusual high transmissibility of Mtb strain in the area compared to those in the cold spot area.

CATCHING BACILLI IN FLIGHT: DIRECT SAMPLING AND ANALYSIS OF MYCOBACTERIUM TUBERCULOSIS AEROSOLS

Warner, Digby, Prof; Dinkele, Ryan, Mr; Gessner, Sophia, Dr; Morrow, Carl, Dr; Kamariza, Mireille, Dr; Bertozzi, Carolyn, Prof; Mizrahi, Valerie, Prof; Kamholz, Andrew, Dr; Bryden, Wayne, Dr; Call, Chuck, Dr; Wood, Robin, Prof

There is renewed interest in the potential for novel interventions to interrupt *Mycobacterium tuberculosis* (*Mtb)* transmission in tuberculosis (TB) endemic regions. While attractive, this is a challenging undertaking: the release of *Mtb* bio-aerosols cannot be predicted, so detection of infectious individuals depends on the volume of exhaled air sampled, efficient capture of respirable particles, and the sensitive identification of viable *Mtb* bacilli.

The practical and biosafety difficulties posed by working with often paucibacillary samples further complicate the development of rapid, reliable, and scalable technologies to detect live bacilli released by *Mtb*-infected individuals independent of TB symptoms. For this reason, most studies to date have focused on smear-positive TB cases, thereby ignoring the potential contribution of sub-clinically infected individuals (that is, those who are minimally symptomatic or even asymptomatic) to *Mtb* transmission.

To address this challenge, we have developed the Respiratory Aerosol Sampling Chamber (RASC), a personal clean-room equipped with advanced, high-efficiency filtration and sampling technologies that allows biosafe, non-invasive capture and isolation of all particulate matter – including *Mtb* bacilli – released during natural breathing and (non-induced) cough. By combining liquid capture and live-cell fluorescence imaging, we have demonstrated the capacity to detect, quantify, and obtain preliminary morphological and metabolic data from viable *Mtb* bacilli released in respirable aerosols by confirmed TB patients.

Current work is focused on optimizing the RASC platform for rapid, semi-quantitative detection of viable *Mtb* bioaerosols in large numbers of individuals, irrespective of symptoms – a first for direct studies of *Mtb* transmission. Our goal is to model the contribution of sub-clinical *Mtb* transmission to TB prevalence rates, in turn informing the design of implementable interventions to reduce the TB burden in endemic settings. Notably, this approach also suggests the potential to use the RASC to understand the impact of TB chemotherapy on *Mtb* bioaerosol release.

CULTURE-INDEPENDENT WHOLE GENOME SEQUENCING MTB ISOLATES DIRECTLY REVEALS WITHIN-PATIENT HETEROGENEITY.

Koch, Anastasia, Dr; Gessner, Sophia, Dr; Rockwood, Neesha, Dr; Goldstone, Robert, Mr; Wood, Robin, Prof; Wilkinson, Robert J., Prof; Warner, Digby F., Prof

Whole-genome sequencing (WGS) has uncovered surprising levels of genotypic diversity within infecting Mycobacterium tuberculosis (Mtb) populations in individual patients (PMID:25418686). Even dynamic changes in the relative frequencies of specific mutations, including those conferring drug resistance (DR), have been observed (PMID:28424085, PMID:31141643). Recent observations that Mtb in sputum may not represent the within-patient population (PMID:26620446), coupled with evidence that culture of sputum-derived bacilli can select for specific (sub-) lineages (PMID:23936157), further implies that genetic diversity in infecting populations might be underestimated (PMID:31109296, PMID:31214242 This has important implications for the use of WGS to detect DR (PMID:31141643) and to infer patterns of TB transmission (PMID:27798613).

To investigate this issue, a proof-of-concept study was designed in which WGS was applied to two unique collections of clinical Mtb isolates: i) longitudinal DR-TB samples in which Mtb genomes were sequenced without prior culture (direct-WGS) and compared to corresponding WGS data from cultured isolates from the same samples (8 sample pairs) and ii) Mtb isolates from a TB transmission project in which sputum and bioaerosol samples were cultured to compare the genetic diversity in the respective compartments (18 samples).

From a subset of matched bioaerosol-sputum samples, major genetic differences were observed following pairwise genome comparisons. This indicates that sputum may not be representative of the transmitted population of bacilli, potentially biasing the use of this sample type to infer TB transmission networks. Only two direct-WGS samples provided data of sufficient quality; however, this analysis revealed that culture prior to WGS masked heterogeneity. While further optimization is required, these data indicate the capacity for direct-WGS of clinical samples, supporting the potential to reveal true levels of heterogeneity within clinical Mtb populations.

INTRAMACROPHAGIC EXPRESSION PROFILE OF THE SMALLRNA NCRV0757C IN DIFFERENT M. TUBERCULOSIS LINEAGES

Chiacchiaretta, Matteo, Dr; Bresciani, Nadia, Dr; Russo, Giulia, Dr; Cirillo, Daniela Maria, Dr; Miotto, Paolo, Dr

The contribution of the host variability and of the smallRNAs (sRNAs) to the pathogenesis of *M. tuberculosis (Mtb)* remain largely unknown. We characterized the role of *ncRv0757c*, a sRNA cis-encoded to *phoP*, a gene part of the phoPR two-component system, involved in the pathogenesis of tuberculosis. We used Mtb different strains for *in vitro* infection of THP-1 derived classically (M1) and alternatively activated (M2) macrophages. Strains were grouped by phylogeny (ancient and modern) and virulence (reference: H37Rv; more virulent: Beijing, CDC1551; less virulent: Africanum, EAI, H37Ra, Bovis). Macrophages were polarized with either LPS (M1-like) or IL-4 (M2-like) prior to the infection. Intramacrophagic profiling of *ncRv0757c*, *phoP* and *phoR* genes was assessed by TaqMan qPCR at 4h, 24h and 48h post-infection. We performed MTB CFUs count on macrophage lysate at 4h post infection.

Compared to H37Rv, in M1 cells *ncRv0757c* was found to be upregulated in all strains at 4h (modern: 80X; ancient: 5X; less virulent: 3X, more virulent: 100X). *phoP* showed a similar trend. After 24h, we observed no differences for both *ncRv0757c* and *phoP*. In M2 cells the sRNA expression remains unchanged in all the conditions. CFUs count shows that the percentage of bacteria that enters in the macrophages is below 10% (effective MOI is 1:1). M2 cells are more easily infected with mycobacteria rather than M1.

Our data highlight that different Mtb isolates show different intramacrophagic expression profiles of key regulators of pathogenesis. In M1 cells the sRNA exerts its regulatory function early during infection, and more virulent strains show an up-regulation of phoP. In M2 cells the sRNA doesn't change its expression in any strain selected. Strains carrying the overexpression plasmid pMV261 will help us to shed some light on the mechanism of action of this molecule.

Author Index

Bold indicates presenting author

A

Aamotsbakken R. EP-10-196-01
Aarnoutse R. LB-2921
Abdrasuliev T. LB-2976
Abdula A. **EP-16-250-02**
Abdulkarim S. **EP-11-201-02**, PS-26-787-01
Abdullah M.Y. OA-08-359-31
Abdur-Razzaq H. OA-01-302-31
Abebe G. SOA-14-1138-01
Abera F. PS-10-603-31
Abeysundara S.R. **SOA-12-1120-01**
Abikoye E. SOA-04-1035-31
Abimiku A. PS-14-648-31
Abraha M. **SOA-02-1014-31**, **SOA-10-1103-01**, **PS-21-725-01**, **PS-23-748-01**
Abubakar I. OA-18-429-01
Achanta S. OA-27-482-02, **SOA-01-1002-31**, EP-08-172-01, EP-08-175-01, **PS-22-745-01**, **PS-30-824-02**
Achar J. **OA-26-477-02**, **PS-41-956-02**, **LB-2976**
Acharya S. SOA-11-1105-01, EP-05-140-31
Achwoka D. EP-15-235-02
Acquah R. OA-17-419-01
Adak D. PS-18-699-01
Adakun A.S. PS-15-656-01
Adakun S. OA-26-474-02
Adakun Akello S. PS-36-899-02
Adamashvili N. PS-03-527-31
Adams C. SOA-16-1158-02
Adamu I.-T. PS-30-830-02
Adamu Y. SOA-04-1035-31
Adanto A. PS-40-938-02
Ade S. EP-07-165-01, PS-22-737-01, PS-40-938-02
Adé S. PS-21-730-01
Adebayo A.M. OA-12-394-01
Adedotun A. OA-12-394-01
Adelakun Y. **SOA-06-1061-31**
Adeoti A. EP-02-119-31
Adepoyibi T. OA-11-387-31
Adepu R. OA-06-341-31, PS-11-613-31
Adesokan H. **PS-17-686-01**
Adeyomoye A. PS-27-794-01
Adibo E. **EP-12-211-02**, EP-12-215-02, PS-07-570-31
Adithya C. OA-10-375-31
Adjobimey M. **OA-07-351-31**, OA-14-403-01, OA-14-406-01, OA-14-408-01, **EP-07-165-01**, **PS-22-737-01**, **PS-40-938-02**, **PS-40-942-02**
Adjoh K.S. PS-40-942-02
Adnan F. PS-27-793-01
Adnan S. EP-04-130-31
Adonis Koffy L. PS-41-952-02
Affolabi D. OA-15-416-01, EP-07-165-01, PS-06-564-31, **PS-07-572-31**, **PS-18-693-01**
Afifah N. OA-27-485-02, EP-01-109-31, **PS-10-607-31**, PS-32-860-02
Afzal S. OA-03-316-31
Agarwal P. PS-16-674-01, **PS-34-881-02**, PS-38-918-02
Agbaje A. PS-14-648-31, PS-18-690-01, PS-23-755-01
Ager E. PS-16-679-01
Aggarwal R. OA-11-385-31
Aghi M.B. SOA-12-1122-01
Agizew T. **SOA-17-1176-02**, LB-2908
Agodokpessi G. EP-07-165-01, PS-07-572-31, PS-22-737-01, PS-40-938-02, PS-40-942-02
Agogo E. PS-07-575-31
Agrawal L. PS-34-885-02
Agrawal N. PS-30-834-02
Aguilar G. PS-03-530-31
Aguilar M. EP-09-182-01
Aguirre S. PS-03-530-31
Aguolu R. PS-07-575-31
Ahmad S. **SOA-18-1180-02**
Ahmad Y. EP-10-195-01
Ahmad Khan F. SOA-17-1178-02
Ahmadzada N. SOA-11-1107-01, EP-02-118-31, EP-11-200-02, PS-14-654-31
Ahmadzadah N. SOA-15-1151-02, PS-22-744-01
Ahmatov M. **PS-11-610-31**
Ahmed J. **PS-41-959-02**
Ahmed S. OA-28-496-02, SOA-08-1079-31, SOA-08-1081-31, **SOA-14-1140-01**, **SOA-18-1183-02**, **EP-04-130-31**, PS-01-503-31, PS-09-590-31, PS-18-697-01, **PS-35-894-02**
Ahmedov S. SOA-06-1055-31
Ahn Y.-M. SOA-10-1100-01
Ahuja C.K. PS-16-676-01
Ahuja S. EP-01-103-31, PS-21-733-01
Aina T. PS-11-619-31
Aiyenigba B. EP-16-246-02
Aiylchiev S. OA-28-492-02
Ajawaila S. SOA-17-1171-02
Ajayi P. EP-08-171-01
Ajiboye F. **PS-27-794-01**
Akande H. **EP-02-119-31**
Akerfeldt K. SOA-10-1104-01
Akhmedova G. OA-06-344-31
Akhtar M.W. OA-05-338-31
Akinmulero O. PS-14-648-31
Akinseye V. PS-17-686-01
Akkerman O.W. SOA-06-1060-31
Akobye W. LB-2990
Akpomiemie O. OA-12-393-01
Aksenova V. PS-16-675-01
Akulov V. EP-01-104-31
Akumu B. OA-11-387-31
Alagna R. **PS-09-594-31**
Alahi M.A. PS-41-955-02
Alam M. SOA-08-1081-31
Alam M.S. OA-08-361-31, **EP-03-123-31**
Alam M.-U. EP-09-186-01, PS-01-507-31, PS-14-650-31
Alam S. SOA-04-1039-31, SOA-14-1140-01, PS-12-626-31
Alarcon M. SOA-14-1144-01
Alassani A. PS-21-730-01
Alatise M. **PS-11-619-31**
Albuquerque Montenegro R. PS-35-888-02
Alekseeva G. PS-06-557-31
Alem A. SOA-17-1168-02
Alemu A. SOA-17-1168-02
Alemu D. PS-10-603-31
Alexander M. EP-07-160-01, EP-07-162-01, **EP-07-163-01**, EP-07-164-01, **PS-22-739-01**
Alexander N. PS-28-801-02
Alffenaar J.-W. OA-28-493-02, SOA-06-1060-31, SOA-10-1098-01
Al-Hajoj Al-Nakhli S. **PS-35-896-02**
Ali H. PS-27-793-01
Ali K. OA-18-432-01
Ali Z. EP-04-130-31
Ali Ligali M. PS-06-564-31
Alisjahbana B. **OA-27-485-02**, EP-01-109-31, **EP-05-146-31**, EP-15-238-02, PS-10-607-31, PS-32-860-02
Aliyu I. EP-02-116-31
Al-Jahdali H. OA-14-406-01
Aljayyoussi G. OA-17-425-01
Alkabab Y.M. PS-01-503-31
Allam R.R. **OA-11-385-31**
Allen R. PS-37-915-02
Al-Mutairi N. SOA-18-1180-02
Alobu I. PS-18-696-01
Alphonsus C. PS-01-504-31
Alsdurf H. **OA-14-407-01**
Altunay K. SOA-03-1027-31
Alvarado K. SOA-16-1164-02, PS-29-813-02, PS-29-814-02
Alvarez-Hernandez X. OA-20-439-01
Alves J.D. OA-18-433-01, EP-08-173-01, PS-03-528-31
Alves L.S. PS-03-528-31, PS-03-533-31, PS-37-914-02

Alves Y.M. PS-03-533-31
Alyes H. EP-09-185-01
Ama M.C.G. SOA-18-1181-02
Ama M.C. PS-38-924-02
Amalia B. **OA-25-472-02**
Amanullah F. PS-27-793-01, PS-41-959-02
Amarsaikhan B. LB-3037
Amazue-Ezeuko I. SOA-04-1035-31
Ambule P. **OA-07-355-31**
Amico K.R. PS-18-694-01
Amin M.D. **PS-31-840-02**
Amin M.J. SOA-04-1039-31
Amofa-Sekyi M. **EP-04-134-31**
Amos-Kuma A. PS-26-786-01
Amrutha Y. PS-41-954-02
Anagonou S. PS-07-572-31
Anaman J. EP-05-147-31, **EP-13-224-02**
Anand S. SOA-01-1002-31, EP-08-175-01, EP-12-208-02
Ananthakrishnan R. OA-09-370-31, OA-23-461-01, OA-27-483-02, **OA-27-484-02**, **PS-33-867-02**
Anbalagan S. PS-16-671-01
Andama A. SOA-16-1166-02, PS-06-566-31, PS-39-930-02
Andersen P. PS-16-669-01
Andersen P.H. PS-25-771-01
Andrade B.B. PS-12-630-31
Andrade B.D.B. PS-28-802-02
Andrade H.L. EP-08-169-01, PS-37-914-02
Andrade B. B. OA-21-442-01
Andres S. SOA-16-1167-02
Andrews J. SOA-01-1001-31, SOA-02-1011-31, SOA-06-1057-31, SOA-18-1188-02, EP-11-197-02, EP-14-229-02
Andrews J.R. PS-26-779-01, PS-26-781-01
Andriani K. PS-33-868-02
Angamuthu D. PS-04-542-31
Angappan S.K. PS-41-954-02
Angarita B. SOA-14-1136-01
Angayarkanni B. EP-10-187-01
Anguzu G. EP-15-237-02
Aniwada E. PS-01-504-31, PS-23-750-01
Antari N. SOA-17-1171-02
Anthonisamy J.J.J. OA-27-484-02
Anthony J. EP-14-230-02
Anthony R. OA-06-345-31
Anthwal D. OA-13-398-01, SOA-16-1157-02, SOA-16-1162-02, SOA-16-1165-02
Antonov N. LB-2892
Anwar A. PS-27-793-01
Anyanti J. OA-04-329-31
Anyim M. PS-01-504-31
Appleby Y. SOA-03-1029-31
Arago Galindo M. OA-26-479-02, SOA-08-1084-31, SOA-18-1185-02
Arakaki-Sanchez D. EP-16-248-02, PS-26-779-01, PS-26-781-01
Araújo D.N. OA-21-442-01
Arcêncio R.A. **OA-18-433-01**, **EP-08-169-01**, **EP-08-173-01**, **PS-03-528-31**, **PS-03-533-31**, **PS-11-622-31**, **PS-37-914-02**
Arcoverde M.A.M. PS-03-528-31, PS-03-533-31, PS-37-914-02
Ardizzoni E. SOA-18-1185-02, **PS-29-817-02**
Arefin N. SOA-08-1081-31, PS-14-653-31
Arefin Saki N. **EP-09-186-01**, **PS-01-507-31**, **PS-14-650-31**
Arekpa K. PS-06-564-31
Arinaitwe W.J. PS-15-666-01
Arinaitwe Samuel A. **EP-15-237-02**
Arinaminpathy N. OA-22-453-01, EP-15-243-02, PS-39-937-02
Ariunzaya S. LB-3037
Armimi A. EP-12-213-02
Armistad A. PS-15-656-01
Armstrong-Hough M. **OA-07-348-31**, SOA-06-1065-31, EP-15-236-02
Arora J. OA-13-398-01
Arora R. **PS-11-621-31**
Arriaga M. PS-01-512-31, **PS-12-630-31**
Arriaga M.B. OA-21-442-01
Arroyave Zuluaga I.D. PS-03-529-31
Arroyo L.H. OA-18-433-01, EP-08-169-01, EP-08-173-01, PS-03-533-31
Arscott-Mills T. OA-04-330-31
Arsenault C. PS-10-597-31
Artawan W.G. EP-06-151-01
Artawan Eka Putra I.W.G. **PS-05-546-31**, **PS-19-703-01**
Articona M. PS-13-636-31
Arumugam D. PS-10-598-31, PS-25-775-01
Arun Kumar K. **PS-07-577-31**
Aryal T.P. PS-33-866-02
Aseresa M.M. PS-14-654-31
Asfaw M. OA-21-448-01, **OA-28-490-02**
Ashalew M. PS-10-603-31
Asienzo J. EP-15-237-02
Asif K. PS-27-793-01, PS-41-959-02
Asnely Putri F. EP-05-146-31
Assao Neino M.M. SOA-18-1184-02
Assefa B. EP-02-119-31
Assis I.S. EP-08-173-01, PS-03-528-31, PS-37-914-02
Assis I.S.d. PS-03-533-31
Assoumani Y. PS-13-634-31
Astuti P.A.S. **SOA-12-1116-01**, PS-19-703-01
Atchemyan H. OA-10-377-31, PS-34-884-02
Ather F. PS-09-590-31
Atiku Abubakar F. PS-26-787-01
Atkins S. PS-13-643-31
Atre S. EP-09-179-01
Atshemyan H. PS-18-701-01
Atta A. PS-10-603-31
Atterfelt F. PS-16-669-01
Attinsounon C.A. **PS-21-730-01**
Atwood S. OA-26-478-02
Aubry A. **OA-03-322-31**, OA-17-420-01, OA-20-438-01
Audu I. PS-14-646-31
Auguesteen S. OA-27-483-02
Augusteen S. OA-27-484-02
Aulia D. EP-12-213-02
Aung H. PS-14-652-31
Aung H.L. PS-29-818-02
Aung S.T. SOA-14-1142-01, SOA-15-1149-02, EP-01-106-31, PS-14-652-31, PS-29-818-02
Aung W.W. **SOA-14-1142-01**, **PS-06-563-31**
Aung Y.K. **PS-04-538-31**, PS-30-828-02
Avadenii I. PS-24-759-01
Avagyan N. PS-34-884-02
Avaliani Z. OA-21-447-01, SOA-03-1024-31, PS-03-527-31, PS-11-617-31, PS-18-698-01, PS-34-883-02
Avanashvili M. PS-22-743-01
Avsar K. EP-11-198-02
Awe A. **PS-08-585-31**
Awe A.O. PS-04-544-31
Ayalew A. SOA-02-1014-31
Aydin M. SOA-02-1012-31
Aye S. SOA-15-1149-02
Ayelo P. PS-40-942-02
Ayles H. OA-12-388-01, SOA-03-1028-31, EP-02-110-31, EP-04-134-31, LB-3050
Ayong C. EP-03-126-31
Ayorinde A. **PS-16-668-01**
Ayoubi M.K. PS-14-654-31
Aytmurzaeva G. SOA-05-1053-31
Ayyamperumal M. PS-28-802-02
Azad A.K. OA-08-362-31, **EP-03-122-31**
Azam K. **PS-14-649-31**, PS-27-795-01
Azamova S. PS-32-857-02
Azger V.N.D. **EP-10-187-01**

B

Babaley M. SOA-14-1136-01
Babawale V. PS-18-696-01
Babbar N. EP-05-144-31, EP-12-208-02, PS-34-882-02
Babu R. PS-23-756-01
Babu S. EP-10-194-01, PS-39-929-02
Bacelar Gomes A. OA-25-470-02
Bacha J. SOA-06-1055-31, SOA-15-1147-02
Bachir M. **OA-17-420-01**
Baddeley A. EP-07-159-01
Bader L. PS-23-749-01
Badman S. PS-26-786-01
Baena I.G. SOA-09-1087-31
Baijnath P. OA-03-320-31
Bailon N. SOA-16-1164-02, PS-29-813-02, **PS-29-814-02**
Baird M. PS-17-680-01
Bajiya M. PS-21-733-01
Baker B. OA-03-318-31
Bakesiima R. PS-07-576-31
Bakker R. OA-22-452-01
Bakuli A. OA-04-326-31
Bal H.B. **PS-09-589-31**
Bal S.K. PS-09-592-31
Balachandra S. SOA-02-1015-31
Balaji S. PS-09-591-31, PS-09-591-31, PS-17-683-01, PS-39-934-02

Balaji V. OA-06-346-31
Balakrishnan S. SOA-13-1134-01, PS-20-713-01
Balasubramanian D. **OA-10-378-31**, **PS-12-623-31**, PS-41-954-02
Balate A. OA-12-395-01
Baldé M.P. SOA-11-1110-01
Baldwin A. EP-03-129-31
Baliashvili D. **EP-04-131-31**, **PS-03-527-31**
Baliga S. **PS-29-823-02**
Balkan S. PS-18-701-01
Ball A. **PS-29-821-02**
Ballayira Y. **PS-21-727-01**
Balloux F. OA-06-343-31
Baloyi O. PS-38-923-02
Baloyi T. PS-38-923-02
Bam T.S. PS-19-703-01
Bamrah Morris S. OA-14-404-01, SOA-04-1042-31
Banda G. OA-20-440-01
Bangoura A.M. SOA-11-1110-01
Bano R. EP-16-247-02, PS-30-826-02
Bansal A. EP-10-195-01
Banu R.S. SOA-04-1039-31, PS-01-503-31, PS-14-653-31
Banu S. SOA-01-1008-31, SOA-04-1039-31, SOA-14-1140-01, PS-01-503-31, PS-09-590-31, PS-35-894-02
Banurekha V. EP-10-194-01, **EP-15-242-02**, PS-09-591-31, PS-15-663-01, PS-16-671-01
Banzakadilo C. **OA-21-443-01**, **PS-28-811-02**
Barash J. OA-18-432-01
Barbier M. OA-06-340-31
Barholomay P. EP-16-248-02
Barman C. PS-05-548-31
Barnes D. EP-05-149-31
Barreda Ponce N. OA-21-442-01, **PS-01-512-31**
Barrios Lopez B. PS-29-821-02
Barry S. PS-15-660-01
Barry lll C. SOA-10-1100-01
Barton H.E. EP-04-136-31
Barua S. SOA-04-1039-31
Baruwa E. EP-13-220-02, PS-07-570-31, PS-13-637-31
Bascuna J.E. **PS-38-924-02**
Basham C.A. **PS-03-523-31**
Bashar M.S. SOA-14-1140-01, EP-09-186-01, PS-01-503-31, PS-01-507-31, PS-14-650-31
Basilea W. EP-15-242-02
Basillo R. PS-38-924-02
Baskaran D. EP-10-194-01, PS-39-929-02
Basset T. OA-03-320-31
Bassey E.E. SOA-01-1003-31
Bassey E.N. PS-16-677-01, PS-30-830-02
Bastard M. **OA-21-447-01**, OA-28-492-02, **SOA-08-1084-31**, **SOA-18-1185-02**, PS-11-614-31, PS-18-701-01, PS-29-817-02, **PS-34-883-02**, PS-34-884-02, LB-2909
Bastos M. OA-14-406-01
Basu S. PS-35-891-02
Bateson A. SOA-16-1167-02
Batra S. **EP-01-103-31**, EP-01-103-31, PS-11-620-31, PS-21-733-01, PS-21-733-01
Battaglia S. OA-15-411-01
Battaglioli T. PS-22-742-01
Batte C. SOA-09-1087-31
Batur S. OA-12-394-01
Bava H. EP-11-199-02
Becerra M.C. OA-01-300-31, OA-09-369-31
Beckwith P.G. PS-26-785-01
Bedru A. PS-23-757-01
Beebe D.J. EP-10-196-01
Beenish R. **PS-39-932-02**
Behanzin L. PS-21-730-01
Behr M. PS-17-682-01
Behrends U. EP-11-198-02
Beishenbiev T. PS-11-610-31
Bekang Angui F. EP-11-199-02
Bekele D. EP-11-203-02
Bekou W. EP-07-165-01, PS-22-737-01
Bele A. SOA-11-1111-01
Beliaeva E. OA-20-437-01
Belilovskiy E. PS-16-675-01
Belinga E. EP-11-199-02
Bell D. SOA-16-1166-02
Bella Devaleenal D. EP-15-242-02
Bellbrant J. PS-16-669-01
Belskikh A. OA-20-435-01
Ben Dayan D. PS-01-506-31
Benedetti A. SOA-04-1038-31
Benedictus L. PS-17-680-01
Bennett C. SOA-16-1166-02
Berger C. **SOA-03-1032-31**, PS-25-777-01
Bergstrom M. PS-37-906-02
Berland J.-L. SOA-01-1008-31
Bernaola L. SOA-16-1164-02, PS-29-813-02, PS-29-814-02
Bernardo J. PS-38-925-02
Berra T.Z. EP-08-173-01, PS-03-533-31
Berry S. EP-10-196-01
Best A. **OA-11-381-31**, OA-23-463-01
Beulah F. PS-23-750-01
Beyeler N. OA-10-372-31
Bezuidenhout C. SOA-03-1023-31, SOA-13-1135-01, **SOA-17-1172-02**, PS-05-547-31, PS-08-582-31, **PS-08-583-31**, PS-20-715-01, PS-27-789-01
Bhalla M. OA-13-398-01, SOA-16-1162-02
Bhan C. PS-01-502-31
Bhanot A. EP-01-102-31
Bharaswadkar S. PS-30-829-02
Bharatwal M. EP-10-189-01
Bhardwaj A.K. PS-05-552-31
Bhardwaj M. SOA-03-1022-31, PS-08-580-31, PS-14-647-31
Bhardwaj R. PS-35-890-02
Bhargava A. PS-29-812-02, PS-37-913-02
Bhargava M. **PS-37-913-02**
Bhargavi G. **PS-39-934-02**
Bhat N. OA-04-326-31
Bhat P. **EP-12-214-02**
Bhatnagar A. PS-34-882-02
Bhatnagar H. PS-10-597-31
Bhatnagar P.C. EP-12-214-02
Bhatt G. **EP-03-128-31**, PS-02-515-31
Bhatt N. PS-28-806-02, PS-41-952-02
Bhattrai R. PS-26-778-01, PS-41-951-02
Bhering M. OA-22-455-01
Bhosale R. EP-07-160-01, EP-07-162-01, EP-07-163-01, EP-07-164-01, PS-22-739-01
Bhuniya S. PS-09-592-31
Biagini G. OA-17-425-01
Bichashvili T. **PS-18-698-01**
Biermann O. **PS-13-643-31**
Bill C. OA-12-389-01
Billiew T. OA-17-424-01
Bimba J. SOA-01-1003-31
Birabwa E. EP-12-210-02, PS-13-632-31, PS-14-651-31, PS-36-904-02
Biranthabail D. PS-29-823-02
Biremon M. SOA-05-1053-31
Birhane N. PS-10-603-31
Bissell K. OA-25-466-02, OA-25-468-02, SOA-12-1123-01
Bisson G. OA-03-321-31
Biswas D.K. PS-04-541-31
Biswas S. SOA-01-1008-31, **PS-01-503-31**
Black J. SOA-05-1049-31, SOA-05-1052-31
Blackman A. PS-29-819-02
Blasco P. PS-21-726-01
Blumberg H. PS-03-527-31
Bo Z.W.Y. PS-04-538-31
Boada E. SOA-16-1158-02
Bodi O. PS-06-564-31
Boehme C. OA-15-412-01
Boeree M.J. **LB-2921**
Boffa J. SOA-03-1025-31, EP-13-227-02, PS-10-600-31, PS-10-601-31, PS-32-861-02
Bogati H. PS-21-726-01
Boiditswe S. OA-04-330-31
Bollela V.R. OA-18-433-01
Bond V. SOA-03-1028-31, **EP-09-185-01**
Bonnet M. SOA-17-1173-02, SOA-18-1186-02, PS-41-948-02, PS-41-952-02
Bonnewell J. PS-12-629-31
Bonsu F. PS-09-596-31, PS-32-852-02
Bontuyan E. PS-13-636-31
Boodhram R. PS-18-694-01, PS-28-799-02
Boot C. PS-38-920-02
Borand L. PS-41-948-02
Borgdorff M. PS-23-746-01
Borkar V.V. PS-41-958-02
Bornheimer S. **OA-05-338-31**
Bosch C. SOA-06-1058-31
Boshoff H. SOA-10-1100-01
Bosman N. OA-15-415-01
Boukary I. SOA-18-1184-02
Boulle A. OA-12-389-01, PS-32-850-02
Boulware D. OA-21-445-01
Bourassa C. PS-20-723-01
Bouzouita I. SOA-14-1145-01, PS-06-556-31
Boyd A. PS-28-807-02
Boyle D. PS-27-798-01
Boyles T. **LB-2861**
Bozzani F. OA-02-308-31
Bresenham D. SOA-17-1172-02, **PS-05-547-31**, **PS-08-582-31**, PS-08-583-31, **PS-20-715-01**, PS-27-789-01
Bresges C. OA-18-426-01
Brien K. OA-06-343-31
Brightman H. PS-15-666-01
Brilleman S. PS-03-534-31
Brito de Souza A. LB-2904
Brode S.K. SOA-18-1186-02

Broger T. PS-38-921-02
Bronson G. PS-05-551-31
Brooks M.B. OA-01-300-31, OA-09-369-31
Brossier F. OA-03-322-31, OA-17-420-01
Brostrom R. **OA-14-409-01**
Bruchfeld J. OA-17-423-01, OA-28-493-02, SOA-10-1097-01, SOA-10-1098-01, PS-12-631-31, PS-16-669-01
Brunette M.J. PS-38-925-02
Brust J. OA-26-480-02
Bryant J.E. SOA-01-1008-31
Bryer S. PS-18-692-01, **PS-34-885-02**
Buck W.C. **SOA-15-1150-02**
Bucsan A. OA-20-439-01
Budhathoki G. SOA-11-1105-01
Budhathoki G.R. EP-05-140-31
Budi Wicaksono D. EP-05-146-31
Bui L. **OA-02-313-31**
Bui T.T.H. SOA-17-1175-02
Bulage L. PS-37-910-02
Bullen C. OA-25-466-02, OA-25-468-02, SOA-12-1123-01
Bulti A.B. LB-2957
Bupachat S. PS-04-535-31
Burdakov V. OA-20-437-01
Burhan E. SOA-09-1086-31
Burnett J.M. LB-3050
Burua A. **SOA-05-1051-31**, PS-10-602-31, PS-33-863-02
Burza S. PS-28-801-02
Busenga M. EP-01-100-31
Butcher P.D. SOA-16-1158-02
Buu T.N. OA-14-408-01
Buziashvili M. **PS-11-617-31**, PS-18-698-01
Bwana D. PS-11-620-31
Bwembya J. EP-12-207-02, PS-14-645-31, PS-15-661-01, PS-21-729-01, **PS-30-833-02**, PS-32-853-02, PS-33-869-02
Byrnes S. SOA-16-1166-02

C

C. Alffenaar J.-W. SOA-10-1097-01
Cabibbe A.M. **OA-15-411-01**
Cabral P. EP-03-129-31
Cáceres T. PS-29-819-02
Cachay R. EP-09-180-01, PS-29-819-02
Cadmus S. PS-17-686-01
Cajazeiro J. LB-2976
Calderon M. OA-18-427-01, EP-04-136-31, EP-04-138-31
Calderon R. OA-05-336-31
Calderon R.I. PS-26-780-01
Calderon Espinoza R. **OA-21-442-01**, PS-01-512-31
Calderwood C.J. OA-18-427-01, **SOA-13-1129-01**, **PS-37-906-02**
Caldwell J. SOA-01-1009-31
Calligaro G. LB-3062
Camara F. PS-21-727-01
Camara S. SOA-11-1110-01, SOA-11-1110-01
Camioli C. SOA-01-1001-31
Campbell A. OA-26-480-02
Campbell J.R. OA-07-351-31, **OA-14-406-01**, **OA-17-418-01**, OA-17-421-01, **OA-17-422-01**, SOA-04-1041-31, SOA-08-1075-31, **SOA-18-1186-02**, EP-07-165-01
Campos H. EP-09-182-01
Campoy L.T. OA-18-433-01, PS-03-533-31, PS-37-914-02
Canagasabey D. OA-21-443-01, PS-28-811-02
Candari C. OA-12-392-01
Cangelosi G. **PS-06-566-31**
Cantera J. **PS-27-798-01**
Cao Y. PS-38-925-02
Capochichi D. PS-22-737-01
Caporale C. SOA-09-1089-31
Cardoso J. OA-12-395-01
Carpio I. **OA-26-478-02**
Carrillo Montenegro L.V. OA-09-369-31
Carter J. PS-15-656-01
Carvalho C. PS-25-771-01
Casenghi M. PS-41-954-02
Cassamo A. PS-28-806-02
Castañeda-Orjuela C. SOA-05-1050-31, PS-03-529-31
Castano-Villegas N. OA-18-427-01
Castelnuovo B. PS-03-525-31
Castro M. LB-2948
Catabi O. PS-17-685-01
Cattamanchi A. SOA-02-1019-31, SOA-02-1020-31, SOA-03-1032-31, SOA-16-1166-02, SOA-17-1174-02, EP-15-236-02, PS-03-525-31, PS-06-566-31, PS-07-567-31, PS-08-584-31, PS-25-777-01, PS-39-930-02
Cavalcante J.R. SOA-04-1038-31
Cavalheiro A.P. PS-41-956-02
Caws M. OA-01-303-31, SOA-11-1105-01, SOA-11-1113-01, EP-05-140-31, PS-08-587-31, PS-13-643-31, PS-33-866-02, PS-33-873-02
Cazabon D. OA-01-301-31, SOA-01-1000-31, PS-10-597-31, PS-23-747-01
Cele N. PS-28-799-02
Celina Ribeiro da Silva C. EP-14-229-02
Cepuch C. SOA-10-1104-01
Chaddha S. OA-15-412-01
Chadha K. EP-01-102-31, PS-05-548-31
Chadha S. PS-15-664-01, PS-33-872-02
Chafulumira H. PS-13-635-31
Chakroun A. PS-29-815-02
Chalwe V. PS-30-833-02
Chan E.D. OA-17-422-01
Chan H.-H. OA-13-397-01
Chan P.C. SOA-08-1076-31
Chan P.-C. **PS-28-809-02**
Chand P. OA-25-467-02
Chandanwale A. EP-07-161-01
Chandra S. EP-05-144-31, EP-12-208-02, PS-29-816-02, PS-34-882-02
Chandra Reddy S. PS-22-745-01
Chandra Shekar V. SOA-09-1088-31
Chandrasekaran P. EP-09-177-01
Chandrashekaran P. PS-28-802-02
Chang C.L. SOA-14-1142-01, PS-06-563-31
Chang H.-Y. SOA-09-1085-31
Chang S. **OA-01-302-31**, OA-21-444-01
Chani K. OA-11-387-31
Chapurishvili L. SOA-03-1024-31
Charalambous S. SOA-02-1017-31, SOA-13-1129-01, EP-01-105-31, EP-05-147-31, EP-13-224-02, EP-14-228-02, PS-10-608-31, PS-26-785-01
Charifker Schindler H. **PS-35-888-02**
Chatterjee D. PS-38-920-02
Chaubey J. PS-29-816-02
Chauffour A. OA-20-438-01
Chavan A. OA-03-323-31
Chavan V. OA-28-489-02
Chea M. EP-14-231-02
Chedid C. SOA-01-1008-31
Chegou N. OA-03-318-31
Chegou N.N. LB-2965
Chemtob D. OA-02-313-31
Chen B. SOA-09-1085-31
Chen H. OA-10-373-31
Chen L. OA-10-373-31
Chen L.-C. OA-04-327-31
Chen N. PS-20-720-01
Chen S.-H. PS-12-628-31
Chen W. EP-08-167-01, PS-20-720-01
Chen W.W. PS-22-738-01
Chen X. PS-11-612-31
Cheng J. PS-15-658-01
Cheng S. PS-17-684-01
Chernokhaeva I. OA-20-437-01
Chetty S. OA-11-382-31
Chetty-Makkan C. EP-01-105-31, PS-10-608-31
Chhetry T. PS-26-778-01, PS-41-951-02
Chiang C.-Y. SOA-09-1085-31
Chiang S. SOA-06-1059-31, SOA-15-1146-02
Chiang T.-Y. OA-13-397-01
Chiappe Gonzalez A. PS-29-820-02
Chiaravalloti-Neto F. PS-03-528-31
Chiau R. OA-26-479-02, SOA-08-1082-31
Chibinga F. PS-14-645-31
Chibinga Mwiinga F. EP-12-207-02
Chicovore J. PS-15-665-01
Chidacua M. OA-07-352-31
Chien J.-Y. **OA-04-327-31**
Chihaye F. PS-03-531-31
Chijioke-Akaniro O. OA-01-302-31, EP-02-119-31, PS-18-690-01
Chijioke-Akaniro O.O. **SOA-17-1170-02**, **PS-30-831-02**
Chikovore J. SOA-03-1025-31, EP-13-227-02, PS-10-600-31, PS-10-601-31, PS-32-861-02
Chimatira F. PS-26-782-01
Chimatira R. **PS-26-782-01**
Chimhundu C. SOA-11-1109-01
Chimoyi L. **SOA-02-1017-31**
Chimzizi R. PS-13-641-31
Chingandu A. EP-05-149-31
Chinnakali P. PS-28-808-02

Chinthika P. SOA-12-1119-01
Chinweuba C. PS-18-696-01
Chiranjeevi M. SOA-13-1132-01, PS-11-616-31
Chirehwa M.T. OA-26-473-02, **SOA-10-1096-01**, **SOA-10-1101-01**
Chitalia V. LB-2991
Chittenden L. SOA-04-1035-31
Chittiboyina S. **OA-06-341-31**, PS-11-613-31
Chituku P. PS-18-692-01, PS-34-885-02
Chiwenkha P. PS-04-537-31
Chkhaidze I. EP-06-157-01
Chobotar O. PS-34-878-02, PS-34-879-02
Choi D.H. **EP-10-191-01**
Choi K. SOA-02-1018-31
Chomutare H. OA-07-354-31
Chong F. **SOA-05-1054-31**
Chongo C. **PS-33-869-02**
Chongsuvivatwong V. OA-10-373-31, LB-2922
Choo L. SOA-17-1177-02
Chopra K.K. EP-05-144-31, EP-12-208-02, **PS-34-882-02**
Chopra R. OA-27-486-02, EP-02-117-31
Chorba T. OA-14-404-01, SOA-04-1042-31
Choto R. SOA-02-1015-31
Choub S.C. OA-01-301-31, **OA-12-391-01**, SOA-11-1112-01, PS-23-747-01, PS-36-898-02
Choudhary S.K. PS-31-848-02
Choudhury S. PS-09-590-31
Chowdhury G.I. SOA-04-1039-31
Christie A. PS-36-897-02, PS-36-903-02
Chry M. **SOA-01-1000-31**, **SOA-11-1112-01**
Chryssanthou E. PS-16-669-01
Chu P.-W. SOA-09-1085-31
Chugh M. PS-06-562-31
Chukwu J. PS-01-504-31
Chukwuemeka C. EP-13-220-02
Chukwulobelu U. PS-18-696-01
Chukwuogo O. OA-01-306-31
Chungu C. **PS-13-641-31**
Churchyard G. SOA-06-1056-31, EP-04-131-31, EP-05-147-31, EP-13-224-02
Churchyard G.J. PS-26-785-01
Cikobe V. PS-28-811-02
Cillie I. **PS-04-539-31**, **PS-33-864-02**
Cilloni L. **OA-22-453-01**
Cirillo D.M. OA-15-411-01, PS-09-594-31
Cissé A. PS-21-727-01
Citro B. OA-23-458-01
Ciza F. PS-18-695-01
Claassens M. EP-02-110-31
Clark T.G. SOA-18-1181-02
Clemente J. OA-03-317-31
Coakley P. SOA-04-1035-31
Codlin A.J. OA-01-303-31, SOA-03-1031-31, SOA-04-1033-31, **SOA-05-1048-31**, SOA-11-1106-01, SOA-15-1148-02, EP-14-233-02, EP-16-251-02, PS-08-587-31, PS-13-640-31, PS-23-754-01, PS-33-873-02
Coelho Hamene H.E. PS-14-649-31, PS-27-795-01
Cohen A. PS-37-908-02
Cohen J. OA-08-360-31
Cohen J.E. SOA-12-1114-01, SOA-12-1124-01, EP-06-154-01
Cohen T. OA-02-315-31, OA-20-441-01, SOA-18-1187-02, EP-11-197-02
Cohn J. PS-41-954-02
Coit J. OA-05-336-31, PS-16-679-01
Coker E. OA-07-348-31, PS-16-668-01
Colaco L. **PS-23-749-01**
Cole D.C. EP-16-244-02
Colman R. OA-15-411-01, **SOA-16-1159-02**
Colorado A. PS-15-656-01
Combary A. PS-09-594-31
Conjera J. PS-23-749-01
Conjera J.L. **EP-08-174-01**
Connelley T. PS-17-680-01
Connelly J. SOA-16-1166-02, PS-29-821-02
Conradie F. SOA-08-1075-31, PS-05-551-31
Conteras C. **EP-09-182-01**
Cook C. OA-28-496-02, PS-18-697-01
Cook G.M. PS-29-818-02
Cook V. OA-14-408-01, SOA-04-1037-31
Cook V.J. OA-14-406-01
Cook-Scalise S. OA-06-342-31, OA-22-454-01
Cooper D. OA-11-381-31
Corbett E. OA-20-440-01
Corbett E.L. OA-22-452-01
Cordeiro-Santos M. LB-2904
Cordon O. PS-11-609-31, PS-12-626-31
Cords O. SOA-02-1011-31, SOA-06-1057-31, EP-11-197-02
Correia-Neves M. PS-16-669-01
Cotes Cantillo K.P. SOA-05-1050-31
Court R. **OA-26-473-02**, SOA-10-1096-01, SOA-10-1101-01
Cowan J. OA-07-352-31, OA-26-479-02, SOA-08-1082-31
Cox C. PS-11-620-31
Cox G. PS-12-629-31
Cox H. SOA-05-1049-31, SOA-05-1052-31, SOA-08-1077-31
Cox S. **LB-2948**
Crampin A.C. LB-2965
Cresswell F. OA-21-445-01, SOA-17-1177-02
Creswell J. OA-07-352-31, OA-26-479-02, OA-27-483-02, OA-27-484-02, SOA-01-1000-31, SOA-08-1082-31, PS-26-784-01
Crispim J.A. PS-03-528-31
Crispim J.D.A. OA-18-433-01, PS-03-533-31
Croda J. SOA-01-1001-31, **SOA-18-1188-02**, EP-04-137-31, EP-11-197-02, **EP-14-229-02**, PS-26-779-01, PS-26-781-01
Crook A. SOA-17-1177-02
Cross A. OA-27-482-02
Crowder R. OA-10-375-31, PS-25-777-01
Cruz R. **OA-12-392-01**, PS-13-636-31
Cubillos-Angulo J.M. PS-12-630-31
Cucho C. PS-29-820-02
Cudahy P.G.T. **OA-20-441-01**
Cuevas L.E. **SOA-01-1003-31**
Cui J. **OA-21-449-01**
Cui X. OA-21-449-01
Cumbi N. OA-26-479-02
Cumburidze N. PS-11-614-31, PS-34-883-02
Cunha E. SOA-01-1001-31, SOA-18-1188-02
Cunningham B. OA-11-383-31, PS-09-596-31
Cunningham C.K. OA-04-330-31
Currie B. OA-15-417-01

D

Da Silva K.E. SOA-18-1188-02
Da Silva P. **OA-15-415-01**, EP-08-171-01
Da Silva Santos A. EP-04-137-31, EP-14-229-02
Daftary A. OA-11-382-31, SOA-03-1025-31, EP-13-227-02, PS-10-597-31, PS-10-600-31, PS-10-601-31, PS-18-694-01, PS-28-799-02, PS-28-810-02, PS-32-861-02
Daga C.M. PS-38-924-02
Dalal A. **OA-28-489-02**, PS-18-699-01
Dalawangbayan K. **PS-13-636-31**
Dale K. **EP-04-133-31**, **PS-37-907-02**
Dale K.D. PS-34-875-02
Dália Alves J. PS-11-622-31
Dam T. SOA-03-1031-31
Damanik F. PS-33-868-02
Dambe I. PS-13-635-31
Danelia M. SOA-03-1024-31
Daniels B. SOA-03-1025-31, EP-13-227-02, PS-10-600-31, PS-10-601-31, PS-32-861-02
Daniels J. **SOA-03-1023-31**, **SOA-13-1135-01**
Danielyan N. OA-21-447-01, PS-34-883-02
Danjuma A. OA-12-393-01, PS-30-830-02
Dao N.V. OA-20-434-01
Dao T. EP-16-251-02
Dapakekar S. PS-30-829-02
Dara M. OA-28-494-02, EP-01-104-31
Dare D.J. **EP-11-203-02**
Daroch P. PS-38-918-02
Daru P. OA-12-392-01, PS-13-636-31, PS-23-751-01
Das A. PS-23-756-01
Das B.R. EP-06-153-01
Das D. PS-09-589-31
Das M. OA-28-489-02, SOA-08-1078-31, **SOA-13-1127-01**
Das P. **OA-01-307-31**, PS-28-801-02, PS-29-812-02
Das R. EP-10-195-01
Das R.R. PS-16-673-01

Das S. EP-03-121-31
Das V.N.R. PS-28-801-02
Datiko D. **SOA-17-1168-02**, EP-11-203-02, **PS-25-770-01**
Datta B. PS-05-553-31
Datta S. SOA-16-1164-02, PS-20-718-01, PS-29-813-02, PS-29-814-02, PS-29-820-02, LB-3028
Daum L.T. **OA-13-396-01**
Dave P. SOA-09-1092-31
David A. OA-15-415-01
Davidson R. PS-22-735-01
Davies G. OA-20-440-01
Davies M. PS-15-660-01
Davies Forsman L. OA-17-423-01, **OA-28-493-02**, SOA-10-1097-01, **SOA-10-1098-01**
Davis J.L. OA-07-348-31, SOA-06-1065-31
Davitashvili M. SOA-03-1024-31
Dawkore M. LB-3021
Dawood H. OA-11-382-31
Dawson R. LB-2921
Dayal R. **EP-13-219-02**, PS-13-638-31
De P. **PS-38-920-02**
De Azevedo V. OA-17-419-01, SOA-08-1077-31, SOA-15-1154-02, EP-09-184-01
De Bruyne K. SOA-16-1160-02
De Carvalho E. PS-41-952-02
De Haas P. LB-3050
De Jager V. LB-2921
De Jong B. PS-13-634-31
De Jong B.C. OA-13-399-01, OA-15-416-01, PS-06-564-31
De Kock M. SOA-10-1101-01
De la Flor A. EP-09-180-01
De Morais L. PS-14-649-31, PS-27-795-01
De Neeling A. OA-06-345-31
De Rauw K. SOA-16-1160-02
De Rijk W.B. OA-13-399-01
De Seram S. **PS-31-844-02**, PS-31-847-02
De Vos M. SOA-16-1163-02, PS-06-559-31
De Vries N. OA-26-473-02, SOA-10-1096-01, SOA-10-1101-01
De Zwaan R. OA-06-345-31
Dean A. SOA-18-1187-02
DeAtley T. **EP-07-159-01**
Degner N. EP-04-137-31
Delgerekh B. LB-3037
Delogu G. SOA-01-1008-31
Deluca A. EP-07-161-01
Delyuzar H. PS-25-774-01
Demers A.-M. SOA-17-1177-02
Demidov I. LB-2892
Demisse M. PS-37-912-02
Deng G. **PS-24-760-01**
Deng S. PS-13-642-31
Denholm J. OA-22-450-01, EP-04-133-31, **EP-15-239-02**, PS-37-907-02
Denholm J.T. PS-34-875-02
Denkinger C. OA-06-342-31, OA-13-400-01, OA-22-454-01, SOA-01-1009-31, SOA-16-1159-02, EP-10-190-01, PS-38-921-02, PS-39-937-02
Denkinger C.M. SOA-17-1178-02
DeNormandie J. EP-16-246-02
Denti P. SOA-10-1096-01, SOA-10-1101-01
Deo S. PS-08-580-31
Deogan C. PS-08-588-31
Depargo N. PS-28-799-02
Der J. **PS-32-852-02**
Derendinger B. **SOA-16-1163-02**, PS-06-559-31
Des Jarlais D.C. SOA-05-1045-31
Desai C.R. PS-18-699-01
Deshpande M. EP-16-247-02, PS-30-826-02
Deshpande P. OA-03-323-31, EP-07-164-01
Deshpandey S. OA-25-467-02
Destito M. OA-26-475-02
Destura R. PS-25-777-01
Dev P. **PS-10-606-31**
Devezin T. SOA-06-1055-31, SOA-15-1147-02
Devi C. PS-11-613-31
Devi U. PS-35-889-02
Dewi R.K. **EP-12-213-02**
Dey A. PS-30-834-02
Deyala C. PS-21-729-01
Dhanalakshmi A. EP-15-242-02
Dhanapal S.R. PS-10-598-31, PS-25-775-01
Dharmshale S. **PS-35-890-02**
Dharuman K. PS-10-598-31, PS-25-775-01
Dhawan S.R. PS-16-676-01
Dheda K. LB-2904, LB-3062
Dhillon D. SOA-06-1055-31, SOA-15-1147-02
Dhillon J. SOA-16-1158-02
Dhiman A. EP-10-195-01
Dhital R. **SOA-11-1105-01**, SOA-11-1113-01, EP-05-140-31, PS-33-866-02
Dhliwayo P. OA-18-431-01, PS-04-539-31, PS-36-900-02
Dholakia Y. PS-10-606-31, **PS-18-699-01**, **PS-30-825-02**
Dhole T.N. PS-34-877-02
Dhumal G. EP-07-161-01
Diack A. SOA-17-1173-02
Diacon A.H. LB-2921
Diallo A.O. **EP-16-252-02**, PS-33-870-02
Diallo B. EP-16-252-02, PS-33-870-02
Dian Kurniasari N.M. PS-02-514-31
DiAndreth L. OA-21-446-01
Diaz-Jimenez D. SOA-05-1050-31
Dicks K. PS-12-629-31
Dickson-Hall L. SOA-05-1049-31, **SOA-05-1052-31**
Didik V.S. PS-33-862-02
Diefenbach-Elstob T. PS-24-761-01, PS-38-917-02, PS-39-931-02
Diergaardt C. PS-10-605-31
Dikko A.A.b. **EP-02-116-31**
Dina N. EP-15-242-02
DiNardo A. SOA-06-1055-31
Dinda M.K. PS-30-834-02
Dineshkumar P. OA-08-358-31, SOA-12-1121-01, EP-03-120-31, PS-31-838-02
Dinh T.H. **OA-15-413-01**
Dione A. PS-33-870-02
Diouf N.O. EP-16-252-02
Dioukhane E.H.M. PS-33-870-02
Dioukhane E.M. EP-16-252-02
Diricks M. **SOA-16-1160-02**
Diro Ejara E. OA-13-399-01
Dissanayake S. PS-36-905-02
Dissou A. EP-15-240-02
Dixit A. EP-09-179-01
Dixit K. SOA-11-1105-01, SOA-11-1113-01, **EP-05-140-31**, **PS-33-866-02**
Dixit P. SOA-14-1141-01, PS-06-555-31
Dixon R. PS-06-566-31
Djetigenova A. SOA-05-1053-31
Djurdjev O. SOA-04-1037-31
Dlamini B. SOA-05-1046-31
Dlamini C. PS-18-691-01, PS-41-950-02
Dlamini N. EP-11-205-02, PS-03-531-31
Dlamini S. SOA-15-1147-02
Dlamini T. OA-07-354-31, EP-11-205-02
Dlamini Z. PS-04-539-31
Dlamini Z.L. **EP-01-108-31**
Dlodlo R. PS-07-574-31
Do D.A.T. OA-20-434-01
Do G.C. SOA-15-1148-02, EP-14-233-02, EP-16-251-02, PS-08-587-31
Do T.T. **PS-13-640-31**
Doan T. OA-22-450-01
Dobbin J. OA-21-445-01
Dobrikov G. PS-39-935-02
Dockhorn Costa F. EP-16-248-02
Doctor T. OA-18-432-01
Dodd P. EP-04-133-31
Dodd W. EP-16-244-02
Dolby T. OA-15-415-01, SOA-01-1010-31, SOA-16-1163-02
Doltu S. PS-05-550-31
Dolynska M. SOA-06-1059-31, **EP-04-132-31**
Dolynskyi G. EP-04-132-31
Domingo A.K. EP-09-184-01
Dominguez J. SOA-01-1003-31
Dominic N. **OA-27-486-02**
Donchuk D. PS-33-862-02
Dong T.T.T. **SOA-04-1033-31**, SOA-05-1045-31, SOA-05-1048-31, PS-13-640-31, **PS-23-754-01**
Donkor S. PS-15-660-01
Donville B. OA-21-446-01
Dorjravdan M. PS-37-915-02
Dos Santos P.C. SOA-18-1188-02
Dos Santos Peixoto A. PS-35-888-02
Dovgaluk I. EP-10-193-01
Dovonou C.A. PS-21-730-01
Dowdy D. OA-01-304-31, OA-06-342-31, OA-06-347-31, OA-10-376-31, OA-22-454-01, EP-08-168-01, PS-07-567-31, PS-08-581-31, PS-10-608-31, PS-12-624-31, PS-32-855-02
Dowdy D.D. SOA-02-1019-31
Dowdy D.W. SOA-02-1020-31, PS-08-584-31

Dowi R. PS-24-761-01, PS-38-917-02, PS-39-931-02
Drain P. OA-21-444-01
Drain P.K. EP-10-196-01
Dramé M. PS-21-727-01
Draoui H. SOA-14-1145-01, PS-06-556-31
Draper H.R. SOA-15-1155-02
Dravniece G. SOA-08-1083-31
Drew E. SOA-13-1135-01
Drobniewski F. OA-18-429-01
Drummond Marques da Silva G. EP-16-248-02
Du J. OA-28-495-02
Du X. EP-08-167-01
Du Cros P. OA-26-477-02, PS-41-956-02, LB-2976
Du Preez K. EP-02-113-31, PS-41-957-02
Duan J. **EP-06-150-01**, EP-06-152-01
Duana I.M.K. PS-19-703-01
Duana M.K. EP-06-151-01
Duarte R. OA-22-455-01
Dubey A. PS-30-826-02
Dudley L. **SOA-13-1133-01**
Duffy S. **PS-17-682-01**
Dugan G. OA-14-409-01
Dugyala R. PS-41-954-02
Duka M. PS-33-862-02
Dukhlii T. EP-04-132-31
Duman D.D. SOA-03-1027-31
Dumbre Y. EP-09-179-01
Dumicho A. LB-2957
Dunbar R. EP-02-113-31, PS-41-957-02
Duong H.T.T. SOA-05-1045-31
Dusmatova Z.S. PS-41-956-02
Dusthackeer VN A. PS-29-822-02
Dycoco-Cam J. PS-13-636-31
Dyers R. SOA-13-1133-01
Dymov G. PS-41-956-02

E

Eang C. EP-14-231-02
Eang M.T. **PS-13-642-31**
Ebere G. PS-17-686-01
Eberts N. PS-36-897-02
Edimani E. EP-12-209-02
Edor J. **EP-16-246-02**
Edry N. PS-17-685-01
Eduardo I. OA-07-352-31
Edwards T. SOA-01-1003-31, LB-2948
Egbule D. OA-12-393-01, PS-07-575-31, PS-30-830-02
Egemberdieva D. SOA-05-1053-31, PS-11-610-31
Egere U. **OA-04-328-31**, PS-16-668-01
Ehimanre C. PS-27-794-01
Ei P.W. SOA-14-1142-01, PS-06-563-31
Eisenberg G. EP-08-171-01
Ekanem E. EP-13-220-02, PS-07-570-31, PS-13-637-31
Ekeke N. PS-01-504-31
Ekesi E.O. PS-19-704-01, **PS-19-705-01**
Elf J. **OA-21-446-01**
Elhadj Adam D. **EP-03-127-31**
Ellis J. OA-18-426-01, **OA-21-445-01**, EP-04-136-31
Ellner J. OA-05-334-31
Ellner J.J. PS-01-510-31
El-Sadr W. SOA-06-1062-31
Elsony A. OA-04-328-31
Emery J.C. OA-22-451-01, **PS-34-875-02**
Emperor U. EP-02-116-31
Enache C.F. **OA-09-368-31**
Endo A. EP-04-138-31
Endtz H. SOA-01-1008-31
Eneogu R. **OA-01-306-31**, OA-12-394-01, PS-07-569-31
Engelbrecht M. OA-07-349-31
England K. **PS-14-644-31**
Enock F. **PS-16-677-01**
Erisen D. SOA-03-1027-31
Erkens C. PS-23-746-01
Esmail A. **LB-2904**, **LB-3062**
Esmail H. OA-22-451-01
Essalah L. SOA-14-1145-01, PS-06-556-31
Esse M. EP-07-165-01
Estigarribia G. **PS-03-530-31**
Etoundi Evouna A. EP-11-199-02
Ette U. PS-23-750-01
Evans C. PS-20-718-01
Evans C.A. SOA-16-1164-02, PS-29-813-02, PS-29-814-02, PS-29-820-02, LB-3028
Evdokimova N. PS-06-557-31
Eves T. PS-36-903-02
Eyangoh S. SOA-17-1173-02
Eyo A. PS-23-750-01
Eze C. PS-01-504-31
Ezzati M. OA-02-310-31

F

Faerstein E. SOA-04-1038-31
Faisel A.J. PS-12-626-31
Falconer J. OA-18-426-01, EP-04-138-31
Fall A.N. EP-16-252-02, PS-33-870-02
Fall F. EP-16-252-02
Falzon D. OA-17-422-01, EP-01-104-31, EP-07-159-01, EP-15-240-02, PS-18-693-01
Fandohan M. PS-07-572-31
Faqih M. EP-09-179-01
Farhat M. OA-13-402-01, EP-09-179-01
Faroun H. OA-23-462-01
Farr K. SOA-03-1032-31, PS-07-567-31
Farrow L. **PS-12-629-31**
Fattah D. EP-01-109-31
Fauzi R. PS-31-839-02
Feemster K.A. OA-04-330-31
Feng J.-Y. PS-01-511-31
Feng T.-Y. PS-28-809-02
Ferdous S.S. PS-35-894-02
Ferguson O. **OA-10-376-31**
Ferlazzo G. OA-17-419-01, OA-28-489-02, SOA-08-1077-31, SOA-08-1078-31, SOA-13-1127-01
Fernandes A. PS-10-605-31
Fernández E. OA-25-472-02
Fernando I. OA-08-358-31, SOA-12-1119-01, EP-03-120-31, PS-31-838-02
Fernando I.B. SOA-12-1121-01
Fernhout J. OA-17-424-01
Ferrari D. SOA-18-1188-02
Ferreira T. OA-12-395-01, EP-05-141-31
Ferreira-Guerrero E. PS-24-765-01
Fewer S. OA-10-372-31
Fida N. SOA-06-1055-31
Fidler S. OA-12-388-01
Fiebig L. **PS-11-620-31**
Fielding K. OA-18-426-01, SOA-02-1017-31, PS-10-608-31, PS-38-921-02
Fielding K.L. **OA-18-427-01**, SOA-13-1129-01, **EP-04-136-31**, EP-04-138-31, PS-26-785-01
Filatov M. OA-20-437-01
Filipe E. PS-28-806-02
Finlay A. OA-14-409-01, SOA-17-1175-02, PS-24-758-01, PS-24-766-01
Fiorati R.C. EP-08-169-01
Firdaus S. PS-09-592-31
Fischer G.W. OA-13-396-01
Fisher D. OA-14-408-01
Fisher J. SOA-10-1100-01
Flanagan C. OA-26-478-02, EP-09-182-01
Flegg J. PS-03-534-31
Fleming M.F. EP-03-129-31
Florez de Sessions P. SOA-18-1181-02
Floyd S. OA-12-388-01, LB-3050
Fononda A. EP-14-228-02
Fonseka A.D. SOA-12-1120-01
Forse R.J. OA-01-303-31, SOA-03-1031-31, SOA-04-1033-31, SOA-05-1048-31, SOA-11-1106-01, **SOA-15-1148-02**, EP-14-233-02, EP-16-251-02, PS-08-587-31, PS-13-640-31, PS-23-754-01, **PS-33-873-02**
Fortune D. PS-15-656-01
Fourie B.P. PS-38-926-02
Fourie P.B. OA-13-396-01, PS-39-933-02
Fournier Le Ray L. OA-20-438-01
Fox G.J. PS-22-740-01
Fox M.P. SOA-13-1125-01
Franke M. OA-26-478-02, PS-26-780-01, LB-2909
Franke M.F. **OA-05-336-31**, SOA-08-1080-31, PS-16-679-01
Fraser-Hurt N. **SOA-13-1125-01**
Frederix K. SOA-06-1062-31
Fregonese F. OA-14-406-01, OA-14-408-01, SOA-04-1038-31, EP-15-238-02, PS-22-740-01
Frescas R. OA-12-395-01, EP-05-141-31
Freschi L. OA-13-402-01
Frick M. OA-10-379-31
Friedland G. SOA-02-1018-31, PS-18-694-01, PS-28-799-02
Friedrich G. **PS-19-708-01**
Frieze J. PS-41-953-02
Fröberg G. **PS-16-669-01**
Fu H. **EP-15-243-02**
Fu L. PS-24-760-01, **PS-34-874-02**
Fu M. OA-25-472-02
Fuady A. **SOA-09-1086-31**, **PS-08-586-31**
Fujiwara P.I. PS-17-681-01
Fukutani K.F. PS-12-630-31
Fuqua E. OA-18-432-01
Furin J. OA-20-436-01, SOA-15-1154-02, LB-2957
Fynn S. PS-18-691-01

G

Gabisonia I. **SOA-03-1024-31**
Gabuzzi J. PS-26-786-01
Gacheri S. EP-12-209-02
Gachie T. **OA-12-388-01**, PS-33-869-02

Gadtia R. **PS-02-521-31**
Gafar F. **SOA-06-1060-31**
Gaikwad S. EP-09-177-01, EP-10-189-01
Gaikwad U. **PS-29-812-02**
Gajjar I. SOA-18-1182-02
Gala N. LB-2991
Galabada Dewage N. PS-30-832-02
Galea J.T. OA-01-300-31, OA-09-369-31
Galligan A. SOA-15-1146-02
Galloway M. OA-09-366-31
Galvez Sanchez T. PS-39-928-02
Gamage N.S. **SOA-12-1117-01**, **PS-31-847-02**
Gamara D. PS-27-792-01, PS-29-815-02
Gamkrelidze A. EP-06-158-01
Ganatra S. **OA-20-439-01**
Gandaho P. EP-15-240-02, PS-18-693-01
Gandhi N. OA-26-480-02, EP-04-131-31
Gandhi R. EP-02-117-31
Gandhi R.K. **OA-27-488-02**, **EP-13-218-02**, PS-30-827-02
Ganesh J. EP-10-194-01
Ganmaa D. **LB-3037**
Gantsetseg G. LB-3037
Ganu H. PS-09-596-31
Gao J. OA-28-495-02
Gao M. OA-28-495-02, PS-06-565-31
Gao Q. PS-26-783-01
Gao Y. OA-21-449-01, **SOA-10-1097-01**
Garcia R. PS-23-751-01
Garcia-Garcia L. **PS-24-765-01**
Garcia-Prats A. SOA-06-1064-31, SOA-15-1154-02
Garcia-Prats A.J. SOA-15-1155-02
Garfin A.M.C. PS-25-777-01
Garfin C. LB-2948
Garg T. **SOA-03-1022-31**, **PS-08-580-31**, **PS-14-647-31**
Gasana M. EP-02-112-31, PS-18-693-01, PS-24-762-01, PS-27-796-01
Gaskell K.M. **PS-37-915-02**
Gaurav K. PS-07-568-31
Gautam R. PS-41-958-02
Gbadamosi D. OA-12-394-01, PS-11-619-31
Geard N. OA-02-312-31
Gebrehiwot T. SOA-02-1014-31, PS-23-748-01
Gebremariam A. SOA-10-1103-01
Gebremedhin A. SOA-02-1014-31, SOA-10-1103-01, PS-21-725-01, PS-23-748-01
Geetha R. EP-10-187-01
Geldmacher C. EP-11-198-02
Geliukh E. **SOA-05-1044-31**
Gemechu D. SOA-02-1014-31, SOA-10-1103-01, PS-23-748-01
Geocaniga-Gaviola D.M. PS-25-777-01
George A.M. PS-10-598-31, PS-25-775-01
George G. PS-41-953-02
George O. **EP-01-102-31**, PS-05-548-31
Gerasimova A. PS-24-759-01
Germamo N. PS-23-757-01
Getnet F. **PS-37-912-02**
Ggita J. SOA-03-1032-31
Ghafari S. OA-09-371-31
Ghariani A. SOA-14-1145-01, PS-06-556-31, PS-27-792-01
Ghati L. **PS-20-722-01**
Ghodousi A. SOA-16-1167-02
Ghorbel A. PS-27-792-01, PS-29-815-02
Ghosh B.S. PS-26-784-01
Ghosh S. **OA-26-475-02**
Ghule V. **PS-33-872-02**
Gibba M.I. PS-15-660-01
Gidado M. OA-01-306-31
Gill O.P.K. **PS-19-711-01**
Gillespie S. LB-2921
Gilman R. LB-3028
Giraldo J. SOA-14-1144-01
Girardi E. **SOA-09-1089-31**
Girma B. PS-04-537-31
Girma Tefera M. SOA-10-1095-01
Giske C. OA-28-493-02, SOA-10-1098-01
Gizynski K. SOA-16-1158-02
Glaziou P. PS-24-758-01, PS-24-766-01
Glockner K. SOA-03-1023-31, SOA-13-1135-01
Gnanou S. OA-14-403-01
Gobena T. PS-37-912-02
Godebo M. **PS-10-603-31**
Godfrey E. PS-17-681-01
Godfrey-Faussett P. EP-02-110-31
Godreuil S. SOA-17-1173-02
Gody J.-C. OA-14-403-01
Goel S. EP-03-128-31, **PS-02-515-31**, PS-05-554-31
Gogen S. EP-14-232-02, PS-15-657-01
Goldberg D. PS-18-692-01, PS-34-885-02
Goldberg E. OA-05-338-31
Goletti D. SOA-01-1008-31
Goliath C. OA-12-389-01
Golin R. SOA-06-1055-31
Golub J. OA-21-446-01, EP-10-189-01
Goma R. PS-14-645-31
Gomathi N. PS-16-671-01
Gomathi N.S. PS-09-591-31, PS-15-663-01
Gombe M.M. **SOA-11-1109-01**
Gomes I. PS-12-624-31
Gomes V.F. SOA-04-1043-31
Gomez G. OA-02-308-31, OA-06-347-31
Gomez M.P. EP-10-190-01
Gonçalves C. SOA-01-1001-31, EP-14-229-02
Gonçalves C.C.M. PS-26-779-01, PS-26-781-01
Gondwe M. **SOA-03-1028-31**, EP-09-185-01
González Ochoa E. PS-22-742-01
Goodall R. OA-28-496-02, SOA-18-1183-02
Goodridge D. OA-23-464-01
Goodwin M. SOA-10-1100-01
Goosby E. OA-10-372-31, PS-03-532-31
Gordon J. OA-23-464-01
Gorgens M. SOA-13-1125-01
Gorla M. SOA-01-1002-31, PS-22-745-01, PS-30-824-02
Goswami A. OA-09-370-31
Goswami N.D. OA-17-422-01
Gotham D. OA-10-379-31
Gottesfeld P. **PS-40-939-02**
Gotuzzo E. PS-29-819-02
Goupehou Wandji A. OA-14-403-01
Gous N. OA-11-383-31, PS-09-596-31
Govender A. EP-01-100-31, EP-14-228-02
Govender I. EP-04-136-31
Govender S. EP-01-100-31, EP-14-228-02
Govindan S A. PS-16-673-01
Govindarajan S. EP-10-187-01
Goyal J. PS-32-859-02
Graham H. EP-07-162-01, PS-22-739-01
Grandjean L. OA-18-428-01
Grankina N. PS-34-878-02, PS-34-879-02
Grankov V. OA-28-494-02, EP-01-104-31
Grant A. OA-02-314-31, OA-06-343-31, SOA-05-1049-31, SOA-05-1052-31, PS-10-608-31, PS-32-852-02, **PS-37-911-02**
Grant A.D. SOA-13-1129-01, **PS-26-785-01**
Grant B. PS-29-821-02
Grant I.R. PS-17-681-01
Grant K. OA-23-463-01
Graulus P. PS-29-817-02
Greenberg L. PS-28-806-02
Gregg M. EP-04-136-31
Grew E. SOA-03-1023-31
Grewal H. OA-05-335-31
Grewal N. **OA-23-464-01**
Griesel R. LB-2861
Griffin T. PS-38-925-02
Griffiths M. OA-27-483-02
Grint D. PS-32-852-02
Groenheit R. OA-17-423-01, SOA-10-1098-01, SOA-16-1167-02
Grossman R. PS-17-685-01
Gualano G.A. SOA-09-1089-31
Guernier V. PS-24-761-01
Guerra D. PS-26-780-01
Guglielmetti L. OA-17-420-01, OA-20-438-01, SOA-18-1186-02
Guha U. **PS-05-548-31**
Guilengue S. PS-14-649-31
Guillermo S.P. OA-01-305-31
Gula B. PS-24-761-01, PS-38-917-02, PS-39-931-02
Gumbo T. OA-03-321-31, OA-26-473-02, SOA-10-1096-01, SOA-10-1101-01
Gumede N.P. PS-04-539-31
Gumma V. OA-15-412-01
Gummar N.V. OA-15-413-01
Gunarathna H. PS-02-517-31
Gunasekara S. PS-02-517-31
Gunawardena P. PS-36-905-02
Gune M. EP-14-230-02
Guo H. EP-08-167-01, PS-15-658-01
Gupta A. OA-03-323-31, SOA-06-1056-31, SOA-18-1182-02, EP-04-131-31, EP-07-160-01, EP-07-161-01, EP-07-162-01, EP-07-163-01, EP-07-164-01, EP-09-177-01, EP-10-189-01, PS-22-739-01

Gupta A.K. PS-05-552-31
Gupta H. EP-11-206-02
Gupta N. OA-27-482-02
Gupta N.K. SOA-16-1157-02
Gupta P.C. SOA-12-1124-01
Gupta R. **SOA-16-1162-02**, PS-05-552-31
Gupta R.K. **OA-18-429-01**, SOA-16-1157-02, SOA-16-1165-02
Gupta R.S. OA-11-385-31
Gupta S. EP-02-117-31, PS-26-784-01
Gupta V. OA-04-324-31
Gupta-Wright A. PS-38-921-02
Gupte A.N. SOA-18-1182-02
Gupte H. OA-25-471-02
Gupte N. OA-03-323-31, EP-07-163-01, EP-07-164-01, EP-09-177-01, EP-10-189-01
Guruge D. LB-3003, LB-3014
Guruge G.N.D. PS-02-517-31, PS-36-905-02
Gurung S. SOA-11-1105-01, SOA-11-1113-01
Gurung S.C. EP-05-140-31, PS-33-866-02
Guryev O. OA-05-338-31
Gutierrez-Clavijo J. SOA-05-1050-31
Gychka S. SOA-15-1146-02

H

Ha D. PS-24-764-01
Ha J.H. SOA-01-1006-31
Ha Thai S. OA-02-313-31
Habibu A. EP-02-116-31
Habibu B. SOA-06-1061-31
Hachicha S. PS-27-792-01, PS-29-815-02
Hadgu A. PS-25-770-01
Hadisoemarto P. OA-14-408-01, **EP-01-109-31**, EP-15-238-02
Hadisoemarto P.F. OA-27-485-02, PS-10-607-31, PS-32-860-02
Haeusler I.L. **OA-18-428-01**
Hafalla J.C. SOA-18-1181-02
Hafidhah B. PS-02-520-31
Hafkin J. OA-26-475-02
Haihuie T. OA-11-387-31
Haile L. SOA-15-1146-02
Hakim A. SOA-02-1015-31
Haldar S. OA-13-398-01, **SOA-16-1157-02**, SOA-16-1162-02, SOA-16-1165-02, EP-10-195-01
Hall J. SOA-03-1029-31
Hall P. PS-14-646-31
Hamasur B. **PS-38-922-02**
Hamda S. **LB-2908**
Hamid M. PS-27-793-01
Hamid S. PS-12-626-31
Hamim A. OA-01-305-31, SOA-15-1152-02, EP-11-200-02, **EP-16-249-02**
Hamzeh ali S. **OA-09-371-31**
Hangoma P. OA-01-304-31
Hanh N. PS-24-764-01
Hanif M. **EP-12-208-02**, PS-34-882-02
Hanna L. PS-16-671-01
Hannah H. OA-21-444-01
Hanrahan C. OA-01-304-31, PS-08-581-31, **PS-32-855-02**
Hanson-Nortey N.N. **EP-05-147-31**, EP-13-224-02
Hapolo M. OA-11-387-31
Haq H. SOA-15-1147-02
Harding J. OA-26-473-02, SOA-10-1096-01, SOA-10-1101-01
Hari A. PS-35-889-02
Hariprasad R. PS-19-707-01
Harries A.D. PS-15-655-01
Harrington P. OA-26-480-02
Harris R. OA-02-308-31
Harris R.C. **OA-02-309-31**, **OA-18-426-01**, OA-18-427-01, EP-04-136-31, EP-04-138-31
Harris R.J. PS-25-771-01
Harris V. PS-14-652-31
Harshana A. PS-28-801-02
Hasan M.M. PS-31-840-02
Hasibul Huq K.M. PS-02-516-31
Hasker E. PS-13-634-31
Hasnain A. EP-02-111-31
Hassan A. PS-08-585-31, PS-30-831-02
Hassan S. PS-39-934-02
Hassen H.M. **PS-40-941-02**
Hatam Khan W. OA-17-424-01
Hatherill M. OA-14-410-01
Haumba S. PS-03-531-31
Hausler H. OA-11-381-31, OA-23-463-01, SOA-02-1017-31, EP-14-228-02
Hayes C. OA-15-415-01
Hayes N. EP-03-129-31
Hayes R. OA-12-388-01, EP-04-134-31
Hayward A. SOA-03-1029-31
Heekes A. OA-12-389-01
Hegde A. OA-27-486-02, EP-02-117-31
Hegde-Shetiya S. **OA-25-471-02**
Heinrich N. SOA-14-1139-01, EP-11-198-02, PS-16-678-01
Hemanth Kumar A.K. EP-10-187-01
Hendricks P. PS-32-850-02
Heng S. PS-17-684-01
Herce M. SOA-02-1017-31
Hernandez H. PS-01-508-31
Herrera B. SOA-16-1164-02, PS-29-813-02
Herrera-Flores E. **PS-01-508-31**
Hesseling A. SOA-06-1056-31, SOA-06-1062-31, EP-04-131-31, PS-32-850-02, PS-41-957-02
Hesseling A.C. SOA-06-1058-31, SOA-15-1155-02, EP-02-113-31
Heunis C. **OA-07-349-31**
Heupink T. SOA-14-1138-01
Hewison C. **OA-10-377-31**, OA-21-447-01, OA-28-492-02, **PS-11-614-31**, PS-18-701-01, PS-34-883-02, **PS-34-884-02**, **LB-2909**
Heysell S. **OA-20-435-01**
Heysell S.K. PS-01-503-31
Hibberd M.L. SOA-18-1181-02
Hilario-Huapaya N. LB-3065
Hill A. PS-12-624-31
Hill J. OA-14-409-01
Hill P. OA-14-406-01, OA-27-485-02, SOA-04-1038-31, EP-01-109-31, EP-15-238-02
Hill P.C. PS-10-607-31, PS-32-860-02
Hillery N. SOA-16-1159-02
Hinson V. PS-40-938-02, PS-40-942-02
Hippner P. **PS-10-608-31**
Hirani N. PS-06-562-31
Hirsch-Moverman Y. **SOA-06-1062-31**, **PS-41-953-02**
Hiruy N. SOA-02-1014-31, EP-11-203-02
Hissar S. EP-10-194-01, **PS-09-591-31**, **PS-16-671-01**
Hittel N. OA-26-475-02
Hnin Hnin Phyu E. OA-17-424-01
Ho C. OA-14-404-01, SOA-04-1042-31
Ho V.A. SOA-17-1175-02
Hoa N.B. OA-22-452-01
Hoa V.D. OA-17-425-01
Hoang G.T. SOA-05-1045-31
Hoang L.M.T. OA-01-303-31, PS-33-873-02
Hoang T.H. **OA-20-434-01**
Hochberg N. OA-05-334-31
Hochberg N.S. PS-01-510-31
Hoddinott G. SOA-03-1028-31, SOA-06-1064-31
Hoelscher M. OA-04-326-31, PS-16-678-01, LB-2921
Hoeppner V. OA-23-464-01
Hoffmann C. SOA-02-1017-31, EP-14-228-02
Hoffmann C.J. PS-26-785-01
Hoffmann H. EP-11-198-02
Hoffmann J. SOA-01-1008-31
Hoffner S. SOA-10-1097-01
Hogarth P.J.,. PS-17-680-01
Holder T. PS-17-680-01
Holmberg R. OA-05-336-31
Hölscher M. EP-11-198-02
Holtzman D. **OA-21-448-01**, OA-28-490-02
Horna-Campos O. EP-11-202-02
Horne R. SOA-03-1029-31
Horowitz Y. PS-17-685-01
Horsburgh C.R. SOA-06-1059-31, SOA-15-1146-02, EP-04-132-31
Horsburgh Jr R.C. PS-01-510-31
Horton K.C. **OA-22-452-01**
Hossain A. SOA-08-1081-31
Hossain F. PS-12-626-31, PS-41-955-02
Hossain S.T. PS-11-609-31
Hossein M. **OA-08-362-31**, EP-03-122-31
Hota P.K. EP-12-212-02, EP-16-253-02
Hou P. PS-26-786-01
Hou S. PS-11-612-31, PS-11-615-31, PS-20-720-01
Houben R. SOA-18-1187-02, EP-04-133-31
Houben R.M.G.J. OA-22-451-01, OA-22-452-01, PS-34-875-02
Houeto S. PS-06-564-31
Houweling T.A.J. SOA-09-1086-31
Hove S. PS-07-574-31
Hovhannisyan L. OA-10-377-31, PS-34-884-02
Howard A.A. SOA-06-1062-31, PS-41-953-02
Hsueh P.-R. OA-04-327-31
Htut Aung S. PS-07-578-31
Htwe K.K. SOA-15-1149-02
Htwe M.M. SOA-14-1142-01, PS-06-563-31
Hu J. PS-24-763-01

Hu Y. SOA-10-1097-01, **PS-39-936-02**, PS-39-936-02
Huang C.-C. PS-12-628-31
Huang H.-L. **SOA-10-1099-01**
Huang S. EP-06-150-01
Huang W. OA-05-338-31
Huang W.C. PS-22-738-01
Huang X. SOA-04-1034-31, PS-22-736-01
Huang Y. EP-06-150-01, **EP-06-152-01**
Huang Y.C. PS-28-809-02
Huang Y.F. SOA-08-1076-31
Huang Y.-F. SOA-09-1085-31, PS-28-809-02
Huang Y.W. **PS-22-738-01**
Huang Z. OA-10-373-31
Huaroto Valdivia L.M. PS-29-820-02
Huber A.N. SOA-13-1125-01
Huddart S. **PS-03-524-31**, **PS-03-526-31**
Huerga H. OA-21-447-01, **OA-28-492-02**, PS-11-614-31, **PS-18-701-01**, PS-34-883-02, PS-34-884-02, LB-2909
Huff D. LB-3028
Hughes G. **OA-28-496-02**, **PS-18-697-01**
Hughes J. SOA-15-1154-02
Hughes M. SOA-06-1056-31, EP-04-131-31
Huitema I. PS-27-794-01
Human W. OA-09-366-31
Hurevich H. OA-28-494-02, EP-01-104-31
Hurwitz S. OA-18-432-01
Hussain H. PS-12-626-31, PS-25-776-01, PS-41-955-02
Hussain T. EP-16-245-02
Huynh H.B. SOA-03-1031-31, **SOA-11-1106-01**

I

Iacobelli M. OA-08-360-31, SOA-12-1124-01
Ibeziako V. EP-12-215-02
Ibeziako V.C. PS-23-755-01
Ibna Mohsin S.M. **PS-04-541-31**
Ibraeva A. PS-11-610-31
Ibrahim H. OA-04-328-31
Idris Tari A. OA-12-393-01
Idrissova M. OA-11-386-31, SOA-08-1083-31
Igbabul S.-A. OA-01-302-31
Igbinoba R. **OA-23-465-01**
Ignatowicz L. PS-38-922-02
Ikebudu J. PS-01-504-31
Ikpeazu A. PS-07-575-31
Ilter H. EP-14-232-02
Ilyasova E. EP-01-104-31
Imran A. **PS-23-751-01**
Imsanguan W. **PS-04-535-31**
Inobaya M. PS-38-924-02
Inolopu J. LB-3065
Inomata Bruce A.T. PS-11-622-31
Iragena J. EP-02-112-31, **PS-27-796-01**
Iragena J.D.D. PS-24-762-01
Irfan M. OA-03-316-31
Iroko A. EP-13-220-02, PS-07-570-31, PS-13-637-31
Isaakidis P. OA-17-419-01, OA-28-489-02, SOA-08-1078-31, SOA-13-1127-01, EP-09-184-01, PS-33-862-02, LB-2957
Isabirye J. OA-07-353-31, PS-32-851-02
Ishaq S. OA-17-424-01
Ishengoma L. EP-05-143-31, EP-13-222-02, **PS-04-540-31**
Islam A. EP-13-223-02, PS-02-516-31, **PS-02-516-31**
Islam M.A. SOA-03-1030-31, **EP-05-145-31**, EP-13-223-02, PS-04-541-31, **PS-27-790-01**, PS-28-804-02
Islam M.R. PS-11-609-31
Islam M.S. EP-09-186-01, PS-01-507-31, PS-04-541-31, PS-04-541-31, PS-11-609-31, PS-12-626-31, PS-14-650-31, PS-14-653-31, PS-41-955-02
Islam S. OA-11-387-31, SOA-03-1030-31, SOA-08-1081-31, EP-05-145-31, EP-13-223-02, PS-04-541-31, PS-27-790-01, PS-28-804-02
Islam Z. SOA-05-1044-31
Ismoiliva J. EP-11-204-02
Isooba D. EP-08-168-01
Ivanova O. **OA-04-326-31**
Ivaturi V. OA-03-321-31
Iwakun M. **PS-14-648-31**
Iwuoha E. **OA-11-380-31**
Iyer A. SOA-08-1078-31

J

J Valamparampil M. OA-04-331-31, SOA-13-1134-01
Jackson C. OA-18-429-01
Jackson J. SOA-01-1010-31
Jacobsen M. PS-16-670-01
Jaffré J. OA-03-322-31, OA-17-420-01
Jaganath D. **OA-10-375-31**, **PS-39-930-02**
Jagirdar A. EP-14-230-02
Jagtap J. **EP-09-179-01**
Jagwer G. OA-18-431-01, SOA-05-1046-31, SOA-06-1063-31, EP-01-108-31, PS-10-604-31, **PS-18-691-01**, PS-33-864-02, PS-36-900-02, PS-38-923-02, **PS-41-950-02**
Jain A. **SOA-14-1141-01**, **PS-06-555-31**
Jain D. EP-07-161-01, EP-07-163-01, EP-07-164-01
Jain R. PS-05-553-31
Jain Y. SOA-13-1131-01
Jaintilal D. PS-14-649-31, **PS-27-795-01**
Jaiswal A. PS-05-553-31
Jajou R. **OA-06-345-31**
Jaju J. **OA-27-482-02**, EP-08-172-01, **EP-08-175-01**
James J. OA-27-487-02
Janardhana Naga Sai K. SOA-01-1002-31
Jansson L. **PS-12-631-31**
Jaramillo A. OA-12-395-01, EP-05-141-31
Jarlier V. OA-17-420-01, OA-20-438-01
Jarrett B. OA-21-446-01
Jassat W. SOA-05-1052-31
Jawahar M.S. PS-15-663-01
Jayakody M. PS-30-832-02
Jayakody W. **PS-30-832-02**
Jayaraman D. PS-41-958-02
Jayasinghe T.B. PS-36-905-02
Je J.H. EP-10-191-01
Jena P. OA-03-316-31, OA-08-357-31, **EP-03-121-31**
Jena P.K. PS-02-521-31
Jenkins H. SOA-06-1059-31, SOA-15-1146-02
Jenkins H.E. EP-04-132-31
Jensen P.A. PS-15-658-01
Jereb J. OA-14-404-01
Jerene D. PS-25-770-01
Jha N. PS-03-524-31
Jha P. **PS-08-579-31**
Jha S.N. OA-23-460-01
Ji L. PS-26-783-01
Jia C. PS-20-720-01
Jiang Q. **PS-26-783-01**
Jikia D. PS-05-550-31
Jimenez Guevara J. OA-01-300-31, OA-09-369-31, PS-01-509-31
Jiménez-Corona E. PS-24-765-01
Jimoh K. SOA-17-1170-02
Jo Y. **OA-01-304-31**, OA-10-376-31, **PS-12-624-31**
Jobe D. EP-10-190-01
Joel D. LB-2908
Jogewar P. OA-27-481-02
Jogewarr P. PS-30-829-02
John J. SOA-14-1139-01
John S. EP-11-201-02, **PS-26-787-01**
Johnson K. OA-10-376-31
Johnson S. SOA-13-1129-01, PS-26-785-01
Johnson S.-M. PS-37-906-02
Johnson W.E. **OA-05-334-31**
Johnston J. SOA-04-1037-31, PS-03-523-31
Johnston J.C. SOA-17-1178-02
Johnstone D. PS-22-735-01
Jokwiro J. SOA-11-1109-01
Joloba M. SOA-17-1177-02, EP-12-210-02, PS-14-651-31, PS-38-919-02
Joloba M.L. PS-28-803-02
Jondhale V. EP-02-117-31, PS-30-827-02
Jone J. EP-13-221-02
Jone Zacarias J. EP-08-174-01
Jones J. OA-07-352-31
Jonnala S. SOA-10-1100-01
Jonsson J. OA-28-493-02, SOA-10-1098-01
Jonsson Nordvall M. OA-17-423-01
Jooste S. PS-15-665-01
Jorjoliani N. PS-22-743-01
Jorwal P. PS-29-816-02, PS-40-945-02
Jose M.B. PS-04-544-31
José B. **OA-07-352-31**
Joseph C. PS-07-577-31
Joseph K. PS-30-831-02
Joseph N. OA-05-334-31, PS-35-887-02
Joshi A. PS-06-562-31
Jou R. **OA-13-397-01**
Juan A. PS-33-868-02
Jumayeva J. SOA-13-1127-01

K

K Gopal B. OA-04-331-31
K Singh S. OA-27-487-02
Kabango L. EP-12-207-02
Kabasakal E. SOA-02-1012-31, EP-14-232-02, PS-15-657-01

Kabeya R. PS-21-729-01
Kabir S. **PS-09-590-31**, PS-35-894-02
Kabra S.K. OA-05-335-31
Kabugo J. **OA-15-414-01**
Kadam D. EP-07-161-01
Kadhiravan T. **PS-22-741-01**, **PS-35-887-02**
Kadianda C. OA-21-443-01
Kadota J. SOA-02-1019-31, **PS-08-584-31**
Kadu A. **PS-30-829-02**
Kadyrov A. PS-11-610-31
Kaemala F. EP-12-209-02
Kaewmamuang K. PS-04-535-31
Kagal A. EP-10-189-01, PS-35-890-02
Kagan L. OA-22-457-01
Kagujje M. OA-01-304-31
Kagwisagye M. LB-2990
Kahwa A. PS-11-620-31
Kak N. PS-23-751-01
Kakeeto A. PS-14-651-31
Kakodkar P. OA-25-471-02
Kalema N. **EP-15-236-02**
Kalia M. **PS-41-958-02**
Källenius G. PS-16-669-01
Kalliyath A. SOA-13-1134-01
Kally J.S.N. **PS-33-870-02**
Kalon S. OA-28-489-02, SOA-08-1078-31, SOA-13-1127-01
Kalottee B. EP-13-218-02, **EP-13-226-02**
Kalpana S. EP-10-194-01
Kalra A. PS-33-872-02
Kamala R. OA-04-331-31
Kamarli C. PS-11-610-31
Kamble S. OA-27-481-02, PS-10-606-31, PS-30-825-02
Kamdolozi M. OA-20-440-01
Kamene M. OA-10-374-31
Kamenska N. SOA-05-1044-31
Kamerhe D. PS-28-811-02
Kammoun S. PS-27-792-01, PS-29-815-02
Kamoga N. PS-10-605-31
Kampmann B. EP-10-190-01, PS-16-668-01, PS-16-678-01
Kamst M. OA-06-345-31
Kamya M.R. SOA-02-1019-31, SOA-02-1020-31
Kanagat N. PS-30-834-02
Kanchar A. EP-07-159-01, EP-15-240-02
Kandeepan S. OA-08-358-31, SOA-12-1119-01, **SOA-12-1121-01**, **EP-03-120-31**, PS-31-838-02
Kang H.Y. EP-10-191-01
Kankya C. PS-17-681-01
Kannan M. PS-16-671-01
Kannan T. EP-10-187-01, PS-16-671-01
Kant S. **EP-11-206-02**, PS-34-877-02
Kanth S. LB-2991
Kantipudi K. **OA-05-332-31**
Kanyerere H.S. PS-04-537-31
Kao K. PS-14-652-31
Kapungu K. SOA-02-1016-31
Kapur V. PS-17-682-01
Kara F. PS-15-657-01
Karad A. EP-13-217-02
Karane M. SOA-18-1182-02
Karat A. PS-21-731-01
Karat A.S. OA-18-426-01, OA-18-427-01, SOA-13-1129-01, EP-04-136-31, EP-04-138-31, PS-26-785-01
Karnik A. OA-09-364-31
Karunarathna N. PS-02-517-31
Karunarathne N. LB-3003
Karunarathne R. **LB-3014**
Karyakarte R. PS-35-890-02
Kasaie P. OA-06-347-31
Kasapo C. PS-32-853-02
Kasavan K. PS-29-821-02
Kasongo F. PS-14-645-31
Kassa D. LB-2965
Kassa F. PS-22-737-01
Kaswa M. **SOA-11-1111-01**
Kaswandani N. PS-12-627-31
Katahoire A. SOA-02-1019-31
Katahoire A.R. SOA-02-1020-31
Katamba A. OA-07-348-31, SOA-02-1019-31, SOA-02-1020-31, SOA-03-1032-31, SOA-06-1065-31, SOA-17-1174-02, EP-08-168-01, PS-03-525-31, PS-07-567-31, PS-07-576-31, PS-08-584-31
Katana A. EP-15-235-02
Katelaris A.L. OA-18-429-01
Kathamuthu G.R. **PS-39-929-02**
Kathiresan J. SOA-09-1092-31
Katjao I. PS-27-797-01
Katjau I. **PS-20-721-01**
Katlholo T. OA-23-463-01
Kato S. SOA-18-1181-02
Kato-Maeda M. PS-25-777-01
Katongole S.P. PS-37-910-02
Katwesigye E. PS-15-666-01
Katz S. OA-17-421-01
Katz Z. OA-15-412-01
Kaur N. EP-03-128-31, PS-02-515-31
Kaushal D. OA-20-439-01
Kawasaki M. OA-26-475-02
Kawen M. OA-21-443-01
Kay A. **SOA-06-1055-31**, SOA-15-1147-02, PS-03-531-31
Kazgan Arica Z. SOA-02-1012-31
Kazibwe A. SOA-05-1047-31, PS-04-536-31
Kazmi S. PS-28-801-02
Keam T. **OA-11-387-31**
Kekitiinwa A. LB-2990
Kelly M.S. OA-04-330-31
Kelly-Hanku A. **PS-26-786-01**
Kempker R. SOA-18-1186-02, PS-03-527-31, PS-18-698-01, PS-22-743-01
Kendall E. **OA-06-342-31**, OA-06-347-31, **OA-22-454-01**, SOA-17-1174-02, EP-08-168-01
Kendrick P. **OA-04-324-31**
Kennedy R.D. SOA-12-1114-01
Kereu V. **EP-12-209-02**
Kerndt P. PS-28-806-02
Kerschberger B. EP-11-205-02, PS-03-531-31
Keshavjee S.A. OA-01-300-31, OA-09-369-31
Keskin T. SOA-02-1012-31
Ketema L. PS-23-757-01
Keysers J. OA-13-399-01
Khachatryan N. OA-10-377-31, PS-11-614-31, PS-18-701-01, PS-34-884-02
Khader S. OA-20-439-01
Khaebana M. SOA-05-1046-31
Khaidarkhanova Z. OA-26-477-02
Khaled Seddiq M. OA-17-424-01
Khaliq A. OA-03-316-31, OA-05-338-31
Khama M. PS-35-892-02
Khan A. OA-27-483-02, OA-27-484-02, PS-26-784-01, PS-41-959-02, **LB-3052**
Khan A.H. SOA-14-1140-01, EP-09-186-01, PS-04-541-31, **PS-14-653-31**
Khan I. OA-03-316-31, OA-05-338-31, PS-39-930-02
Khan M.H. **PS-25-776-01**
Khan P. EP-04-130-31, LB-2909
Khan P.Y. SOA-08-1081-31
Khan U. **SOA-08-1081-31**, EP-02-111-31, EP-04-130-31, LB-2909
Khan Amirzada H. OA-17-424-01
Khandelwale A.S. SOA-13-1132-01
Khandewale A.S. PS-11-616-31
Khaneja R. PS-16-674-01, PS-38-918-02
Khanna A. **EP-05-144-31**, EP-12-208-02, PS-11-621-31, PS-34-882-02
Khanna V. EP-05-144-31, PS-11-621-31
Khaparde K. **EP-16-247-02**, **PS-30-826-02**
Khatgaonkar V. OA-27-481-02
Khatun F. SOA-03-1030-31, **EP-13-223-02**, PS-27-790-01, **PS-28-804-02**
Khayumbi J. PS-06-560-31
Khieu T.T.N. SOA-17-1175-02
Khieu Thi Thuy N. PS-24-758-01, PS-24-766-01
Khillare K. PS-41-954-02
Khokhar A. PS-40-943-02
Kholikulov B. OA-28-492-02
Khondowe S. SOA-04-1040-31
Khonelidze I. SOA-03-1024-31, PS-11-617-31
Khoo S. OA-20-440-01
Khosa C. OA-04-326-31, PS-41-948-02, PS-41-952-02
Khowaja S. **EP-02-111-31**
Khuat O.T.H. SOA-05-1045-31
Khulan D. LB-3037
Khursheed N. PS-27-793-01
Khwaja S. EP-07-162-01, PS-22-739-01
Kibballi Madhukeshwar A. **SOA-09-1088-31**, **PS-33-865-02**
Kidane Z. SOA-10-1103-01
Kielmann K. SOA-13-1130-01, **PS-21-731-01**, PS-37-911-02
Kigozi G. OA-07-349-31
Kikonyogo R. PS-15-666-01
Kikvidze M. OA-28-492-02
Kiluba J.-C. OA-21-443-01, PS-28-811-02
Kim C.T. LB-2895
Kim H.J. EP-10-191-01
Kim H.W. **SOA-01-1006-31**
Kim J.-R. EP-10-191-01
Kim J.S. SOA-01-1006-31
Kim K.H. SOA-01-1006-31
Kim S. **SOA-06-1056-31**, EP-04-131-31
Kimenye M.K. PS-15-656-01
Kimono N. OA-09-365-31

King D. PS-18-698-01
Kinikar A. EP-07-162-01, PS-22-739-01
Kinter A. OA-05-333-31
Kintu Nsangi B. PS-32-851-02
Kipp A. SOA-13-1135-01, PS-05-547-31
Kipp A.M. SOA-03-1023-31
Kiptai T. **OA-09-365-31**, OA-12-390-01
Kirakosyan O. OA-10-377-31, OA-21-447-01, PS-18-701-01
Kirenga B. SOA-09-1087-31
Kirenga B.J. PS-07-576-31
Kiria N. PS-11-617-31, PS-15-656-01, PS-34-883-02
Kirirabwa N. OA-26-474-02, OA-26-476-02, PS-33-863-02
Kisamba H. **PS-04-545-31**
Kishore G. SOA-18-1182-02
Kistnasamy B. **PS-20-714-01**
Kitane M. EP-16-252-02
Kitata M.E. OA-13-399-01
Kitenge M. OA-12-389-01
Kitonsa P.J. EP-08-168-01
Kityamuwesi A. SOA-03-1032-31
Kiyemba T. **EP-02-115-31**, **EP-08-176-01**, **PS-07-573-31**
Kizito E. **PS-36-899-02**
Kizito S. SOA-06-1065-31
Klaos K. OA-06-340-31
Kliescikova J. PS-41-956-02
Klimuk D. OA-28-494-02, EP-01-104-31
Klinkenberg E. LB-3050
Kloprogge F. **OA-20-440-01**
Knight G. SOA-18-1187-02
Knight G.M. OA-02-309-31
Knudsen S. OA-05-334-31, PS-01-510-31
Ko A.I. PS-26-781-01
Ko E. OA-14-409-01
Koch A. PS-04-539-31
Kocharyan L. OA-10-377-31, PS-34-884-02
Kock Y. OA-17-419-01, SOA-15-1154-02, PS-18-692-01
Ködmön C. PS-25-771-01
Kohli M. **OA-13-400-01**
Koiri P. EP-02-117-31
Kokhreidze E. **PS-22-743-01**
Kolomiyets L.M. PS-33-862-02
Komrska J. **OA-22-456-01**, PS-11-611-31
Komujuni H. PS-36-899-02
Konaté B. PS-21-727-01
Konelios-Langinlur M. OA-14-409-01
Kontogianni K. SOA-01-1003-31
Korinchuk L. SOA-06-1059-31
Kort F. OA-20-438-01
Köser C. SOA-16-1167-02
Koshcheyev M. OA-20-435-01
Kosloff B. EP-04-134-31, LB-3050
Kotalwar S.G. **PS-05-553-31**
Kotey T. PS-19-704-01, PS-19-705-01
Kothari A. EP-13-225-02
Kotrikadze T. PS-34-883-02
Koura K. SOA-11-1111-01
Koura K.G. OA-14-403-01
Kozikott S. **PS-05-551-31**
Krainski E.T. OA-18-433-01
Kravchenko A. PS-06-557-31
Krishna Jha S. OA-01-307-31
Krishnan N. OA-23-461-01, OA-27-483-02, OA-27-484-02, PS-33-867-02
Krishnan V. PS-35-893-02
Kritski A. **OA-22-455-01**
Kritski A.L. PS-12-630-31
Kuaban C. PS-18-689-01
Kuate Kuate A. **EP-11-199-02**
Kübler L. **EP-11-198-02**
Kuchukhidze G. SOA-03-1024-31, PS-03-527-31, PS-11-617-31
Kudale A. PS-01-501-31
Kudlay D. PS-16-675-01
Kudzawu S. **PS-09-596-31**
Kuhlin J. **OA-17-423-01**, SOA-10-1098-01
Kula N. PS-36-900-02, PS-41-950-02
Kulane A. PS-12-631-31
Kular J. PS-34-881-02
Kulikova O. PS-24-759-01
Kulkarni V. **OA-03-323-31**, **EP-07-164-01**
Kuma A. OA-11-387-31
Kumar A. OA-23-460-01, EP-10-195-01
Kumar A.M. SOA-15-1149-02
Kumar A.M.V. PS-15-655-01, PS-28-808-02
Kumar G. OA-01-307-31, OA-13-398-01
Kumar K. PS-20-713-01
Kumar M. SOA-03-1022-31, SOA-10-1102-01
Kumar N. OA-15-412-01, EP-08-175-01, EP-12-208-02, PS-17-683-01
Kumar P. PS-40-945-02
Kumar R. EP-08-175-01, **PS-05-554-31**, PS-14-645-31, **PS-15-661-01**, PS-21-729-01, PS-28-808-02, PS-30-833-02, PS-32-853-02, PS-33-869-02
Kumar S. **OA-09-370-31**, OA-23-461-01, SOA-03-1022-31, PS-05-552-31, PS-14-647-31, **PS-20-713-01**, PS-25-775-01, PS-29-816-02, PS-29-822-02
Kumar V. SOA-13-1132-01, SOA-14-1141-01, PS-11-616-31, PS-19-707-01, PS-29-812-02
Kumar AK H. PS-29-822-02
Kumar Mondal R. PS-29-822-02
Kumara S. PS-02-517-31, LB-3003
Kumarasingam K. PS-35-889-02
Kumari A. OA-23-460-01
Kumari P. SOA-16-1165-02
Kumari S. PS-34-881-02
Kumbhalwar A. OA-25-471-02
Kunoor A. **OA-27-487-02**
Kupul M. PS-26-786-01
Kurada J. OA-06-341-31, **PS-11-613-31**
Kurniasari N.M.D. SOA-12-1116-01
Kurniati N.M. SOA-12-1116-01, **PS-02-514-31**
Kusainova R. SOA-08-1083-31
Kusimo O. PS-08-585-31
Kuspekova M. SOA-08-1083-31
Kuwatada J. EP-14-234-02
Kuzin I. SOA-06-1059-31
Kwan A. SOA-03-1025-31, EP-13-227-02, PS-10-600-31, PS-10-601-31, PS-32-861-02
Kweyamba M. PS-13-632-31
Kwon D. OA-03-320-31
Kyaw K.W.Y. **SOA-15-1149-02**
Kyaw N.T.T. SOA-15-1149-02
Kyi Lay K.Z. PS-11-614-31
Kyokutamba H. **PS-33-871-02**

L

Lago H. EP-02-112-31, **PS-24-762-01**, PS-27-796-01
Laker E. EP-15-237-02
Lakmal S. OA-08-358-31, SOA-12-1119-01, EP-03-120-31, PS-31-838-02
Lakmal S.C. SOA-12-1121-01
Lakshmanan S. PS-28-802-02
Lalvani A. OA-18-429-01
Lamorde M. EP-15-237-02
Lan Z. OA-17-418-01
Langer R. OA-20-436-01
Langley I. SOA-10-1095-01
Laniado Laborin R. SOA-18-1186-02
Lapaix A.Z. PS-13-634-31
Largen A. OA-14-409-01
Lau L. **EP-16-244-02**
Laureillard D. SOA-05-1045-31
Laushkina Z. **PS-40-944-02**
Lavania S. SOA-16-1157-02, SOA-16-1165-02
Lavanya J. EP-15-242-02
Law S. **OA-11-382-31**, PS-28-810-02
Lawal I. SOA-04-1035-31
Lawan I.M. SOA-18-1184-02
Lawanson A. OA-01-306-31, SOA-17-1170-02, EP-02-119-31, PS-18-696-01, PS-30-831-02
Lawason A. EP-16-246-02
Lawson L. SOA-01-1003-31
Laxmeshwar C. PS-33-862-02
Lay L.C. PS-13-642-31
Le G.T. SOA-03-1031-31, SOA-11-1106-01, SOA-15-1148-02, EP-14-233-02, EP-16-251-02, PS-08-587-31
Le H.V. SOA-04-1033-31, SOA-05-1045-31, SOA-05-1048-31, SOA-11-1106-01, SOA-15-1148-02, EP-14-233-02, PS-13-640-31, PS-23-754-01
Le N.T.T. SOA-15-1148-02
Le N.T.N. SOA-15-1148-02
Le Roux S. SOA-05-1052-31
Lebelo L. SOA-06-1062-31
Lebina L. OA-21-446-01, PS-08-581-31, PS-32-855-02
Lebona L. **SOA-05-1046-31**, **PS-36-900-02**
Lecca L. OA-01-300-31, OA-05-336-31, OA-09-369-31, OA-26-478-02, EP-09-182-01, PS-01-512-31, PS-26-780-01, PS-39-928-02
Lecca Garcia L. OA-21-442-01
Lecca García L. PS-01-509-31
Lechuti T. EP-01-100-31
Lee C.-H. **PS-12-628-31**
Lee G. **SOA-06-1065-31**
Lee H.M. **LB-2895**
Lee J.S. SOA-14-1142-01, PS-06-563-31
Lee M.-R. SOA-10-1099-01

Lee P.H. **SOA-08-1076-31**
Lee S. EP-16-244-02
Leekha S. PS-37-915-02
Leimane I. OA-11-386-31
Lemos E. SOA-01-1001-31, EP-14-229-02
Lemvik G. SOA-04-1043-31
Lerefolo M. EP-14-228-02
Leseka T. EP-01-100-31
Lessells R. PS-10-608-31
Lessem E. OA-10-379-31
Lestari B. EP-01-109-31
Lestari B.W. OA-27-485-02, PS-10-607-31, **PS-32-860-02**
Leta A. OA-21-448-01, OA-28-490-02
Leung C.C. OA-17-422-01
Levin A. SOA-04-1037-31
Levine H. OA-02-313-31
Levy J. OA-01-306-31, **PS-07-569-31**, **PS-07-575-31**
Levy-Braide B. **OA-12-394-01**, PS-11-619-31
Lewis J. LB-3028
Li J. PS-26-783-01
Li L. OA-28-495-02, PS-11-615-31
Li Q. PS-06-565-31
Li R. **OA-02-311-31**
Li T. **EP-08-167-01**
Li Y. OA-03-317-31, **OA-05-337-31**, **PS-11-615-31**, **PS-18-700-01**, PS-35-886-02
Liao Y. **EP-09-178-01**
Liashko V. SOA-03-1026-31
Liebenberg H. PS-10-604-31
Likhovole C. **PS-06-560-31**
Likichoru J. OA-26-474-02
Lillis L. PS-27-798-01
Lim D. PS-38-924-02
Lim D.R. **SOA-18-1181-02**
Lima dos Santos F. PS-11-622-31
Limberis J. LB-3062
Limirio Souza L.L. EP-08-169-01, PS-11-622-31
Limo J. **PS-30-835-02**
Lin H.-H. OA-02-310-31, SOA-09-1085-31, EP-02-110-31, PS-32-858-02
Lin M. SOA-04-1034-31
Lin W.-H. OA-13-397-01
Lin Y.D. LB-2976
Lin Tun Z. PS-07-578-31
Lipman M. OA-18-429-01, PS-21-731-01, LB-2904
Lisa S. EP-08-174-01
Lisboa M. **SOA-02-1013-31**
Lisboa Bastos M. **SOA-04-1038-31**, **SOA-04-1041-31**
Lister D. LB-2976
Liu B. PS-38-925-02
Liu C. PS-38-925-02
Liu C.H. SOA-08-1076-31
Liu K.-Y. SOA-09-1085-31
Liu Q. **EP-02-114-31**, **PS-01-505-31**, PS-26-783-01
Liu W. PS-20-720-01
Liu X. SOA-04-1034-31, PS-11-612-31
Liu Y. **OA-28-495-02**
Liu Y.-J. PS-12-628-31
Liverko I. EP-11-204-02
Livingstone D. **PS-15-659-01**, **PS-20-717-01**
Llorente B. SOA-12-1118-01, PS-19-708-01
Lo H.-Y. SOA-09-1085-31
Loa R. **PS-20-719-01**
Lobato M. OA-14-404-01
Lobo S. PS-14-649-31
Lochoro P. SOA-09-1087-31
Lodha R. OA-05-335-31
Lomtadze N. PS-03-527-31, PS-11-617-31, PS-22-743-01
Lone A. PS-33-872-02
Long R. OA-14-408-01
Lonnroth K. OA-01-303-31, PS-33-873-02
Lönnroth K. OA-02-310-31, SOA-11-1113-01, PS-08-588-31, PS-12-631-31, PS-13-643-31
Lopes da Silva M.A. PS-35-888-02
Lopes de Melo F. PS-35-888-02
Lopez E. PS-25-777-01
Lopez Tamara K. OA-21-442-01
López-Gatell H. PS-24-765-01
López-Luna F. PS-24-765-01
López-Ridaura R. PS-24-765-01
Lopez-Valencia G. PS-17-687-01
Loret de Mola C. EP-09-181-01
Lounnas M. **SOA-17-1173-02**
Loveday M. SOA-05-1049-31, SOA-05-1052-31
Lu P. EP-02-114-31, PS-01-505-31, PS-12-625-31
Lu W. EP-02-114-31, PS-01-505-31, PS-12-625-31
Lu X. OA-10-373-31
Lubamba P. SOA-11-1111-01
Luciana M. PS-12-627-31
Lugo P. OA-05-333-31
Lukanga D. **SOA-05-1047-31**, **PS-04-536-31**
Lungren M. LB-2861
Lungu P. SOA-02-1016-31, SOA-04-1040-31, PS-13-641-31
Lusiba P. PS-07-576-31, PS-38-919-02
Luyen L.T. OA-17-425-01
Lwanga I. EP-15-237-02
Ly C. OA-01-301-31, OA-12-391-01, PS-36-898-02
Ly S. PS-23-747-01
Lyimo J. EP-05-143-31, EP-13-222-02
Lytvynenko N. **PS-33-862-02**, **PS-34-878-02**, **PS-34-879-02**
Lyytikäinen O. PS-25-771-01

M

Ma J. OA-21-449-01
Maama B.L. SOA-06-1062-31
Maama L. OA-21-448-01, OA-28-490-02
Maartens G. OA-26-473-02, OA-26-480-02, SOA-10-1096-01, SOA-10-1101-01, LB-2861
Mabaso M. PS-15-665-01
Mabena M. OA-11-381-31
Mabota-Rapholo P. EP-01-108-31, PS-18-691-01
Mac T.H. SOA-05-1048-31
Macé A. EP-10-190-01
Macek C. **OA-11-383-31**, SOA-17-1170-02
Macgregor H. PS-37-911-02
Machado D. SOA-16-1167-02
Machmud R. **PS-25-774-01**
MacLean E. OA-13-400-01
Maclean E. **SOA-17-1178-02**
MacNeil A. PS-14-646-31
Mactaggart I. EP-09-185-01
Macuacua B. **EP-13-221-02**
Maculuve B. PS-28-806-02, PS-41-949-02
Madan D. SOA-16-1166-02, PS-06-566-31
Madan J. SOA-10-1095-01
Madela K. PS-04-539-31
Madhav P. PS-18-692-01, PS-34-885-02
Madhumali A. LB-3003
Madhvi A. **OA-03-318-31**
Madoyan A. OA-10-377-31
Mafaune P. SOA-11-1109-01
Mafeto M. OA-18-431-01
Mafukidze A. PS-41-953-02
Maganda A. LB-2990
Magassouba A.S. **SOA-11-1110-01**
Magcaba Z.P. EP-10-196-01
Magee M. PS-03-527-31, PS-18-698-01
Maglakelidze M. EP-06-157-01
Maglakelidze N. **EP-06-157-01**, EP-06-158-01
Maglakelidze T. EP-06-157-01
Magomere R. **PS-37-909-02**
Magri R. **EP-03-129-31**
Mahajan R. **PS-28-801-02**
Mahamba V. PS-04-540-31
Mahande M. PS-28-805-02
Maharjan B. PS-06-561-31
Mahasirimongkol S. PS-04-535-31
Mahesh P. EP-02-117-31
Mahiga H. PS-16-678-01
Mahinca I. PS-29-817-02
Mahizhaveni B. EP-10-187-01, PS-29-822-02
Mahomva A. PS-25-773-01
Mahsusriyanti M. SOA-17-1171-02
Mahto R. SOA-03-1022-31
Mahyoub E. OA-23-462-01
Mainga T. SOA-03-1028-31, EP-09-185-01
Majhi G. PS-33-866-02
Majumdar K. OA-23-461-01
Majwala R.K. PS-37-910-02
Makabayi Mugabe R. PS-13-632-31
Makabayi-Mugabe R. **PS-15-666-01**, **PS-38-919-02**
Makaka J. OA-28-490-02
Makasa M. PS-15-661-01, PS-21-729-01, PS-33-869-02
Makgopa G. PS-36-900-02
Makhmudova M. PS-32-857-02
Makola L. PS-15-665-01
Makombe R. EP-08-174-01, PS-23-749-01
Maksud A.K.M. **OA-08-359-31**
Makwambeni V. PS-15-661-01
Malakyan K. PS-33-862-02
Malama K. SOA-04-1040-31
Maldonado N. **SOA-12-1118-01**, PS-19-708-01
Maleche A. PS-20-722-01
Malgas L. OA-12-389-01
Malhotra S. OA-06-342-31, OA-22-454-01
Malhotra V. SOA-16-1157-02
Maliha U.T. PS-35-894-02
Malik A. PS-41-959-02
Malik K. OA-03-316-31
Malik P. OA-27-481-02
Malik S. PS-09-593-31
Malinga L.A. PS-38-926-02
Mallick G. **EP-12-212-02**, **EP-16-253-02**
Mallick G.C. **EP-14-234-02**
Mallik V. OA-09-364-31
Maltha J. PS-07-575-31, PS-32-857-02
Malukutu M. EP-12-207-02
Mambo P. OA-12-395-01, EP-05-141-31
Manabe Y.C. PS-03-525-31, PS-28-803-02

Mandal A. LB-2991
Mandalakas A. SOA-15-1147-02
Mandalakas A.M. SOA-06-1055-31
Mandindi P. EP-01-100-31
Maneshku S. PS-17-685-01
Manga Ze M. EP-11-199-02
Mangeni R. **EP-12-210-02**, **PS-14-651-31**, PS-38-919-02
Mangla A. PS-05-553-31
Mangtani P. OA-18-429-01
Manhica I. PS-23-749-01
Manhiça I. OA-07-352-31, **OA-26-479-02**, SOA-08-1082-31, SOA-08-1084-31, SOA-15-1150-02, SOA-18-1185-02, EP-13-221-02
Mani D. PS-35-893-02
Mani I. PS-40-945-02
Maningi N.E. **PS-38-926-02**, PS-39-933-02
Mankar S. SOA-08-1078-31
Mannan S. OA-01-307-31
Mansjö M. OA-17-423-01
Mansoor H. SOA-13-1127-01
Mansukhani R. OA-18-426-01, OA-18-427-01
Mansyur M. SOA-09-1086-31
Mantell J.E. SOA-06-1062-31, PS-41-953-02
Manu M.S. OA-04-331-31, **SOA-13-1134-01**
Manyama C. SOA-14-1139-01
Manzoor L. SOA-15-1152-02, EP-11-200-02, EP-16-249-02
Mao T.E. SOA-11-1112-01, PS-41-948-02
Maokola W. PS-28-805-02
Mapamba D. SOA-14-1139-01
Maphalala N. PS-38-926-02
Maphumulo T. PS-04-539-31
Mapuranga T. SOA-11-1109-01, PS-15-667-01, PS-25-773-01
Mar Aung K. PS-07-578-31
Marais F. SOA-13-1133-01
Marbaniang I. OA-03-323-31
Marcy O. SOA-17-1173-02, PS-41-948-02, PS-41-952-02
Maria Lapa Montenegro L. PS-35-888-02
Marin D. SOA-05-1054-31
Markovcius L. PS-36-902-02
Marks S. PS-12-624-31
Marks S.M. OA-17-422-01
Maro A. EP-05-143-31, EP-13-222-02
Marokane P. OA-15-415-01
Marouane C. PS-27-792-01, PS-29-815-02
Marquardt T. PS-21-726-01
Martel Chávez B. **PS-01-509-31**
Martin A. OA-26-475-02
Martin M. EP-11-202-02
Martineau A. PS-22-735-01, LB-3037
Martinez L. **SOA-02-1011-31**, **SOA-06-1057-31**, EP-04-137-31, **EP-11-197-02**, PS-26-781-01
Martinez M. EP-03-129-31
Martínez Rodríguez A. **PS-22-742-01**
Martins Araújo R. PS-35-888-02
Martinson N. OA-21-446-01, PS-08-581-31, PS-32-855-02
Martoreli Júnior J.F. EP-08-173-01
Maruri F. PS-29-819-02
Marx F. SOA-01-1009-31
Marx F.M. **OA-02-315-31**
Mary Philip J. OA-27-487-02
Marzouk N. SOA-14-1145-01
Maschilla L. PS-10-604-31
Mase S. OA-06-341-31, OA-14-404-01, OA-27-481-02, SOA-01-1002-31, PS-07-568-31, PS-11-613-31, PS-22-745-01, PS-29-816-02, PS-30-824-02, PS-30-829-02
Maseed B.A. OA-01-305-31, SOA-15-1152-02
Maseko S. **EP-01-100-31**
Mashizha S. SOA-11-1109-01, **PS-25-773-01**
Masini E. OA-10-374-31
Masini T. SOA-10-1104-01
Masiuk L. SOA-05-1044-31
Massou F. PS-06-564-31, PS-07-572-31
Masuku S. EP-11-205-02, PS-03-531-31, **PS-40-947-02**
Mathad J. EP-07-160-01, **EP-07-162-01**, EP-07-163-01, PS-22-739-01
Mathad J.S. EP-07-164-01
Mathebula U. SOA-17-1176-02
Mathew B. OA-09-364-31, **PS-31-846-02**
Mathew J. PS-16-674-01, PS-38-918-02
Mathew M. OA-07-355-31
Mathews M. OA-27-482-02, EP-08-175-01
Mathews M.E. **EP-08-172-01**
Mathias Alves Y. PS-11-622-31
Mathiasen V.D. **PS-37-908-02**
Mathur P. PS-05-548-31
Matji R. SOA-05-1046-31, SOA-06-1063-31, EP-01-108-31, PS-36-900-02, PS-38-923-02
Matshaba M. SOA-06-1055-31
Matta S. PS-34-882-02
Mattoo S.K. PS-12-623-31, PS-41-954-02
Maug A.K.J. PS-04-541-31
Maurya A.K. **PS-34-877-02**
Maurya B. **PS-40-940-02**
Mave V. OA-03-323-31, EP-07-161-01, EP-07-163-01, EP-09-177-01, EP-10-189-01
Mavhunga F. **EP-02-112-31**, EP-15-240-02, PS-18-693-01, PS-24-762-01, PS-27-796-01
Mawarire R. SOA-17-1172-02, PS-05-547-31, PS-08-582-31, PS-08-583-31, PS-20-715-01, PS-27-789-01
Mayanja-Kizza H. PS-28-803-02, LB-2965
Mayaphi L. SOA-05-1046-31
Mbairo N. EP-03-127-31
Mbassa V. EP-11-199-02, **PS-18-689-01**
Mbate Mutemba C. SOA-08-1082-31
Mbeha B. LB-2908
Mbelle N.M. OA-13-396-01, PS-38-926-02
Mbendera K. PS-13-635-31
Mbewe W. PS-13-641-31
Mboizi R. SOA-17-1177-02
Mbumba Ngimbi R. PS-24-762-01
McAlister S. OA-27-485-02
McAllister S. PS-10-607-31, PS-32-860-02
McAnaw S. OA-28-490-02
McBryde E. OA-02-312-31, OA-22-450-01, PS-03-534-31, PS-24-761-01, PS-38-917-02, PS-39-931-02
McCann N. PS-38-921-02
McCartney-Melstad A. EP-16-246-02
McCreesh N. **OA-02-314-31**, OA-18-427-01, **EP-04-138-31**, PS-37-906-02
McGurk D. SOA-16-1158-02
McIlleron H. OA-26-473-02, SOA-10-1096-01, SOA-10-1101-01
McKenna L. **OA-10-379-31**
McMullin K. OA-23-464-01
McNeil E. OA-10-373-31, LB-2922
McQuaid C.F. **SOA-18-1187-02**, PS-34-875-02
Medina-Marino A. SOA-03-1023-31, SOA-13-1135-01, SOA-17-1172-02, PS-05-547-31, PS-08-582-31, PS-08-583-31, PS-20-715-01, **PS-27-789-01**
Meehan C. SOA-14-1138-01
Meehan S.-A. **PS-32-850-02**
Meharwal S.K. EP-12-213-02
Mehiri E. SOA-14-1145-01, PS-06-556-31
Mehra N. PS-16-673-01, **PS-16-676-01**, PS-38-918-02, PS-41-958-02
Mehra S. OA-20-439-01
Mehrotra R. PS-19-707-01
Mehrpouyan M. OA-05-338-31
Mehta K. SOA-09-1092-31
Mehta S. **EP-07-160-01**
Meier N.R. **PS-16-670-01**
Meintjes G. OA-26-480-02
Meka A. **PS-01-504-31**
Melese M. OA-01-305-31, SOA-15-1151-02, SOA-17-1168-02, EP-11-203-02, PS-22-744-01
Melgar M. **SOA-02-1016-31**, **SOA-04-1040-31**
Melikyan A. OA-10-377-31
Melikyan N. OA-21-447-01, OA-28-492-02, PS-18-701-01, PS-34-883-02, PS-34-884-02
Memela S. PS-18-691-01
Mencarini P. SOA-09-1089-31
Mendel C.M. SOA-16-1167-02
Mendelson M. LB-2861
Mendoza M. OA-05-336-31
Mendoza-Ticona A. SOA-06-1056-31
Mendy A. PS-16-668-01
Mendy F. PS-16-668-01
Meneguetti Pieri F. EP-08-169-01
Meneguim A.C. OA-28-489-02
Menon J. PS-41-958-02
Mensah M.N. EP-05-147-31, EP-13-224-02
Menzies D. OA-07-351-31, OA-11-382-31, OA-14-406-01, OA-14-407-01, OA-17-418-01,

OA-17-421-01, OA-17-422-01, SOA-04-1038-31, SOA-04-1041-31, SOA-08-1075-31, SOA-18-1186-02, EP-15-238-02, PS-22-740-01, PS-37-907-02
Menzies N.A. OA-02-315-31
Meredith S. OA-28-496-02, SOA-08-1079-31, SOA-18-1183-02, PS-18-697-01
Meribe S. **SOA-04-1035-31**
Merker M. **OA-06-340-31**
Merle C. OA-15-416-01, EP-07-165-01, EP-15-240-02, PS-18-693-01, PS-30-831-02
Merle C.S.C. PS-21-727-01
Mermin J. OA-14-409-01
Merrifield C. LB-3052
Mesic A. **OA-17-424-01**
Mesman A. OA-05-336-31
Mesman A.W. **PS-16-679-01**
Messadi Akrout F. PS-27-792-01, PS-29-815-02
Meya D. SOA-17-1177-02
Meyanti F. EP-05-146-31
Meyer A.J. SOA-06-1065-31
Meyerson K.A. **SOA-06-1064-31**
Mezochow A. OA-22-457-01
Mfungwe V. PS-33-869-02
Mgbemena C. PS-23-755-01
Mgode G. PS-11-620-31
Mhiri E. PS-27-792-01
Mi F. OA-28-495-02
Michael E. SOA-02-1014-31, SOA-10-1103-01, PS-21-725-01, PS-23-748-01
Michael J. OA-06-346-31
Michael J.S. PS-17-682-01, **PS-35-893-02**
Micheni M. OA-11-384-31
Middelkoop K. EP-04-137-31
Migeto S. PS-04-540-31
Miheret A. LB-2965
Mikponhoue R. PS-40-938-02, PS-40-942-02
Mikusova S. PS-28-806-02
Milenge P. OA-21-443-01
Millard J. OA-06-343-31
Millones Gomez A.K. OA-01-300-31
Minnaard A. PS-17-680-01
Minnies S. PS-09-595-31
Mintop A. EP-11-199-02
Mirarai S. SOA-18-1181-02
Mirtskhulava V. **OA-11-386-31**, PS-24-758-01, PS-24-766-01
Mirzayev F. PS-18-693-01
Mishra B. PS-09-592-31
Mishra B.K. PS-07-568-31
Mishra D.K. **PS-19-712-01**, **PS-31-836-02**, **PS-31-837-02**, **PS-31-848-02**
Mishra G. SOA-11-1113-01, **LB-3021**
Mishra H. OA-03-318-31, OA-14-405-01, OA-18-430-01, **SOA-01-1009-31**
Mishra P. OA-09-370-31, OA-23-461-01
Mishra S. EP-12-212-02, EP-16-253-02
Mishra S.K. EP-10-195-01
Mishyna K. SOA-15-1146-02
Mistry N. OA-03-319-31, PS-10-606-31, PS-30-825-02, LB-2991
Mitchell E.M.H. OA-11-386-31
Miti S. **PS-32-853-02**
Mitnick C. OA-18-432-01, OA-26-478-02, OA-28-490-02, EP-09-182-01
Mitnick C.D. SOA-08-1080-31, PS-01-509-31, LB-2909
Mitrani L. SOA-05-1052-31
Mkhabela T. **OA-07-354-31**
Mkhombo T. SOA-03-1025-31, **EP-13-227-02**, PS-10-600-31, PS-10-601-31, **PS-32-861-02**
Mleoh L. PS-11-620-31
Mlilo N. SOA-09-1090-31, SOA-09-1091-31
Mmanga M. **PS-13-635-31**
Mmolawa L. PS-08-581-31, PS-32-855-02
Mndzebele P. EP-11-205-02
Modak P.K. SOA-14-1140-01, EP-09-186-01, PS-01-507-31, PS-11-609-31, PS-14-650-31, PS-14-653-31, PS-35-894-02
Modi B. SOA-09-1092-31
Modi M. SOA-01-1004-31, SOA-16-1161-02
Modongo C. OA-03-321-31
Moe M.M. PS-14-652-31
Mogale S. PS-40-947-02
Moh R. PS-41-948-02, PS-41-952-02
Mohammed J. EP-01-100-31
Mohanta D. OA-09-364-31
Mohanty P. **OA-08-357-31**
Mohanty S. SOA-11-1108-01, EP-05-142-31, EP-12-212-02, EP-16-253-02, PS-13-633-31, PS-23-756-01, PS-33-867-02
Mohapatra P.R. **PS-09-592-31**
Mohi Uddin M. EP-06-153-01
Mohr E. **OA-17-419-01**, SOA-08-1077-31, **SOA-15-1154-02**, EP-09-184-01
Mohsin S.M.I. SOA-03-1030-31
Moideen K. PS-39-929-02
Moiseeva E. OA-20-435-01
Mokaddas E. SOA-18-1180-02
Mokganyetji T. OA-23-463-01
Mokrousov I. **OA-06-344-31**, PS-24-759-01
Molchanov V. OA-06-344-31
Moleba D. **PS-38-923-02**
Molfino L. SOA-08-1084-31, SOA-18-1185-02, PS-29-817-02
Moll A. SOA-02-1018-31
Mollel E. **PS-28-805-02**
Mom K. SOA-01-1000-31, SOA-11-1112-01
Mon A.S. SOA-14-1142-01, PS-06-563-31
Monamodi G. LB-2908
Monda N. PS-20-722-01
Mondal S. PS-18-694-01
Mongua-Rodríguez N. PS-24-765-01
Monk E. OA-18-426-01
Monk E.J. PS-37-906-02
Montoya R. SOA-16-1164-02, PS-20-718-01, PS-29-813-02, PS-29-814-02, LB-3028
Moodley N. EP-01-105-31
Moodley S. OA-03-317-31
Moon T.D. SOA-15-1153-02
Moore C.M. SOA-16-1158-02
Moore D. OA-18-426-01
Moore D.A.J. EP-04-136-31, EP-04-138-31, PS-37-906-02, PS-37-915-02
Moore M. OA-05-333-31
Mor Z. OA-02-313-31, **PS-01-506-31**, **PS-17-685-01**
Morais K.M. PS-14-649-31
Moran A. OA-18-431-01, PS-36-900-02, PS-41-950-02
Mordovskaya L. PS-06-557-31
Moreira F. SOA-18-1188-02, EP-04-137-31
Moreto L. PS-28-801-02
Moreton J. OA-21-446-01
Morgan G. PS-06-566-31
Morishita F. PS-13-642-31
Moro R. OA-14-404-01, SOA-04-1042-31
Morou S. SOA-18-1184-02
Morris L. OA-11-387-31
Morshed M. SOA-04-1037-31
Morshed M.M. PS-11-609-31
Moses J. PS-37-910-02
Moshabela M. **SOA-05-1049-31**, SOA-05-1052-31
Mosidi T. OA-09-366-31
Motau D. EP-01-105-31
Motley T. SOA-16-1166-02
Mottay L. LB-3062
Motupalli A. PS-20-717-01
Mouzou B. PS-40-942-02
Moyo S. **SOA-03-1025-31**, EP-13-227-02, PS-10-600-31, PS-10-601-31, PS-15-665-01, PS-32-861-02
Mpagama S. OA-04-328-31
Mphahlele M. **OA-18-431-01**, PS-38-923-02
Mpunga J. PS-04-537-31, PS-13-635-31
Mshali K. PS-04-537-31
Msibi F. EP-11-205-02
Msuya S. PS-28-805-02
Mtafya B. SOA-14-1139-01, PS-16-678-01
Mtotha Nindi B. **PS-04-537-31**
Mubiru F. PS-28-803-02
Muchtar M. PS-25-774-01
Muchuro S. PS-37-910-02
Mudaly V. OA-12-389-01, OA-17-419-01, SOA-08-1077-31, SOA-15-1154-02
Mudanang A. SOA-17-1171-02
Muema D. OA-03-320-31
Mugabe F. SOA-09-1087-31
Mugabe R. SOA-05-1051-31
Mugambi L. OA-11-384-31
Mugauri H. **PS-07-574-31**
Mugenyi L. SOA-09-1087-31
Mugoni P. PS-41-950-02
Mugoni P.C. PS-04-539-31
Muhib S. **EP-02-118-31**
Muhiwa A. PS-41-949-02
Muhwezi A. SOA-02-1021-31, EP-15-241-02, PS-32-851-02
Mujeeb Rahman K.K. PS-09-592-31
Mujumbi S. SOA-17-1177-02
Mukami F. **OA-11-384-31**
Mukhamedov K. **EP-11-204-02**
Mukherjee A. **OA-05-335-31**
Mukherjee N. OA-09-364-31
Mukhopadhyay B. **EP-06-156-01**
Mukhopadhyay S. EP-13-221-02
Mukhwana W. PS-37-915-02
Mukiibi J. EP-08-168-01
Mukinda F. SOA-13-1133-01
Mukora R. PS-10-608-31
Mukunda M. SOA-11-1111-01
Mulackal N. EP-16-254-02, PS-20-716-01

Mulder A. OA-06-345-31
Mulder C. PS-23-746-01
Mulders W. OA-15-416-01
Mulenga F. LB-2908
Mulenga J. SOA-04-1040-31, **EP-12-207-02**
Mulenga L. PS-14-645-31
Mullin S. OA-09-364-31
Mullins B. EP-10-196-01
Mulyawan H. EP-06-151-01
Mulyawan I.K.H. PS-19-703-01
Mumtaz R. OA-23-460-01
Mungai M. OA-09-365-31
Munir M.S. EP-12-212-02, EP-16-253-02
Munish V.G. SOA-12-1114-01
Muñiz-Salazar R. **PS-17-687-01**
Munje R. LB-3021
Munkhjargal G. PS-05-550-31
Munsamy V. PS-29-821-02
Munuo G. **EP-05-143-31**, **EP-13-222-02**
Munyangaju I. SOA-15-1150-02, **PS-28-806-02**, PS-41-949-02
Munyinya C. PS-32-853-02
Muquingue H. OA-12-395-01, EP-05-141-31
Mureithi L. SOA-03-1028-31, EP-04-134-31, LB-3050
Murithi S. EP-12-209-02
Murphy-Okpala N. PS-01-504-31
Murray M. OA-02-311-31, OA-05-336-31
Murrill M. EP-07-160-01
Mursida L. EP-12-213-02
Murtala-Ibrahim F. PS-18-690-01, PS-23-755-01
Murton H. PS-06-566-31
Murton H.E. SOA-16-1158-02
Murugan D. OA-06-346-31
Murugesan P. PS-11-616-31
Murukutla N. OA-09-364-31
Murzabekova T. SOA-05-1053-31, PS-11-610-31
Musaazi J. PS-03-525-31
Musau S. **OA-12-390-01**
Musinguzi A. SOA-02-1019-31, **SOA-02-1020-31**, PS-08-584-31
Musuka G. SOA-02-1015-31
Mutaquiha C. OA-07-352-31, OA-26-479-02, **SOA-08-1082-31**, SOA-08-1084-31, SOA-18-1185-02, PS-29-817-02
Mutavhatsindi H. **LB-2965**
Mutayoba B. PS-04-540-31, PS-11-620-31
Mutegi M. OA-11-384-31
Mutemba C. SOA-15-1150-02
Mutengesa E. OA-21-445-01
Mutesasira K. OA-26-474-02, OA-26-476-02, SOA-05-1051-31, EP-12-210-02, PS-10-602-31, PS-14-651-31, PS-33-863-02, PS-33-871-02, PS-36-899-02
Mutlu S.M. EP-14-232-02
Muttamba W. **SOA-09-1087-31**, PS-07-576-31
Mutua J. OA-12-390-01
Muwonge A. EP-15-241-02, PS-17-681-01
Muwonge A.K. SOA-02-1021-31, **PS-32-851-02**
Muyanja S.Z. PS-37-910-02
Muyano S. OA-21-443-01
Muyise R. EP-15-237-02
Muyoyeta M. OA-01-304-31, PS-13-641-31
Muzyamba M. **PS-24-767-01**
Mvusi L. **PS-10-605-31**, PS-34-885-02
Mwakazanga D. SOA-02-1016-31
Mwale C. PS-13-641-31
Mwamba R. PS-28-811-02
Mwambazi E. PS-33-863-02
Mwamsidu C. OA-09-365-31
Mwananyambe N. SOA-02-1016-31
Mwandumba H. OA-20-440-01
Mwanga Amumpaire J. PS-41-948-02
Mwangala E. PS-33-869-02
Mwangala M. PS-33-869-02
Mwansa B. **PS-14-645-31**
Mwanza S. SOA-02-1016-31
Mwanza W. PS-32-853-02
Mwape K. EP-12-207-02
Mwinga A. PS-15-661-01, PS-21-729-01, PS-32-853-02
Myat S. **PS-07-578-31**
Myat Aung M. PS-07-578-31
Myint Z. PS-07-578-31, PS-14-652-31
Myneedu V. OA-13-398-01
Myneedu V.P. SOA-16-1157-02
Myrick N. OA-11-383-31
Myrzaliev B. **SOA-05-1053-31**, PS-11-610-31
Mysore S. OA-25-466-02, OA-25-468-02, SOA-12-1123-01
Mzembaba A. PS-13-634-31

N

Nabawanga H. EP-12-210-02
Nabeta P. SOA-01-1009-31
Nabisere M.R. EP-15-237-02
Nabunje J. SOA-02-1019-31, SOA-02-1020-31, PS-08-584-31
Nacarapa E. **SOA-15-1153-02**, PS-41-949-02
Nachilembo Mulenga L. EP-12-207-02
Nachman S. SOA-06-1062-31
Nafade V. PS-03-526-31
Nag V.L. PS-34-877-02
Nagara Gadde A. OA-09-364-31
Nagaraja S.B. OA-28-489-02
Nagelkerke N. PS-03-534-31
Nagot N. SOA-05-1045-31
Nahid P. LB-3052
Naidoo C. **OA-03-317-31**
Naidoo I. PS-15-665-01
Naidoo J. EP-05-149-31
Naidoo P. EP-02-113-31, PS-41-957-02
Naidoo S. OA-15-415-01
Naik P.R. PS-30-834-02
Naik S. EP-07-160-01, **EP-07-161-01**, EP-07-163-01, EP-07-164-01
Naing T. **PS-14-652-31**
Naing Y.Y. OA-28-492-02
Naing Maung T. PS-07-578-31
Nair D. PS-09-591-31
Nair K. **SOA-10-1102-01**
Nair P. OA-21-447-01
Nair S. OA-04-331-31
Najjingo I. **PS-07-576-31**
Nakanjako D. PS-28-803-02
Nakanwagi F. **PS-10-602-31**
Nakasolya O. EP-08-168-01
Nakaweesa A. SOA-17-1174-02
Nakazzi-Kweyamba M. PS-15-666-01
Naker K. PS-37-915-02
Nakibuuka S. SOA-05-1051-31
Nakiyingi L. **PS-28-803-02**
Nalda R. EP-14-230-02
Nalugwa T. SOA-17-1174-02, PS-07-567-31
Nalunjogi J. PS-07-576-31
Nalutaaya A. EP-08-168-01
Nambiar S. PS-29-823-02
Namutebi J. PS-10-602-31
Namuwenge P. PS-38-919-02
Namwanje Kaweesi H. PS-07-573-31
Nan J. PS-05-551-31, PS-11-611-31
Nana Yakam A. PS-18-689-01
Nantale M. PS-07-567-31
Naraman I. EP-12-209-02
Naranzul D. PS-37-915-02
Narasimhan P.B. PS-01-510-31
Narayanan A. PS-01-510-31
Nardell E. OA-14-405-01, OA-18-430-01, OA-18-432-01, PS-39-928-02
Narendran G. **PS-28-802-02**
Narh C. PS-32-852-02
Narokobi R. PS-26-786-01
Narunsky K. LB-2921
Narvskaya O. PS-24-759-01
Naser A. OA-23-462-01
Nasrin R. PS-09-590-31
Nasseco I. EP-08-174-01
Natalie Nantale M. **SOA-17-1174-02**
Nathavitharana R. OA-09-366-31, **OA-14-405-01**, **OA-18-430-01**, **PS-39-928-02**
Nathella P.K. **EP-10-194-01**
Natrajan M. PS-15-663-01
Nayak S. EP-13-219-02, **PS-13-638-31**
Nazarenko M. OA-20-437-01
Nazari A. OA-09-371-31
Ncube R. SOA-09-1090-31, SOA-09-1091-31, PS-15-667-01
Ndembi N. PS-14-648-31
Ndiaye N. EP-16-252-02
Ndjeka N. OA-17-418-01, **OA-17-421-01**, **SOA-08-1075-31**, **PS-18-692-01**
Ndlovu K. SOA-11-1109-01
Ndlovu S. OA-13-396-01, EP-08-171-01
Ndlumbini C. SOA-05-1046-31
Ndongosieme A. PS-24-762-01
Ndubani P. PS-14-645-31, PS-15-661-01
Ndung'u T. OA-03-320-31
Nduwamahoro E. OA-13-399-01
Nedsuwan S. PS-04-535-31
Negash S. EP-11-203-02, PS-25-770-01
Negi S. PS-29-812-02
Nelson M. EP-16-252-02, PS-33-870-02
Nelson R. SOA-04-1035-31
Nenasheva N. LB-2892
Nepolo E. LB-2965
Nethan S. **PS-19-707-01**
Neto F. J. OA-21-442-01
Neville K. SOA-03-1032-31
Newby R.E. **PS-29-820-02**
Ng A. LB-2861
Ngabonziza J.C.S. **OA-15-416-01**
Ngamvithayapong-Yanai J. PS-04-535-31
Ng'ang'a J. OA-11-384-31
Nga'ng'a J. OA-12-390-01

Ngcelwane N. SOA-03-1023-31, SOA-13-1135-01, PS-08-582-31, PS-08-583-31, PS-27-789-01
Ngidi H. PS-10-605-31
Ngin C. PS-36-898-02
Ngozo J. LB-2957
Ngozo N. EP-01-100-31
Nguyen B.H. PS-22-740-01
Nguyen C. OA-17-425-01
Nguyen C.D.B. SOA-15-1148-02
Nguyen H.B. OA-01-303-31, SOA-03-1031-31, SOA-04-1033-31, SOA-05-1048-31, SOA-11-1106-01, EP-14-233-02, PS-13-640-31, PS-33-873-02
Nguyen H.P. OA-20-434-01
Nguyen H.T. EP-16-251-02, EP-16-251-02, PS-13-640-31
Nguyen L.H. SOA-05-1048-31, SOA-11-1106-01, PS-08-587-31
Nguyen L.P. SOA-04-1033-31, **SOA-05-1045-31**
Nguyen N.T.T. **EP-14-233-02**
Nguyen N.T. **EP-16-251-02**
Nguyen N.V. OA-01-303-31, SOA-03-1031-31, SOA-04-1033-31, SOA-05-1048-31, SOA-11-1106-01, EP-14-233-02, PS-13-640-31, PS-33-873-02
Nguyen T. PS-14-644-31
Nguyen T.A. PS-22-740-01, PS-22-740-01
Nguyen T.K.T. SOA-17-1175-02
Nguyen T.P.C. **SOA-17-1175-02**
Nguyen T.T.T. OA-20-434-01
Nguyen T.V.A. OA-17-425-01
Nguyen V.H. OA-15-413-01, SOA-17-1175-02
Nguyen V.N. OA-15-413-01, PS-22-740-01
Nguyen Binh H. PS-24-758-01, PS-24-766-01
Nguyen Do P. PS-24-758-01, PS-24-766-01
Nguyen Van H. PS-24-758-01, PS-24-766-01
Nguyen Viet H. **PS-24-758-01**, **PS-24-766-01**
Nguyen Viet N. PS-24-758-01, PS-24-766-01
Ngwane N.W. EP-10-196-01
Ngwenya M. SOA-09-1090-31, SOA-09-1091-31
Ngwepe P. SOA-17-1172-02, PS-05-547-31, PS-08-582-31, PS-20-715-01, PS-27-789-01
Nhabanga A. PS-28-806-02
Nham T.T.T. SOA-05-1045-31
Nhangave A.V. PS-41-949-02
Nhat B.S. OA-17-425-01
Nhung N.V. OA-17-425-01, PS-15-656-01, LB-3052
Niang C.T. EP-16-252-02
Niangoran S. PS-41-948-02
Nichols C. PS-14-646-31
Nicol M. SOA-05-1049-31, SOA-05-1052-31, SOA-17-1173-02, PS-38-921-02
Niemann S. OA-06-340-31, SOA-16-1167-02
Niguse S. PS-21-725-01
Nikisi J. EP-12-207-02, PS-15-661-01
Nikolenko N. **PS-16-675-01**
Nikolova Y. PS-39-935-02
Nilgiriwala K. **LB-2991**
Nimer O.-G. PS-18-695-01
Nimmo C. **OA-06-343-31**
Ninan M. **OA-06-346-31**
Ninan M.M. PS-35-893-02
Ning Z. PS-39-936-02
Nirgude A. PS-28-808-02
Nischith K.R. EP-16-247-02
Nishath T. OA-21-446-01
Njeleka F. SOA-14-1139-01, PS-16-678-01
Njeru A. OA-11-384-31
Njie S. PS-15-660-01
Nkambule M. EP-11-205-02
Nkereuwem E. **EP-10-190-01**
Nkhoma W. EP-02-112-31, PS-24-762-01, PS-27-796-01
Nkolo A. OA-26-474-02, OA-26-476-02, SOA-05-1047-31, SOA-05-1051-31, SOA-09-1087-31, EP-02-115-31, EP-08-176-01, EP-12-210-02, PS-04-536-31, PS-04-545-31, PS-10-602-31, PS-13-632-31, PS-14-651-31, PS-15-666-01, PS-33-863-02, PS-33-871-02, PS-36-904-02, PS-38-919-02
Nkundanyirazo P. OA-21-448-01, OA-28-490-02
Noeske J. PS-18-689-01
Noguera-Julian A. LB-2904
Nonyane B. PS-08-581-31
Nonyane B.A.S. PS-32-855-02
Noor Farid M. EP-05-146-31
Nordio F. OA-02-311-31
Norval P. SOA-11-1111-01
Nota M.M. PS-40-939-02
Notobroto H.B. PS-05-546-31
Nsa B. OA-01-306-31, OA-12-394-01, EP-02-116-31, PS-07-569-31, PS-27-794-01
Nsangi B. OA-07-353-31, EP-15-241-02
Nsengiyumva N.P. SOA-04-1041-31
Nsubuga T. PS-04-545-31, PS-33-863-02
Nsubuga Nyombi T. SOA-05-1051-31, PS-36-899-02
Nsubuga-Nyombi T. EP-02-115-31, PS-10-602-31
Ntinginya N.E. OA-04-328-31, SOA-14-1139-01, PS-16-678-01
Ntogwisangu F. EP-05-143-31
Ntudhu S. **PS-33-863-02**
Nuñez Mederos C.S. PS-22-742-01
Nunn A. OA-28-496-02, SOA-08-1079-31, SOA-18-1183-02, PS-18-697-01
Nuno A. OA-05-333-31
Nuno J.L. **OA-05-333-31**
Nurjana *. EP-05-146-31
Nurjannah N. EP-12-213-02
Nuryunawati R. PS-02-520-31
Nwadike P. PS-16-677-01
Nwafor C. PS-01-504-31
Nwagagbo F. EP-13-220-02, PS-07-570-31, PS-13-637-31
Nwana N. OA-14-404-01, SOA-04-1042-31
Nwokoye N. PS-27-794-01
Nyamande K. OA-03-320-31
Nyambati V. OA-12-390-01
Nyamundaya T.H. PS-25-773-01
Nyaruhirira A.U. OA-11-383-31
Nyawo G. OA-03-317-31
Nyimbili S. PS-13-641-31
Nyinoburyo R. **OA-07-353-31**, **SOA-02-1021-31**, EP-15-241-02, PS-32-851-02
Nyirenda A. EP-05-143-31, EP-13-222-02
Nyombi T. EP-08-176-01
Nyunt W.W. SOA-14-1142-01, PS-06-563-31, PS-14-652-31, **PS-29-818-02**
Nzombe P. PS-15-667-01

O

O'Connell C. LB-2861
O'Marr J. EP-11-197-02
O'Reilly A. EP-16-246-02
Obanubi C. EP-13-220-02, PS-07-570-31, PS-13-637-31
Obeng J. OA-14-408-01
Obot V. **PS-23-750-01**
Ocero A. **PS-13-632-31**, PS-15-666-01, **PS-36-904-02**
Ochuko U. SOA-17-1170-02, PS-30-831-02
Ocwero A. PS-33-871-02
Odafe S. PS-28-807-02
Odayar J. PS-37-906-02
Oddie M. OA-23-464-01
O'Donnell M. OA-06-343-31, PS-28-799-02
O'Donnell M.R. PS-18-694-01
Odoun M. PS-06-564-31
Odume B. PS-14-646-31, **PS-28-807-02**
Odusote T. SOA-17-1170-02, EP-13-220-02, PS-07-570-31, PS-13-637-31
Odusote. T. EP-16-246-02
Oduya B. OA-07-353-31
Oeltmann J. LB-3052
Officer K. **PS-17-684-01**
Ofonakara U. **PS-19-704-01**, PS-19-705-01
Ogarkov O. OA-20-435-01, PS-06-557-31
Ogbanufe O. PS-28-807-02
Ogbudebe C. OA-01-302-31, OA-01-306-31, PS-07-569-31
Ogbuji Q. PS-08-585-31
Oghenetejiro A. PS-30-830-02
Ogwu J. PS-14-648-31
O'Halloran J. **SOA-16-1158-02**
Ohikhuai C.A. **PS-18-690-01**, **PS-23-755-01**
Ohler L. LB-2957
Okafor C. PS-18-696-01
Okafor D. PS-18-696-01
Okeji N. SOA-04-1035-31
Okekearu I. EP-12-211-02, **EP-12-215-02**, **EP-13-220-02**, PS-07-570-31, PS-13-637-31
Okello V. **PS-04-543-31**
Okorie O. OA-01-302-31, OA-11-380-31, PS-18-696-01

Okoro C.A. **PS-04-544-31**
Okoye I. SOA-04-1035-31
Okoye M. PS-14-646-31
Oladimeji O. **PS-15-665-01**
Olaniyi B. OA-01-306-31
Olarewaju O. SOA-17-1170-02
Olbrich L. EP-11-198-02
Olea Popelka F. **PS-17-681-01**
Olifant S.L. **PS-39-933-02**
Oliphant R. EP-01-100-31
Oliveira R. SOA-01-1001-31
Oliveira R.D. PS-26-781-01
Olivier D. SOA-03-1023-31, SOA-13-1135-01
Olivier J. SOA-02-1017-31
Olomi W. PS-16-678-01
Olorunju S. PS-40-947-02
Olotu R. PS-04-540-31
Olukolade R. PS-08-585-31
Olusoji D. PS-30-831-02
Olusola-Faleye B. EP-13-220-02, **PS-07-570-31**, **PS-13-637-31**
Olweny F. PS-07-576-31
Omale N. **OA-10-374-31**
O'Marr J. **PS-26-779-01**
Omesa E. OA-10-374-31
Omid A. SOA-11-1107-01
Omondi E. OA-09-365-31
Omoniyi A. SOA-17-1170-02
Omoniyi A.F. PS-04-544-31
Omosebi O. SOA-17-1170-02
Omoz-Oarhe A. SOA-06-1056-31
Ong S. OA-01-301-31, OA-12-391-01
Ongole J.J. PS-18-691-01
Oniani E. SOA-03-1024-31
Onoh M. OA-12-394-01
Onotu D. PS-28-807-02
Onuoha M. **OA-12-393-01**, PS-16-677-01, PS-30-830-02
Onuoha O. **OA-04-329-31**
Onyedinachi O. PS-23-750-01
Onyeje E. EP-12-211-02, EP-12-215-02
Onyemaechi S. SOA-17-1170-02, PS-30-831-02
Onyoh E. PS-32-858-02
Oo N.L. SOA-15-1149-02
Oraegbu A. OA-17-424-01
Ordóñez Monak I.A. PS-03-529-31
Ordway D. PS-38-920-02
Orivis E. OA-18-432-01
Ork C. OA-12-391-01, **PS-36-898-02**
Orkis J. EP-16-246-02
Orne-Gliemann J. **PS-41-952-02**
Ortega C. PS-06-566-31
Ortuno-Gutierrez N. PS-01-502-31, **PS-13-634-31**
Oruganti G. OA-11-385-31
Osakwe C. **PS-18-696-01**
Osho A. PS-08-585-31
Osih R. EP-05-147-31, EP-13-224-02
Osman M. **EP-02-113-31**, PS-32-850-02, **PS-41-957-02**
Osmanova N. **SOA-08-1083-31**
Osorio C. SOA-14-1144-01
Osorio D. SOA-15-1153-02
Osorio D.V. **PS-41-949-02**
Osso E. OA-26-478-02, PS-26-780-01
Ostrander E. EP-03-129-31
Oswal V. OA-03-319-31, SOA-08-1078-31
Otero L. SOA-18-1189-02, EP-09-181-01, PS-20-718-01
Ottenhoff T. PS-16-670-01
Otuba J.P. **OA-26-474-02**, **OA-26-476-02**
Ouattara E. PS-41-952-02
Ouma P.C. PS-06-560-31
Oun S. EP-14-231-02
Ovelar P. PS-03-530-31
Ovung S. PS-10-598-31, PS-25-775-01
Owarwo N. EP-15-237-02
Owolabi O.A. **PS-15-660-01**
Oxlade O. OA-07-351-31, OA-11-382-31, OA-14-407-01, **OA-14-408-01**, SOA-04-1041-31, EP-15-238-02
Oxlade O.A. PS-22-740-01
Oxlade O.O. SOA-04-1038-31
Oyewusi L. OA-21-448-01, OA-28-490-02
Oyuku D. SOA-17-1174-02, **PS-07-567-31**
Ozkan S. SOA-02-1012-31, **SOA-03-1027-31**, **EP-14-232-02**, **PS-15-657-01**
Ozkara S. **SOA-02-1012-31**, EP-14-232-02, PS-15-657-01
Oztomurcuk D. SOA-02-1012-31

P

P Gujral L. **PS-01-502-31**
P Menon V. OA-27-487-02
P Prabhu B. OA-27-487-02
Padayatchi N. OA-11-382-31, PS-18-694-01, PS-28-799-02
Padmini T.J. EP-05-144-31, PS-34-882-02
Pai M. OA-06-347-31, OA-13-400-01, SOA-03-1025-31, SOA-17-1178-02, EP-13-227-02, PS-03-524-31, PS-03-526-31, PS-10-597-31, PS-10-600-31, PS-10-601-31, PS-32-861-02
Pak S. OA-11-386-31, SOA-08-1083-31
Palaniappan N. PS-28-802-02
Palanivel C. SOA-09-1092-31
Palaniyandi K. **PS-17-683-01**, PS-39-934-02
Pallewatte N. PS-30-832-02
Palmer M. SOA-06-1058-31
Palmer Z. OA-03-317-31, SOA-01-1009-31, SOA-01-1010-31
Palmieri F. SOA-09-1089-31
Palparan A. PS-38-924-02
Paluru V. EP-16-245-02
Pambudi I. EP-05-146-31
Pan S.-W. PS-01-511-31
Pan Y. OA-07-348-31
Panda A. OA-09-370-31, OA-23-461-01
Panda B. EP-12-212-02, EP-16-253-02
Panda S. PS-06-562-31
Panda T. PS-27-794-01
Pande T. **PS-10-597-31**
Pandey A. **SOA-12-1122-01**, PS-19-712-01, PS-31-836-02, PS-31-837-02, PS-31-848-02
Pandey A.K. SOA-11-1108-01, EP-05-142-31, PS-13-633-31
Pandey K. PS-28-801-02
Pandey V. OA-03-319-31
Pandit R.N. PS-33-866-02
Pandurangan S. **SOA-11-1108-01**, **EP-05-142-31**, **PS-13-633-31**, PS-23-756-01, PS-33-867-02
Panibatla V. **PS-01-501-31**
Panigrahi M.K. PS-09-592-31
Panigrahi S. **PS-21-733-01**, **PS-35-891-02**
Pant M. **OA-09-364-31**
Pant R. OA-11-385-31
Panteleev A. EP-10-193-01
Papewar A. LB-2991
Papworth D. EP-12-213-02
Paradkar M. EP-09-177-01
Parija D. PS-33-872-02
Park Y. **SOA-10-1100-01**
Parmar M. OA-06-341-31, SOA-01-1002-31, PS-07-568-31, PS-30-829-02
Parpieva N. OA-26-477-02, EP-11-204-02
Parra N. **OA-25-470-02**
Parwati G. EP-05-146-31
Pasangka M. SOA-17-1171-02
Pascoe S. SOA-13-1125-01
Pasipanodya J. OA-03-321-31
Pasupuleti D. SOA-13-1127-01
Patel B. **SOA-09-1092-31**
Patel D. SOA-03-1032-31
Patel L. PS-05-551-31, PS-11-611-31
Patel S.M. **OA-04-330-31**
Patel Y. EP-08-175-01
Pathak R. **PS-07-568-31**
Pathri R. **SOA-01-1005-31**
Pati S. PS-09-589-31
Patil N. EP-07-160-01, EP-07-162-01, EP-07-163-01, EP-07-164-01, PS-22-739-01
Patil S. SOA-13-1131-01, EP-04-137-31
Patkar N. EP-11-197-02
Patnaik B. EP-12-212-02, EP-16-253-02
Patterson B. **PS-22-735-01**
Patwary S.H. **EP-06-153-01**
Paul K.K. SOA-04-1039-31, SOA-14-1140-01, PS-01-503-31, PS-09-590-31
Pavlov N. PS-06-557-31
Pazhanivel P. PS-10-598-31
Peacock S. PS-17-683-01
Pearson M. SOA-02-1015-31
Pearson M.L. PS-15-658-01
Pedrazzoli D. SOA-09-1090-31, SOA-09-1091-31
Pekon S. PS-26-786-01
Pelissari D.M. EP-16-248-02
Pelowa D. OA-15-417-01, PS-24-761-01, PS-38-917-02, PS-39-931-02
Pelzer P.T. **PS-32-857-02**
Peng Y.T. SOA-08-1076-31
Peravali Carel J. SOA-01-1002-31, PS-22-745-01, PS-30-824-02
Perea S. EP-09-182-01, **PS-26-780-01**
Peredelskaya M. **LB-2892**
Pereira C. PS-06-562-31
Perera C. **OA-08-358-31**, EP-03-120-31, **PS-31-838-02**
Perera C.S. SOA-12-1121-01
Perera K.M.N. SOA-12-1121-01
Perera M. OA-08-358-31, SOA-12-1119-01, PS-31-838-02
Perera M.N. EP-03-120-31
Perera S. PS-36-905-02
Perez F. SOA-05-1054-31
Periyannan D. **SOA-12-1119-01**

Periyasamy M. SOA-13-1132-01, PS-10-598-31, **PS-25-775-01**
Perrin C. **SOA-10-1104-01**
Perumpil M. EP-16-254-02
Peters S. PS-14-648-31
Peterson M. **PS-14-646-31**
Petrenko V. SOA-15-1146-02, EP-04-132-31
Peu D. PS-40-947-02
Pham H.V. PS-23-754-01
Pham L.V. PS-13-640-31
Pham T.H. SOA-17-1175-02
Pham T.V. PS-23-754-01
Phan H. LB-3052
Phares C. LB-3052
Phelan J.E. SOA-18-1181-02
Phillips P. OA-28-496-02, **SOA-08-1079-31**, SOA-18-1183-02, LB-2921
Phiri D. EP-12-207-02
Phiri M. OA-12-388-01
Phokojoe M. SOA-13-1125-01
Phu P. PS-24-764-01
Phulke S. PS-41-958-02
Phuong H.L. LB-3052
Phutane M. PS-01-501-31
Phutke G. **SOA-13-1131-01**
Phyo A.P. **EP-01-106-31**
Phyo N.W. **EP-16-255-02**
Pickard R. EP-16-244-02
Picoy J. PS-20-718-01
Pieri F.M. OA-18-433-01, PS-37-914-02
Pillay R. **EP-05-149-31**
Pillay S. SOA-16-1163-02, EP-05-149-31, **PS-06-559-31**
Pillay Y. SOA-13-1125-01, PS-34-885-02
Pinto I. PS-27-795-01
Pinto I.C. EP-08-173-01, PS-03-528-31
Pires Machai M.J. OA-26-479-02, **PS-23-753-01**
Pirmahmadzoda B. PS-41-956-02
Pittalis S. SOA-09-1089-31
Piubello A. SOA-18-1184-02
Podewils L. SOA-02-1016-31, SOA-04-1040-31
Pogrebna M. PS-34-878-02, PS-34-879-02
Polana M. **OA-12-395-01**, **EP-05-141-31**
Polev D. OA-06-344-31
Pollock N. OA-05-336-31
Ponce-de-León A. PS-24-765-01
Poojar B. PS-30-834-02
Poole N. PS-36-903-02
Pooran A. LB-3062
Pooranagangadevi N. EP-15-242-02
Poovalingam R. PS-33-867-02
Popoola A. PS-11-619-31
Post E. EP-05-146-31
Poudel A. **PS-06-561-31**
Pouseele H. SOA-16-1160-02
Prabhakara **OA-25-467-02**
Pradhan N. EP-07-163-01, **EP-10-189-01**
Prakash A.K. PS-05-553-31
Prakash Babu S. **PS-01-510-31**
Prasad B.M. PS-23-756-01
Prasad C. OA-25-466-02, OA-25-468-02, SOA-12-1123-01
Prasad Tripathy S. PS-29-822-02
Prasanna R. EP-16-247-02, PS-30-826-02
Prast-Nielsen S. PS-39-936-02
Pravednaja E. SOA-08-1083-31
Priya S. PS-29-822-02
Priyono B. **PS-02-520-31**
Probandari A. PS-05-546-31
Puchalski Ritchie L.M. OA-23-464-01
Puma Abarca D.V. **OA-01-300-31**, **OA-09-369-31**
Pungrassami P. PS-04-535-31
Puntambekar N. SOA-12-1124-01
Puri V. EP-13-225-02
Purohit G. PS-09-592-31
Purty A.J. EP-16-245-02
Pushkina T. OA-11-386-31
Puspawati N. **PS-31-839-02**
Puta C. OA-05-333-31
Putha P. EP-14-230-02
Putri F.A. **PS-12-627-31**
Puyen Z. **SOA-14-1143-01**, **SOA-14-1144-01**, **SOA-18-1179-02**, EP-10-188-01, **PS-06-558-31**
Pym A. OA-06-343-31, PS-29-821-02

Q

Qader G. SOA-15-1152-02, EP-11-200-02
Qader G.Q. OA-01-305-31, SOA-15-1151-02, EP-16-249-02, **PS-14-654-31**, PS-22-744-01
Qawiy I. OA-22-456-01, **PS-11-611-31**
Qayyum M.S. **OA-23-462-01**
Qin Z.Z. OA-07-352-31, OA-26-479-02, SOA-08-1082-31
Quach K.U. SOA-17-1175-02
Quevedo Cruz L. **PS-20-718-01**
Quinto E. EP-08-176-01
Qureshi F. **SOA-11-1107-01**

R

R.Andrews J. EP-04-137-31
Rachow A. OA-04-326-31
Rade K. OA-27-481-02, EP-13-217-02, PS-07-568-31, PS-30-824-02, PS-30-829-02
Radin E. SOA-02-1015-31
Radut S. OA-09-368-31
Raghavendra R. PS-33-865-02
Ragonnet R. OA-02-312-31, **PS-03-534-31**
Rahman A. PS-35-894-02
Rahman H. OA-08-359-31
Rahman M.B. EP-06-153-01
Rahman M.M. PS-41-955-02, PS-41-955-02
Rahman M.T. **PS-12-626-31**, **PS-41-955-02**
Rahman S. PS-25-776-01
Rahman S.M.M. PS-09-590-31, PS-35-894-02
Rai B. SOA-11-1105-01, SOA-11-1113-01, EP-05-140-31, PS-33-866-02
Rai S. PS-30-825-02
Raibole L. **PS-20-716-01**
Raihan G. EP-05-145-31, PS-27-790-01
Raihan S.M.G. EP-13-223-02
Raikwar V.K. SOA-14-1141-01, PS-06-555-31
Raj A. SOA-13-1134-01, **PS-40-946-02**
Raj D. PS-17-683-01
Raj S. EP-13-218-02, EP-13-226-02
Raj T. **EP-14-230-02**
Rajabzoda A. PS-32-857-02, PS-41-956-02
Rajan J. PS-39-930-02
Rajasuriya M. OA-08-358-31, SOA-12-1119-01, SOA-12-1121-01, EP-03-120-31, PS-31-838-02
Rajendran A. PS-17-683-01
Rajesh M.K. EP-10-187-01
Rajpurkar P. LB-2861
Rakesh P. PS-20-713-01
Rakesh P.S. OA-27-487-02, SOA-13-1134-01
Ramachandaran G. PS-29-822-02
Ramachandraiah H. PS-38-922-02
Ramachandran A. PS-30-832-02
Ramachandran G. SOA-13-1132-01, PS-11-616-31
Ramachandran R. OA-06-341-31, OA-10-378-31, SOA-01-1002-31, EP-08-172-01, PS-11-613-31, PS-12-623-31, PS-29-816-02, PS-30-829-02, PS-40-945-02
Raman S. EP-12-208-02
Ramanlal N. SOA-15-1150-02
Ramarumo E. PS-23-752-01
Ramawela N. PS-10-605-31
Ramchandran R. OA-27-481-02, PS-07-568-31
Ramiro I. OA-07-352-31, PS-41-949-02
Ramos E. LB-3028
Ramos E.S. SOA-16-1164-02, PS-29-813-02, PS-29-814-02, PS-29-820-02
Ramos J.M. SOA-15-1153-02
Ramya N. PS-28-808-02
Ranasinghe D. LB-3003
Randall P. LB-3062
Rangaka M. EP-07-159-01
Rangan S. PS-30-825-02
Ranganathan R. **OA-27-483-02**, OA-27-484-02
Rangaraju C. PS-28-808-02
Rangasamy R. OA-27-484-02
Rangaswamy R. OA-27-483-02
Rangisetty S. PS-41-954-02
Rani S. EP-16-245-02
Rao R. OA-07-355-31, OA-10-378-31, OA-27-482-02, EP-08-172-01, EP-13-217-02, PS-07-568-31, PS-11-613-31, PS-15-663-01, PS-22-745-01
Rao S. SOA-13-1127-01
Rao S.A. PS-22-741-01
Rao V.G. EP-16-245-02
Rapang M. SOA-17-1171-02
Rashidi M.K. **OA-01-305-31**, SOA-15-1151-02, SOA-15-1152-02, **EP-11-200-02**, EP-16-249-02, PS-14-654-31, PS-22-744-01
Rasigade J.-P. OA-06-340-31
Rath S. PS-09-592-31
Rathnayake N. PS-02-517-31, **PS-36-905-02**, LB-3003
Rautenbach C. SOA-06-1058-31, PS-09-595-31
Ravi S. OA-28-489-02, SOA-08-1078-31
Ravimohan S. OA-03-321-31

Ravindran R. **OA-03-316-31**, OA-05-338-31, PS-39-930-02
Ray P. SOA-16-1161-02
Ray Chaudhury M. EP-08-172-01
Rea E. OA-23-464-01
Reaz Hossain K. OA-08-359-31
Rebecca P. **PS-04-542-31**
Reddy B. EP-14-230-02
Reddy K. **PS-38-921-02**
Reddy M.M. **PS-28-808-02**
Reddy vc K. OA-15-412-01
Reeve B. **PS-09-595-31**
Reeve B.W.P. SOA-01-1009-31, **SOA-01-1010-31**
Refaya A.K. PS-17-683-01
Rêgo de Queiroz A.A. EP-08-169-01
Rehman A. EP-13-226-02
Reid M. **OA-10-372-31**, **PS-03-532-31**
Reid S. SOA-02-1017-31
Reja S. SOA-03-1030-31, EP-13-223-02
Reji P. PS-10-603-31, PS-23-757-01
Rengarajan J. OA-20-439-01
Reshu B. EP-11-203-02
Reuter A. OA-17-419-01, **SOA-08-1077-31**, SOA-15-1154-02, **EP-09-184-01**
Reynales L.M. PS-31-841-02
Reza S. EP-05-145-31, PS-27-790-01, PS-28-804-02
Rice M. PS-36-897-02, PS-36-903-02
Rich M. EP-09-182-01, PS-26-780-01, LB-2909
Richards A.S. **OA-22-451-01**, PS-34-875-02
Richardus J.H. SOA-09-1086-31
Ricks S. **PS-39-937-02**
Riese S. PS-38-919-02
Rifat I.A. **SOA-03-1030-31**, EP-05-145-31
Rifat M. PS-04-541-31
Rigouts L. OA-13-399-01, OA-15-416-01, PS-06-564-31, PS-29-817-02
Rios C. PS-03-530-31
Rios J. PS-01-508-31
Ritz N. PS-16-670-01
Rivière E. SOA-14-1138-01
Robart S. EP-16-254-02
Robert J. OA-17-420-01
Robert S. PS-20-716-01
Roberts C. PS-37-915-02
Roberts G. OA-10-372-31, PS-03-532-31
Robsky K. **EP-08-168-01**
Rodrigo T. PS-13-636-31
Rodrigue M. SOA-16-1160-02
Rodrigues A.M.U. PS-03-528-31
Rodrigues C. SOA-18-1182-02, LB-2991
Rodrigues D. SOA-02-1013-31
Rodrigues D.S. OA-17-422-01
Rodriguez C.A. **SOA-08-1080-31**, PS-16-679-01
Rodriguez E. EP-09-184-01
Rodriguez J.D. OA-13-396-01
Rodriguez S. SOA-18-1189-02
Rodwell T. SOA-16-1159-02
Rodwell T.C. OA-15-411-01
Rogers J. SOA-02-1015-31
Roggi A. OA-14-403-01, PS-18-695-01
Rolim Scholze A. EP-08-169-01
Romanowski K. **SOA-04-1037-31**, PS-03-523-31
Romero R. OA-17-421-01
Romero-Sandoval N. **EP-11-202-02**
Rondan P.L. PS-29-820-02
Rosaline Nirmal C. **PS-29-822-02**
Rose C. SOA-04-1037-31
Rosu L. **SOA-10-1095-01**
Roushan M. PS-02-517-31
Rowland D. PS-06-562-31
Roy G. OA-05-334-31, PS-01-510-31
Roy T. PS-12-626-31, PS-25-776-01, PS-41-955-02
Ruan Q. **SOA-04-1034-31**, PS-22-736-01, PS-35-886-02
Rubio G. OA-05-333-31
Rucsineanu O. **PS-05-550-31**
Rucsineanu P. PS-05-550-31
Ruda C. **PS-23-757-01**
Ruhinda N. SOA-02-1021-31, **EP-15-241-02**, PS-32-851-02
Ruhl L. **OA-23-458-01**, **PS-20-723-01**
Ruiz P. EP-09-180-01, EP-09-181-01
Rupali P. OA-06-346-31, PS-35-893-02
Rupasinghe P. PS-29-817-02
Ruperez M. **LB-3050**
Ruperz M. EP-04-134-31
Rusch B. SOA-08-1084-31, SOA-18-1185-02
Rusen I.D. SOA-08-1079-31
Rush C. PS-24-761-01, **PS-38-917-02**, **PS-39-931-02**
Ruslami R. OA-14-406-01, OA-14-408-01, **EP-15-238-02**
Rusu P. OA-09-368-31
Ruswa N. PS-20-721-01, PS-27-797-01
Rutakingirwa M. OA-21-445-01
Ruvwa L. SOA-05-1047-31, PS-04-536-31
Ruwais M. PS-36-905-02
Rybak N. **SOA-06-1059-31**, **SOA-15-1146-02**
Rybak N.R. EP-04-132-31

S

S A. EP-16-245-02
S R. EP-16-245-02
S Majumdar S. EP-01-106-31
Saba S. SOA-14-1140-01, PS-01-503-31
Sabi I. SOA-14-1139-01, **PS-16-678-01**
Sacchi F. SOA-18-1188-02
Sachdeva K. OA-06-341-31
Sachdeva K.S. OA-10-378-31, OA-11-385-31, OA-15-412-01, OA-27-482-02, SOA-01-1002-31, SOA-10-1102-01, EP-08-172-01, EP-08-175-01, EP-13-217-02, PS-12-623-31, PS-22-745-01, PS-30-824-02, OA-07-355-31, EP-12-208-02
Sadanandan R. PS-20-713-01
Sadat S.M. SOA-11-1107-01
Saenz de Miera B. **PS-31-841-02**
Saeze C. OA-12-395-01, EP-05-141-31
Safi D. SOA-15-1152-02, EP-11-200-02
Safi D.A. PS-14-654-31
Safira N. **LB-2922**
Sagili K. **PS-15-664-01**
Sagili K.D. PS-11-621-31
Sah M.K. PS-33-866-02
Saha B. PS-30-834-02
Sahai K.N. PS-07-568-31
Sahay K.N. OA-23-460-01
Sahay R. EP-13-219-02
Sahoo S. PS-09-592-31
Sahrin M. PS-35-894-02
Sahu A. **PS-23-756-01**
Sahu H.S. EP-16-253-02
Saidy B. EP-10-190-01
Saimen A. **EP-01-105-31**
Saini A. PS-16-673-01
Saini S. OA-05-335-31
Saipova M. EP-11-204-02
Sakala E. OA-12-388-01
Sakharova G. LB-2892
Saki N. PS-25-776-01
Saki N.A. SOA-14-1140-01, **PS-11-609-31**
Salagay O. LB-2892
Salama N. PS-12-627-31
Salgame P. OA-05-334-31, PS-01-510-31
Salhotra V.S. SOA-10-1102-01
Salim M.A.H. EP-09-186-01, PS-14-653-31
Salindri A. EP-01-109-31
Salomon A. SOA-03-1025-31, EP-13-227-02, **PS-10-600-31**, **PS-10-601-31**, **PS-28-810-02**, PS-32-861-02
Salomon J.A. OA-02-315-31
Salvatore P. EP-08-168-01
Salvi S. OA-03-323-31
Samadi M.N. **SOA-15-1151-02**, SOA-15-1152-02, EP-11-200-02, **PS-22-744-01**
Sambarey P. EP-07-161-01
Samieva N. PS-11-614-31
Sammann A. SOA-03-1032-31
Sampson A. OA-14-405-01, OA-18-430-01
Samson K. EP-15-240-02, PS-18-693-01
Samsuri M. SOA-17-1171-02
Samudio T. PS-03-530-31
Samuels T. OA-21-445-01
San C.C. SOA-15-1149-02
Sanabria O.M. PS-01-512-31
Sanabria Salazar O. OA-21-442-01
Sanaie A. SOA-11-1107-01
Sanathya K. PS-09-591-31
Sánchez Garavito E. PS-01-509-31
Sánchez-Pérez H. EP-11-202-02
Sanders J. SOA-15-1147-02
Sandoval R. OA-25-470-02
Sandoval-Azuara S.E. PS-17-687-01
Sandy C. SOA-02-1015-31, **SOA-09-1090-31**, **SOA-09-1091-31**, SOA-11-1109-01, PS-15-667-01, PS-25-773-01
Sane M. EP-09-177-01
Sangle S. OA-03-323-31
Sani U. EP-02-116-31
Sankhyan N. PS-16-676-01
Sannino L. **PS-21-726-01**
Sanoussi C.N. **PS-06-564-31**
Santin M. LB-2904
Santos A. SOA-01-1001-31
Santos A.D.S. PS-26-781-01
Santos D. EP-10-188-01
Santos D.T. OA-18-433-01, EP-08-173-01, PS-37-914-02
Santos F.L.d. PS-03-533-31
Santos P. SOA-01-1001-31
Santos Lazaro D. SOA-14-1143-01, SOA-14-1144-01, PS-06-558-31

Santos Lázaro D. SOA-18-1179-02
Santos-Filho E.T. PS-05-550-31
Saoyo T. PS-20-722-01
Sapiyeva Z. OA-11-386-31
Saraf S. **OA-08-360-31**, **SOA-12-1114-01**, **SOA-12-1124-01**, **EP-06-154-01**
Saranya G. PS-35-887-02
Saraswathy J. EP-15-242-02, **PS-15-663-01**
Sargsyants N. PS-18-701-01
Sargsynats N. OA-21-447-01
Sarin R. OA-13-398-01, SOA-16-1157-02, PS-15-656-01
Sarin S. OA-15-412-01, PS-33-872-02
Saritha R. PS-20-713-01
Sarkar S. OA-05-334-31, PS-01-510-31
Sarker S. SOA-04-1039-31
Sarmiento P. OA-12-392-01
Sasya H. EP-05-143-31
Sathar F. EP-14-228-02
Sathoff E. OA-04-326-31
Satpathy N. PS-02-521-31
Satyanarayana S. SOA-15-1149-02, PS-03-526-31, PS-15-655-01, PS-15-664-01
Saunders M. PS-20-718-01
Saunders M.J. **LB-3028**
Savilov E. PS-06-557-31
Savy M. PS-21-727-01
Saw S. EP-01-106-31
Sawadogo L.T. PS-09-594-31
Sawadogo M. **PS-18-695-01**
Saxena A. **PS-40-943-02**
Saxena D. EP-01-103-31
Sayedi S.M. OA-01-305-31, **SOA-15-1152-02**, EP-11-200-02, EP-16-249-02
Sayfullo M. PS-41-956-02
Sayyad K. PS-01-501-31
Sayyed A.A. EP-02-117-31
Schaaf H.S. **SOA-06-1058-31**, SOA-15-1155-02
Schaap A. OA-12-388-01, EP-04-134-31, PS-15-661-01, PS-32-853-02
Scheibe A. OA-11-381-31
Schiff A. OA-03-320-31
Schimmel H. PS-25-771-01
Schmid L. SOA-16-1158-02
Schoeman I. OA-09-366-31
Scholten J. OA-01-306-31, PS-07-575-31, PS-27-794-01
Scholten J.N. PS-07-569-31
Scholze A.R. EP-08-173-01, PS-37-914-02
Schön T. OA-17-423-01, OA-28-493-02, SOA-10-1098-01, PS-37-908-02
Schubert P. PS-09-595-31
Schumacher S. OA-13-400-01, PS-39-937-02
Schumacher S.G. SOA-01-1009-31
Schwalb A. EP-09-180-01, **PS-29-819-02**
Schwartzman K. SOA-04-1041-31
Schwoebel V. **OA-14-403-01**
Scott L. OA-15-415-01, **EP-08-171-01**
Scott N. OA-02-312-31
Scott P. PS-37-906-02
Scriba T. OA-14-410-01
Seas C. SOA-18-1189-02
Sebagadis H. SOA-02-1014-31, PS-23-748-01
Seddiq K. EP-16-249-02
Seddiq M.K. SOA-11-1107-01, SOA-15-1151-02, EP-02-118-31, PS-14-654-31, PS-22-744-01
Seddon J. PS-41-957-02
Seddon J.A. EP-02-113-31, PS-41-956-02
Sediq K. OA-01-305-31
Seed P.C. OA-04-330-31
Seepamore B. OA-11-382-31, **PS-18-694-01**, **PS-28-799-02**
Segal L. OA-03-317-31
Seid J. SOA-17-1168-02
Seilmaier M. EP-11-198-02
Sekaggya-Wiltshire C. EP-15-237-02
Sekirov I. SOA-04-1037-31
Sekyere J.O. PS-38-926-02
Selamolela M.M. PS-39-933-02
Selv K. PS-11-621-31
Selvarjan M. OA-25-467-02
Semeere A. EP-15-236-02
Semitala F. PS-39-930-02
Semitala F.C. **SOA-02-1019-31**, SOA-02-1020-31, PS-08-584-31
Sen D. SOA-03-1022-31, PS-14-647-31
Sen P. PS-10-597-31
Sen S. PS-05-548-31
Senarathne K.D. PS-36-905-02
Senguttuvan T. PS-28-802-02
Senko J. PS-34-878-02, PS-34-879-02
Sequera G. PS-03-530-31
Serobyan A. OA-10-377-31, OA-28-492-02
Sessou L. **EP-03-126-31**
Set R. PS-27-791-01
Sethi S. PS-16-673-01, PS-16-674-01, PS-16-676-01, **PS-38-918-02**
Setkina S. OA-28-494-02
Setlhare V. LB-2908
Setswe G. EP-01-105-31
Seung K. OA-28-490-02, EP-09-182-01, PS-26-780-01, LB-2909
Sevostianova T. PS-16-675-01
Sewwandi N. **LB-3003**
Seyoum B. PS-37-912-02
Shafie A. OA-07-355-31
Shah A. OA-23-461-01, EP-08-170-01
Shah D. **SOA-08-1078-31**, SOA-13-1132-01, **EP-13-225-02**, PS-11-616-31, **PS-27-791-01**, **PS-30-827-02**
Shah J. PS-29-823-02
Shah K. EP-05-140-31
Shah N.S. SOA-06-1056-31, PS-14-646-31
Shah S. EP-02-111-31, EP-04-131-31, PS-10-606-31, PS-16-676-01, PS-30-825-02, PS-30-825-02, LB-2991
Shah S.S. OA-04-330-31
Shah T. **OA-15-412-01**
Shah V. SOA-12-1114-01
Shah Y. PS-06-561-31
Shaikh A. OA-03-319-31
Shainaba A.S. EP-10-187-01
Shalini E. OA-06-346-31
Shanaube K. OA-12-388-01, SOA-03-1028-31, EP-04-134-31, EP-09-185-01, LB-3050
Shani D. OA-20-440-01
Shankar R. SOA-03-1022-31
Shanmugam P. PS-30-834-02
Shanmugam S. PS-17-683-01
Shanta A. PS-07-577-31
Shao L. SOA-04-1034-31, PS-22-736-01
Shapiro A.E. **EP-10-196-01**
Sharipov B. PS-32-857-02
Sharkas G. OA-23-462-01
Sharma A. OA-23-461-01, SOA-01-1004-31, SOA-16-1161-02
Sharma B. PS-19-710-01
Sharma D. OA-09-370-31
Sharma K. **SOA-01-1004-31**, PS-09-593-31, PS-16-676-01
Sharma L.K. SOA-16-1165-02
Sharma M. SOA-01-1004-31, **SOA-14-1137-01**, **PS-09-593-31**
Sharma N. SOA-16-1165-02, EP-05-144-31, EP-10-195-01, PS-11-621-31, PS-34-882-02
Sharma P. **SOA-16-1165-02**
Sharma R. SOA-03-1022-31, EP-13-226-02, PS-29-816-02, **PS-40-945-02**
Sharma R.S. OA-23-460-01
Sharma S. SOA-10-1102-01, EP-05-144-31, PS-19-707-01
Sharma S.K. PS-40-945-02
Sharma T.K. **EP-10-195-01**
Sharma V. **PS-30-834-02**
Sharna K. **SOA-16-1161-02**
Sharon L. PS-29-823-02
Shastri J. PS-27-791-01
Shastri S. PS-28-808-02
Shaweno D. **OA-22-450-01**
Shayo E. OA-04-328-31
Shebl F. PS-38-921-02
Shedrawy J. **PS-08-588-31**, PS-12-631-31
Sheffer R. PS-17-685-01
Shenoi S. **SOA-02-1018-31**
Shenoy S. PS-29-823-02
Shere D. OA-03-323-31
Sherefedin B. SOA-17-1168-02
Sheremeta Y. SOA-06-1059-31, SOA-15-1146-02
Shete P. OA-10-375-31, SOA-17-1174-02, PS-07-567-31
Shewade H. OA-27-481-02, SOA-09-1092-31, PS-07-574-31
Shi L. PS-38-920-02
Shi W. PS-39-936-02
Shigayeva A. LB-2957
Shigut B. PS-13-635-31
Shih Y.-J. EP-02-110-31
Shim T.S. EP-10-191-01
Shin S.S. PS-27-789-01
Shinwana E. PS-38-923-02
Shiraishi R. SOA-02-1016-31, SOA-04-1040-31
Shitikov E. OA-06-340-31
Shiv kumar S.B.Y. EP-09-177-01
Shivakoti R. EP-07-160-01, EP-07-162-01, PS-22-739-01
Shivakumar M. PS-01-502-31
Shivakumar S.V.B.Y. SOA-18-1182-02
Shongwe N. PS-41-953-02
Shongwe S. PS-41-953-02
Shoo A. SOA-14-1139-01
Showket T. PS-33-872-02
Shrestha S. PS-12-624-31, **PS-36-897-02**, **PS-36-903-02**
Shrestha S.K. **PS-26-778-01**, **PS-41-951-02**

Shringarpure K. PS-11-621-31
Shukla P. **EP-08-170-01**, EP-16-247-02, PS-30-826-02
Shukla S. OA-06-341-31, PS-11-613-31
Shukurali kyzy C. PS-11-610-31
Shumba K. OA-07-354-31
Siame W. PS-14-645-31
Sibagadis H. PS-21-725-01
Sibanda E. PS-07-574-31
Sibanda J. OA-07-354-31, PS-03-531-31
Sichone E. **SOA-14-1139-01**, PS-16-678-01
Siddiqui M. PS-28-804-02
Siddiqui S. **PS-27-793-01**, PS-41-959-02
Sidibe K. PS-28-807-02
Sidiq Z. EP-12-208-02
Sifuentes-Osornio J. PS-24-765-01
Sifumba Z. OA-09-366-31
Sikazwe J. EP-12-207-02
Sikder A.S. SOA-04-1039-31
Sikhakhane N. OA-11-382-31
Sillah A.K. PS-16-668-01
Silumesii A. SOA-04-1040-31, PS-13-641-31
Siluyele C. PS-21-729-01
Silva D. OA-23-458-01, PS-20-723-01
Simbaya J. PS-15-661-01, PS-32-853-02
Simionato de Assis I. PS-11-622-31
Simon K. SOA-15-1147-02
Simone T. PS-28-806-02
Simsek A.C. SOA-03-1027-31
Simsir S. SOA-02-1012-31
Simunovic A. PS-25-771-01
Sim-Yassah B. EP-03-126-31
Sindhu M.P. SOA-13-1134-01
Singh A. OA-08-357-31
Singh A.K. **PS-20-724-01**
Singh B. **PS-29-816-02**
Singh B.K. PS-40-945-02
Singh D. **OA-09-367-31**
Singh G. PS-02-515-31
Singh H. **PS-05-552-31**
Singh J. OA-26-477-02, EP-04-130-31, LB-2976
Singh M. PS-03-524-31, PS-16-673-01, PS-16-674-01, PS-38-918-02
Singh P.K. SOA-14-1141-01, PS-06-555-31
Singh R.M. PS-13-642-31
Singh S. OA-09-370-31, PS-28-810-02, PS-39-932-02
Singh S.K. **OA-23-460-01**
Singh U. SOA-14-1141-01, PS-06-555-31
Singh V. OA-05-335-31
Singh Baghel P. OA-09-370-31
Singh Bam T. EP-06-151-01
Singh Negi N. OA-09-364-31
Singhal R. **OA-13-398-01**
Singla N. PS-34-882-02
Singla R. SOA-18-1186-02, **PS-32-859-02**
Sinha A. OA-26-477-02
Sinha D. PS-19-707-01
Sinha M.K. **PS-19-710-01**
Sinha P.K. SOA-12-1114-01
Sinha S. PS-09-593-31
Siomak O.V. PS-33-862-02
Siqueira N. **SOA-11-1113-01**
Siroka A. PS-08-588-31
Sisam C. EP-04-134-31
Sivanna T. PS-13-642-31
Sivaswami Tyagi J. SOA-16-1162-02
Siwelana T. PS-32-855-02
Siziba N. SOA-11-1109-01
Skrahina A. **OA-28-494-02**, **EP-01-104-31**
Skrip V. PS-36-902-02
Slavchev I. PS-39-935-02
Slim L. PS-27-792-01, PS-29-815-02
Slim-Saidi L. **SOA-14-1145-01**, **PS-06-556-31**
Sloan D. **OA-17-425-01**, OA-20-440-01
Smaoui S. **PS-27-792-01**, **PS-29-815-02**
Smelyanskaya M. OA-12-391-01, SOA-01-1000-31, EP-11-201-02, PS-23-747-01
Smelyanskaya M.S. OA-01-301-31
Smith D. PS-22-735-01
Smith H. SOA-02-1017-31
Smith K. OA-08-360-31, EP-06-154-01
Smith K.C. SOA-12-1124-01
Smith S. PS-03-523-31
Smith S.E. EP-08-167-01, PS-15-658-01
Snow K. PS-37-907-02
Snyman L. EP-09-184-01
Soe K.T. EP-01-106-31
Sohn H. OA-01-304-31, **OA-06-347-31**, PS-07-567-31, PS-10-608-31
Sok S. PS-23-747-01
Soka J. PS-11-620-31
Sokoya O. PS-13-637-31
Solanki D. SOA-09-1092-31
Solari L. **EP-10-188-01**
Soliev A. PS-32-857-02
Solodovnikova V. OA-28-494-02
Solon J. LB-2948
Solovieva N. PS-24-759-01
Somashekar N. OA-15-412-01, PS-28-808-02
Somoskovi A. SOA-16-1166-02, PS-06-566-31, PS-29-821-02
Son V. PS-24-764-01
Sondashi A. PS-32-853-02
Soneja M. PS-29-816-02
Song H. OA-05-337-31
Song N. **EP-14-231-02**
Song S.D. LB-2895
Song Y. **PS-06-565-31**
Soria J. PS-29-820-02
Soriano J. OA-04-324-31
Sorum M. PS-07-570-31
Sorvor F. PS-09-596-31
Sossen B. OA-22-451-01
Soto A. EP-08-174-01, PS-23-749-01
Soto M. OA-05-336-31
Soualhine H. SOA-14-1137-01
Sougakoff W. OA-03-322-31, OA-17-420-01
Souleymane M.B. **SOA-18-1184-02**
Soumya G. **OA-04-331-31**
Soundravally R. PS-35-887-02
Southern J. OA-18-429-01
Souza C.S. PS-03-528-31
Souza L.L.L. EP-08-173-01
Spani M. OA-12-389-01
Spitaleri A. OA-15-411-01
Squire B. OA-04-328-31, SOA-11-1113-01
Squire B.S. SOA-10-1095-01
Squire S.B. OA-01-303-31, PS-33-873-02
Sreelatha V. PS-35-892-02
Sreeramareddy C. **OA-08-356-31**
Sriavstava S. **PS-24-768-01**
Sridhar R. PS-39-929-02
Srikantam A. **PS-35-889-02**
Srikanth Prasad T. EP-10-187-01
Srinivasaiyer A. **OA-25-466-02**, **OA-25-468-02**, **SOA-12-1123-01**
Srinivasalu V.A. PS-28-802-02
Srinivasan A. OA-09-370-31, **OA-23-461-01**
Srinivasan S. PS-17-682-01
Srinivasan V. OA-20-434-01
Sriram S. EP-15-242-02
Sriraman K. **OA-03-319-31**
Srivastava K. PS-34-877-02
Srivastava S. OA-03-321-31
Ssebambulidde K. OA-21-445-01
Ssebunya R. **LB-2990**
Ssemata J.L. SOA-02-1020-31, PS-08-584-31
Ssengooba W. **SOA-17-1177-02**, PS-07-576-31, PS-28-803-02
Ssentongo H. SOA-05-1047-31, PS-04-536-31
Stadelman A. OA-21-445-01
Stagg H. PS-21-731-01
Starshinova A. **OA-20-437-01**, **EP-10-193-01**
Steadman A. **SOA-16-1166-02**
Steinbach S. PS-17-680-01
Sterling T. PS-29-819-02
Sterling T.R. PS-12-630-31
Stevens L. SOA-17-1171-02, EP-14-231-02
Stevens R.H. PS-26-784-01
Stevens W. OA-15-415-01, EP-08-171-01
Stewart B. SOA-04-1042-31
Stewart L. PS-17-681-01
Stewart R.C. EP-09-185-01
Stokes S. PS-37-906-02
Stoltz A.C. PS-39-933-02
Story A. **SOA-03-1029-31**
Stout J. PS-12-629-31
Stracker N. PS-08-581-31
Straetemans M. **PS-25-771-01**
Strauss M. PS-41-953-02
Struminger B. SOA-08-1082-31, **PS-15-656-01**
Struminger B.B. PS-11-617-31
Studhi A. PS-16-671-01
Sturua L. EP-06-157-01, **EP-06-158-01**
Su W.-J. **PS-01-511-31**
Suarez G.P. PS-14-654-31
Suarez P. SOA-02-1014-31, SOA-10-1103-01, SOA-15-1152-02, SOA-17-1168-02, EP-02-119-31, EP-11-200-02, EP-11-203-02, PS-21-725-01, PS-23-748-01, PS-25-770-01
Suarez P.G. SOA-15-1151-02, EP-16-249-02
Suarjana I.K. PS-19-703-01
Suarjana K. **EP-06-151-01**
Subbaraman R. SOA-13-1132-01, **PS-11-616-31**
Subbian S. OA-22-457-01
Subedi B. SOA-11-1105-01, EP-05-140-31
Subhani H.D.S.P. PS-02-517-31
Sudheer S. OA-27-487-02
Sugiharto J. **PS-33-868-02**
Sugumaran V.B. PS-10-598-31
Sukumar V.B. PS-25-775-01
Sulaiman N. PS-33-868-02
Suleman M. OA-03-320-31
Sulis G. SOA-17-1178-02, PS-10-600-31
Sultana S. **SOA-04-1039-31**, SOA-14-1140-01, PS-09-590-31

Sumalgy M. SOA-08-1082-31
Sumiya E. LB-3037
Sumner T. OA-02-309-31, **OA-14-410-01**, OA-22-452-01
Sun F. PS-18-700-01, PS-35-886-02
Suni M. OA-05-338-31
Sunil Kumar M. SOA-13-1134-01
Supply P. OA-06-340-31, OA-15-416-01
Surendran S. EP-13-225-02
Suresh A. OA-15-411-01, SOA-16-1159-02
Suresh C. PS-04-542-31
Suresh R. EP-14-230-02
Suri J. PS-40-943-02
Suryavanshi N. EP-07-160-01, **EP-09-177-01**
Suryawanshi S. **OA-27-481-02**
Sutar N. SOA-08-1078-31
Sutherland J. PS-15-660-01
Sutherland J.S. LB-2965
Sutter T. PS-16-670-01
Suzuki Y. PS-06-561-31
Svadzian A. PS-03-526-31
Svetina P. PS-25-771-01
Svoren A. SOA-11-1109-01
Swamickan R. EP-08-170-01
Swaminathan R.P. PS-22-741-01
Swaminathan S. EP-10-194-01, PS-09-591-31, PS-16-671-01, PS-17-683-01, PS-28-802-02
Swandewi Astuti P.A. PS-02-514-31
Swartz A. PS-32-850-02
Swe P.P. PS-04-538-31, PS-30-828-02
Swindells S. SOA-06-1056-31, EP-04-131-31
Sy K.T.L. SOA-08-1080-31
Sydykova G. SOA-05-1053-31
Szekely R. EP-10-190-01
Szulkin R. PS-16-669-01

T

Tabagabylova K. SOA-08-1083-31
Tachiwenyika E. PS-25-773-01
Tack I. **LB-2957**
Tadepalli M. EP-14-230-02
Tadokera R. PS-15-665-01
Taegtmeyer M. OA-04-328-31
Taguebue J.-V. PS-41-948-02
Tajudeen W. PS-11-619-31
Takamiya M. **SOA-02-1015-31**
Takarinda K. SOA-02-1015-31
Takatshana S. PS-15-665-01
Takiff H. PS-26-783-01
Talavera S. PS-29-814-02
Talekar S. OA-27-488-02, EP-13-225-02
Tambatamba B. PS-13-641-31
Tampi R. PS-08-581-31
Tan F. PS-11-612-31
Tan W. PS-26-783-01
Tana A. PS-22-735-01
Taneja R.L. SOA-16-1165-02
Tang Q. **PS-20-720-01**
Tanha T.I. PS-41-955-02
Tareen N. OA-01-305-31, EP-11-200-02
Tarelakar R. EP-12-212-02, EP-16-253-02
Tashkhodjaeva S. EP-11-204-02
Tasnim H. LB-2976
Tatara M. SOA-18-1188-02
Taune M. OA-11-387-31
Tavares Magnabosco G. **EP-16-248-02**
Tavora Dos Santos Filho E. PS-05-551-31
Taylor M. SOA-06-1059-31
Te Brake L. LB-2921
Team B. EP-14-231-02
Teixeira N. EP-05-140-31
Teixeira Chongo A. PS-14-649-31, PS-27-795-01
Teixeira De Siqueira-Filha N. OA-01-303-31, PS-33-873-02
Teklehaimanot N. PS-21-725-01
Tekumalla R. SOA-01-1002-31, PS-22-745-01, PS-30-824-02
Telisinghe L. OA-12-388-01
Telnov A. SOA-08-1084-31, SOA-18-1185-02, PS-29-817-02
Tembo B. LB-2908
Tembo M. SOA-02-1016-31, SOA-04-1040-31
Tende C. SOA-02-1016-31
Tendo C. OA-21-443-01
Teo A.K.J. OA-01-301-31, OA-12-391-01, PS-23-747-01, PS-36-898-02
Tepori W. EP-12-209-02
Terenciani Campoy L. PS-11-622-31
Terleeva Y. PS-33-862-02
Terleieva I. SOA-03-1026-31, PS-36-902-02
Terry M. PS-17-681-01
Tesfamichael B. PS-10-603-31
Tesfaye D. EP-12-209-02
Tessew Y. PS-11-614-31
Testuzza M. SOA-03-1029-31
Thakker J. **EP-02-117-31**
Thakur C. EP-13-218-02, EP-13-226-02
Thamaga S. PS-38-923-02
Thapa A. SOA-11-1105-01, SOA-11-1113-01, PS-26-778-01, PS-41-951-02
Thapa B.R. PS-41-958-02
Tharyan P. PS-15-664-01
Thawtheong S. PS-04-535-31
Thein S.T. PS-04-538-31, PS-30-828-02
Thekkur P. OA-28-489-02, **PS-15-655-01**, PS-28-808-02, PS-30-834-02
Theodorou H. OA-18-427-01
Theron G. OA-03-317-31, OA-14-405-01, OA-18-430-01, SOA-01-1009-31, SOA-01-1010-31, SOA-16-1163-02, PS-06-559-31, PS-09-595-31
Theron S. PS-10-604-31
Thet M.M. PS-04-538-31, **PS-30-828-02**
Thiagesan R. OA-27-483-02, OA-27-484-02, PS-33-867-02
Thilakarathna S. SOA-12-1120-01
Thior I. OA-05-333-31, OA-21-443-01, PS-28-811-02
Thiruvengadam K. PS-09-591-31
Thoibisana A. PS-35-887-02
Thomas A. PS-20-721-01
Thomas A.M. **PS-27-797-01**
Thomas B. **SOA-13-1132-01**, EP-09-177-01, **EP-16-245-02**, PS-04-542-31, PS-10-598-31, PS-11-616-31, PS-25-775-01
Thomas D.A. PS-17-680-01
Thu M.K. EP-01-106-31
Thuong Thuong N. PS-24-764-01
Thwaites G. OA-20-434-01, PS-24-764-01
Tibesso G. SOA-17-1168-02
Tiemersma E. EP-05-146-31, PS-03-534-31, PS-24-758-01, PS-24-766-01, PS-32-857-02
Tientcheu L. PS-16-668-01
Tierney D. **OA-18-432-01**, PS-39-928-02
Tifase B. EP-02-119-31
Tigga D. **EP-16-254-02**
Tijjani Habibu A. SOA-06-1061-31
Tilek Kyzy B. SOA-05-1053-31
Tillashaikhov M. LB-2976
Tillyashaykhov M. OA-26-477-02
Timire C. SOA-09-1090-31, SOA-09-1091-31
Timm J. **SOA-16-1167-02**
Tinkari B.S. PS-26-778-01, PS-41-951-02
Tintaya K. OA-18-432-01, PS-39-928-02
Tintaya Miñán K. PS-01-509-31
Tisi L. **PS-06-562-31**
Tisile P. OA-09-366-31
Tlali M. SOA-13-1129-01, EP-04-136-31, PS-26-785-01
Todd J. PS-28-805-02
Togun T. EP-10-190-01
Togun T.O. PS-15-660-01
Toktorbaeva N. PS-11-610-31
Toktorboreva N. SOA-05-1053-31
Tolhurst R. OA-04-328-31
Toloba Y. PS-21-727-01
Tomlinson M. SOA-06-1064-31
Tonsing J. PS-15-664-01, PS-23-756-01
Toriola M. EP-13-220-02, PS-13-637-31
Tornheim J.A. **SOA-18-1182-02**
Torobekova A. SOA-05-1053-31
Torrea G. **OA-13-399-01**, OA-15-416-01
Touray A. PS-15-660-01
Tovar M. LB-3028
Tovar M.A. PS-20-718-01
Trajman A. OA-14-406-01, OA-17-422-01, SOA-04-1038-31, SOA-18-1186-02, LB-2904
Tran C. LB-3052
Tran N.B. **PS-22-740-01**
Tran P.N. SOA-04-1033-31, SOA-05-1048-31
Tran P.T.M. **SOA-03-1031-31**
Trang N. PS-24-764-01
Traore H. PS-30-831-02
Traoré N. PS-21-727-01
Trauer J. **OA-02-312-31**, OA-22-450-01, EP-04-133-31, PS-03-534-31, PS-37-907-02
Traverso G. OA-20-436-01
Trébucq A. OA-14-403-01
Trinh T.B.T. OA-20-434-01
Triñona J. EP-14-230-02
Tripathi A. OA-05-335-31
Tripathi G.K. **SOA-12-1115-01**
Tripathy S. EP-15-242-02, PS-15-663-01
Tripathy S.P. PS-28-802-02
Trivino-Duran L. OA-17-419-01, SOA-08-1077-31, SOA-15-1154-02, EP-09-184-01

Tromp G. OA-03-318-31
Truong V.V. PS-08-587-31
Tsai H.-Y. OA-13-397-01
Tschop R. PS-37-912-02
Tsegay G. SOA-10-1103-01
Tsegay T. PS-23-748-01
Tseng H.-K. **SOA-09-1085-31**
Tshabalala M. PS-10-605-31
Tshey P. SOA-11-1111-01
Tshigeng B. OA-18-430-01
Tshikuka J.G. LB-2908
Tsibolane Y. **PS-23-752-01**
Tucker A. OA-10-376-31, PS-07-567-31, **PS-08-581-31**
Tugume L. OA-21-445-01
Tugumisirize D. **PS-37-910-02**
Tujan M.A. SOA-18-1181-02
Tukur M. OA-01-306-31
Tukvadze N. PS-18-698-01, PS-22-743-01
Tumane K. PS-30-829-02
Tumushabe E. PS-10-602-31
Tumwesigye N. OA-07-353-31, SOA-02-1021-31, EP-15-241-02, PS-32-851-02
Tumwesigye P. EP-02-115-31
Tunkara A. PS-15-660-01
Tunsag M. LB-3037
Tuot S. **OA-01-301-31**, OA-12-391-01, **PS-23-747-01**, PS-36-898-02
Turimumahoro P. SOA-03-1032-31
Turyahabwe S. OA-26-474-02, OA-26-476-02, SOA-05-1047-31, SOA-05-1051-31, SOA-09-1087-31, EP-08-176-01, PS-04-536-31, PS-04-545-31, PS-36-904-02, PS-37-910-02, PS-38-919-02
Tweedie I. EP-16-246-02
Tyagi J.S. SOA-16-1157-02, SOA-16-1165-02, EP-10-195-01
Tzanani I. PS-01-506-31

U

Ubochioma E. EP-11-201-02, PS-26-787-01, PS-30-831-02
Uddin M.K.M. **SOA-01-1008-31**, PS-01-503-31, PS-09-590-31, PS-35-894-02
Udwadia Z.F. SOA-18-1182-02
Ugarte C. **EP-09-180-01**, **EP-09-181-01**
Ugarte-Gil C. PS-01-508-31, PS-01-509-31, **PS-38-925-02**, **LB-3065**
Uguge B. OA-12-393-01
Uguge I.B. PS-16-677-01, **PS-30-830-02**
Uju D. PS-23-750-01
Ukasha T. OA-17-424-01
Uko I. EP-16-246-02
Ukwaja K. PS-18-696-01
Ul Alam M. PS-25-776-01
Ulo B. OA-09-365-31, OA-12-390-01
Umutbayeva G. OA-11-386-31
Ung M. PS-23-747-01
Upadhyay V. PS-40-945-02
Uplekar S. OA-15-411-01
Uppal A. SOA-04-1041-31
Urrego M. PS-14-649-31
Useni S. PS-16-677-01, PS-30-830-02
Ushizimpumu B. OA-15-416-01
Utthappa C. OA-11-385-31

V

Vadera B. OA-10-378-31, OA-27-482-02, **EP-13-217-02**
Vadhera B. PS-07-568-31
Vaidya D.C. PS-41-958-02
Vaidya P. PS-16-674-01, PS-38-918-02
Vaidya P.C. **PS-16-673-01**, PS-16-676-01, PS-41-958-02
Valcheva V. **PS-39-935-02**
Valdez C.L. **PS-25-777-01**
Valdivia H. OA-09-369-31
Valencia A. PS-20-718-01
Valencia E. SOA-14-1144-01
Valencia T. SOA-16-1164-02, PS-20-718-01, PS-29-813-02, PS-29-814-02
Valencia-Aguirre S. **SOA-05-1050-31**, **PS-03-529-31**
Valiquette C. SOA-04-1038-31, PS-22-737-01, PS-22-740-01
Vallely A. PS-26-786-01
Valverde E. SOA-15-1153-02
Vambe D. **EP-11-205-02**, **PS-03-531-31**
Van L. **PS-24-764-01**
Van Crevel R. OA-27-485-02, PS-10-607-31
Van Cutsem G. LB-2957
Van de Berg S. OA-11-386-31, **PS-23-746-01**
Van der Laan L.E. SOA-15-1155-02
Van der Laan T. OA-06-345-31
Van der Spuy G. LB-2965
Van der Stuyft P. SOA-18-1189-02, PS-22-742-01
Van der Walt M. PS-27-789-01, PS-40-947-02
Van der Westhuizen A. OA-14-405-01
Van der Westhuizen H.-M. OA-09-366-31
Van der Zalm M. SOA-06-1058-31
Van Deun A. OA-13-399-01, OA-15-416-01
Van Gemert W. **SOA-14-1136-01**
Van Helden P. SOA-01-1010-31
Van Hest R. PS-25-771-01
Van Hoving D. LB-2861
Van Rhijn I. PS-17-680-01
Van Rie A. **SOA-14-1138-01**
Van Soolingen D. OA-06-345-31
Van Zyl A. **SOA-06-1063-31**, **PS-10-604-31**
Van't Boveneind-Vrubleuskaya N. SOA-06-1060-31
Vanderbeke J. SOA-16-1160-02
Varaine F. PS-11-614-31, PS-34-883-02
Varchenko I. **SOA-03-1026-31**
Vargas R. **OA-13-402-01**
Vargas Vasquez D. PS-01-509-31
Varghese B. PS-35-896-02
Variava E. OA-21-446-01
Varsha Joseph M. OA-27-487-02
Varyani M. SOA-03-1022-31, PS-14-647-31
Vassall A. OA-06-347-31
Vasundhara N. PS-22-745-01
Vaswani S. OA-03-319-31
Vedachalam C. EP-16-245-02
Veerasamy M. PS-17-683-01
Veesa K.S. **PS-41-954-02**
Vega V. **SOA-18-1189-02**
Velen K. **EP-14-228-02**, PS-10-608-31
Venkatraman A. PS-16-671-01
Venugopal K. **PS-35-892-02**
Verma A. SOA-16-1157-02
Verma I. PS-16-673-01
Verma M. **OA-20-436-01**
Verma N. PS-28-801-02
Verma R. OA-09-370-31, **SOA-01-1001-31**, **EP-04-137-31**
Vermaak R. EP-04-134-31
Vermeulen M. EP-09-184-01
Versfeld A. **OA-23-459-01**, **OA-23-463-01**
Veziris N. OA-03-322-31, OA-17-420-01, **OA-20-438-01**
Via L. SOA-10-1100-01
Viatushka D. OA-28-494-02
Victor A. PS-15-659-01, PS-20-717-01
Vidal N. PS-21-731-01
Vieira Ramos A.C. EP-08-169-01, PS-11-622-31
Viiklepp P. OA-17-422-01, SOA-18-1186-02
Vijay Kumar R. PS-07-577-31
Vijayageetha M. SOA-09-1092-31
Vijayalakshmi S. PS-09-591-31
Vijayan S. OA-27-486-02, EP-02-117-31, EP-13-226-02, PS-30-827-02
Vikas P. PS-07-577-31
Viljoen C. OA-26-480-02
Villaizan K. PS-38-925-02
Vinayakan E.K. EP-13-226-02
Vincent Allende M. OA-04-330-31
Viney K. PS-13-643-31
Vinh D. PS-24-764-01
Vinnard C. **OA-03-321-31**, **OA-22-457-01**
Vinokurova M. **PS-06-557-31**
Vithanage P.R. SOA-12-1117-01, PS-31-847-02
Vitko S. OA-20-435-01
Vo L.N.Q. **OA-01-303-31**, SOA-03-1031-31, SOA-04-1033-31, SOA-05-1048-31, SOA-11-1106-01, SOA-15-1148-02, EP-14-233-02, EP-16-251-02, **PS-08-587-31**, PS-13-640-31, PS-23-754-01, PS-33-873-02
Voce A. PS-37-911-02
Vogt J.E. PS-16-670-01
Volik M. EP-11-204-02
Volschenk E. SOA-06-1063-31
Von Both U. EP-11-198-02
Von Delft A. **OA-09-366-31**, **OA-12-389-01**, PS-32-850-02
Von Delft D. OA-09-366-31
Vonasek B. **SOA-15-1147-02**
Vordermeier M. **PS-17-680-01**
Vu T.N. SOA-03-1031-31, SOA-11-1106-01, SOA-15-1148-02, EP-14-233-02, EP-16-251-02, PS-08-587-31
Vyas A. **PS-26-784-01**

Vyazovaya A. OA-06-344-31, **PS-24-759-01**

W

W Dowdy D. SOA-17-1174-02
Wachinou A.P. **EP-15-240-02**, PS-07-572-31, PS-18-693-01
Wachinou P. EP-07-165-01, PS-22-737-01
Wademan D. SOA-03-1028-31
Wadhwa M. OA-18-426-01
Wadulo J. PS-36-904-02
Waghmare U. OA-27-488-02, EP-13-225-02
Wagner B. **OA-21-444-01**
Waheed Akhtar M. OA-03-316-31
Wahren Borgström E. PS-16-669-01
Wahyuni C.U. PS-05-546-31
Wahyuningsih W. PS-33-868-02
Walensky R. PS-38-921-02
Walsham A. PS-06-562-31
Walter K. SOA-18-1188-02, EP-11-197-02
Walter K.S. PS-26-779-01, **PS-26-781-01**
Walters E. SOA-06-1058-31
Walzl G. LB-2965
Wambi P. OA-10-375-31
Wan Y. PS-24-760-01
Wan Y.-J.Y. OA-03-316-31
Wanchaithanawong V. PS-04-535-31
Wandeyi G. OA-12-390-01
Wandira C. OA-07-353-31
Wandji A. EP-11-199-02
Wang A. EP-08-167-01
Wang C. OA-10-373-31
Wang F. **SOA-01-1007-31**
Wang I. PS-12-628-31
Wang J.-Y. SOA-10-1099-01
Wang M. **PS-15-662-01**
Wang S.-H. **OA-14-404-01**, SOA-04-1042-31
Wang T. PS-35-886-02
Wang W. PS-34-874-02
Wang Y. **OA-10-373-31**, OA-21-449-01, PS-34-874-02
Waning B. SOA-14-1136-01
Wanjala S. OA-28-492-02, PS-11-614-31
Wankhade A. PS-29-812-02
Wapamesa C. LB-3050
Ward S. OA-17-425-01, OA-20-440-01
Warnares G. SOA-17-1171-02
Warner J. **OA-15-417-01**, **PS-24-761-01**, PS-38-917-02, PS-39-931-02
Warren J. EP-11-197-02
Warren R. OA-03-317-31, SOA-01-1009-31, SOA-01-1010-31, SOA-10-1096-01, SOA-14-1138-01, SOA-16-1163-02, PS-06-559-31, PS-09-595-31
Wasserman S. **OA-26-480-02**
Wathuo M. PS-16-668-01
Watson B. PS-04-542-31, **PS-10-598-31**, PS-25-775-01
Webb R. OA-14-404-01, **SOA-04-1042-31**
Weerasuriya C. **OA-02-308-31**
Wei X. PS-24-763-01
Weich L. EP-09-184-01
Wejse C. **SOA-04-1043-31**, PS-37-908-02
Welch C. PS-11-609-31
Welding K. OA-08-360-31, SOA-12-1124-01, EP-06-154-01
Welishe F. SOA-02-1019-31, SOA-02-1020-31, PS-08-584-31
Welte A. EP-02-113-31, PS-41-957-02
Were N. OA-09-365-31
Werede A. SOA-02-1014-31, PS-21-725-01, PS-23-748-01
Werner P. EP-07-159-01
Werngren J. OA-17-423-01
Wesson P. OA-10-372-31, PS-03-532-31
West N. PS-08-581-31, PS-32-855-02
Weyenga H. **EP-15-235-02**
White H. PS-27-798-01
White K. LB-2957
White L. LB-2948
White R. OA-02-308-31, OA-14-410-01, SOA-18-1187-02
White R.G. OA-02-309-31, OA-02-314-31, OA-22-452-01, PS-34-875-02
Whitelaw A. PS-09-595-31
Wiesner L. OA-26-473-02, SOA-10-1096-01, SOA-10-1101-01
Wig N. PS-29-816-02
Wihardini PS-02-520-31
Wijerathne A. **PS-02-517-31**
Wijesooriya H. SOA-12-1119-01, EP-03-120-31
Wijesuriya H. OA-08-358-31, SOA-12-1121-01, PS-31-838-02
Wijkander M. OA-17-423-01
Wilffert B. SOA-06-1060-31
Willie B. PS-26-786-01
Wilson D. OA-20-441-01, SOA-13-1125-01
Wilson D.P.K. EP-10-196-01
Wilson J. EP-09-182-01, PS-37-906-02
Wilson J.P. **SOA-16-1164-02**, **PS-29-813-02**, PS-29-814-02
Wilson N. OA-12-389-01, OA-23-462-01
Win K.S. EP-01-106-31
Win S.M. SOA-14-1142-01, PS-06-563-31
Winckler J.L. **SOA-15-1155-02**
Wing K. OA-26-477-02
Wingfield T. PS-33-866-02, LB-3028
Wiriyaprasobchok A. PS-04-535-31
Wirth T. OA-06-340-31
Witney A. SOA-16-1167-02
Wittwer T. EP-10-196-01
Wobeser W. OA-23-464-01, PS-20-723-01
Wobudeya E. OA-10-375-31, SOA-17-1173-02, SOA-17-1177-02, **PS-41-948-02**, PS-41-952-02
Wolf A. PS-28-799-02
Wong E. OA-03-320-31
Wood N. PS-26-785-01
Wood R. EP-04-137-31, PS-06-566-31, PS-38-921-02
Woodman M. OA-18-427-01
Wopari B. **SOA-17-1171-02**
Worku A. PS-37-912-02
Wu B. OA-03-317-31
Wu C.-Y. **OA-02-310-31**, **PS-32-858-02**
Wu J. SOA-04-1034-31
Wu M.-H. OA-13-397-01
Wu S. SOA-03-1025-31, EP-06-150-01, EP-13-227-02, PS-10-601-31, PS-32-861-02
Wu S.-B. PS-28-809-02
Wu X. SOA-06-1056-31
Wurie F. SOA-03-1029-31

X

Xaba F. PS-41-953-02
Xu B. PS-39-936-02
Xu S. OA-28-495-02
Xu Z. PS-11-615-31
Xulu B. **OA-03-320-31**

Y

Yaacoub H. OA-23-462-01
Yablonskiy P. OA-20-437-01, EP-10-193-01
Yacat N. PS-23-751-01
Yadav A. PS-30-829-02
Yadav R. EP-16-245-02, PS-16-673-01, **PS-16-674-01**, PS-16-676-01, PS-38-918-02
Yadav S. OA-14-409-01
Yaesoubi R. OA-02-315-31
Yaffe A. PS-01-506-31
Yaha L. EP-07-165-01, PS-22-737-01
Yakasai B.M. EP-02-116-31
Yamamura M. OA-18-433-01, PS-37-914-02
Yang C. PS-11-612-31, PS-11-615-31, PS-20-720-01, PS-26-783-01
Yang C.-C. **EP-02-110-31**
Yang L. EP-08-167-01
Yang Q. SOA-04-1034-31, **PS-11-612-31**, **PS-22-736-01**
Yang S.-L. SOA-09-1085-31
Yang Z. PS-11-612-31
Yaniv Z. OA-05-332-31
Yasin M. PS-23-757-01
Yassin M. PS-10-603-31
Yaya S. EP-03-127-31
Ybanez H. OA-12-392-01
Ye T. PS-24-760-01
Yeghiazaryan L. PS-18-701-01
Yegiazaryan L. OA-10-377-31, PS-34-884-02
Yegin E. SOA-02-1012-31
Yeldandi V.V. OA-11-385-31
Yen Y.-F. PS-01-511-31
Yeole R. EP-13-219-02, PS-13-638-31
Yeraliyeva L. OA-11-386-31
Yi S. OA-01-301-31, OA-12-391-01, PS-23-747-01, PS-36-898-02
Yildirim A. SOA-02-1012-31, PS-15-657-01
Yoon C. PS-39-930-02
You N. EP-02-114-31, PS-01-505-31
Young R.R. OA-04-330-31
Young S. LB-3014
Youngleson M. PS-10-605-31
Yu W. PS-26-783-01
Yuen C.M. OA-01-300-31, OA-09-369-31
Yuengling K. SOA-06-1062-31
Yusuf Audi A. SOA-06-1061-31

Z

Zachraiah R. PS-15-655-01
Zachraias Z. OA-14-409-01
Zafari M. EP-16-249-02, PS-14-654-31
Zagarella R.M. SOA-09-1089-31

Zahirzai A.B. EP-02-118-31
Zaitseva O. **PS-36-902-02**
Zakhura N. EP-01-105-31
Zaki A.M. PS-12-627-31
Zala C. SOA-09-1092-31
Zaman F. EP-06-153-01
Zamboni Berra T. EP-08-169-01, PS-11-622-31
Zameer M. OA-06-341-31
Zawedde-Muyanja S. OA-26-474-02, OA-26-476-02, **PS-03-525-31**, PS-15-666-01, PS-38-919-02
Zawede S. PS-33-863-02
Zekeshov N. SOA-08-1083-31
Zelnick J. PS-18-694-01, PS-28-799-02
Zeng X. EP-06-150-01, EP-06-152-01
Zenner D. PS-24-767-01
Zenteno-Cuevas R. PS-17-687-01
Zentner I. OA-03-321-31, OA-22-457-01
Zetola N. OA-03-321-31
Zhang B. OA-21-449-01
Zhang C. OA-26-480-02, **PS-15-658-01**
Zhang H. OA-02-309-31, EP-08-167-01
Zhang N. PS-38-925-02
Zhang P. PS-24-760-01
Zhang W. SOA-04-1034-31, PS-18-700-01, PS-22-736-01
Zhang W.-H. PS-35-886-02
Zhang X. **PS-24-763-01**
Zhang Y. PS-11-615-31
Zhavoronok S. OA-21-447-01
Zhdanova S. OA-20-435-01, PS-06-557-31
Zheng J. EP-11-197-02
Zheng X. PS-39-936-02
Zhong L. PS-11-615-31
Zhou X. **PS-35-886-02**, LB-3037
Zhu L. OA-05-337-31, EP-02-114-31, PS-01-505-31, **PS-12-625-31**
Zhumanijazova A. SOA-08-1083-31
Zhuravlev V. OA-06-344-31, EP-10-193-01, PS-24-759-01
Zignol M. EP-07-159-01
Ziki P. PS-33-864-02
Zimba N. **PS-21-729-01**
Zindoga P. OA-26-479-02, SOA-08-1082-31, SOA-08-1084-31, SOA-18-1185-02, PS-29-817-02
Zishiri C. SOA-09-1090-31, SOA-09-1091-31, **PS-15-667-01**
Zoidze A. EP-06-158-01
Zou G. **SOA-13-1130-01**
Zubair A. **OA-08-361-31**, EP-03-123-31
Zuma K. PS-15-665-01
Zunt J. PS-29-820-02
Zwama G. PS-37-911-02
Zyambo K. PS-13-641-31