



6th TB and COVID 2021 Virtual Conference 05 – 07 June 2021

Abstract Book



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INDEX

ORAL PRESENTATIONS	7
Track 1	7
Abstract #26	7
Novel urine-based diagnostics for the diagnosis of active TB in minimally symptomatic HIV-positive ART-initiators in Cape Town, South Africa	
Miss Gcobisa Ndlangalavu	
Abstract #27	7
Adherence to anti-TB drugs during hospitalization at drug-resistant TB treatment hospitals in South Africa	
Dr Elize Pietersen	
Abstract #28	8
3D micro- and nano-CT imaging of TB infected and SARS-Cov 2 infected lung.	
Dr Gordon Wells	
Abstract #46	9
What is “subclinical” tuberculosis? A case series of clinic attendees with sputum culture-positive for M. tuberculosis in rural KwaZulu-Natal	
Dr Indira Govender	
Abstract #34	10
Tuberculosis (TB) treatment initiation among patients newly initiating Antiretroviral Therapy (ART) and already on ART in the 27 President’s Emergency Fund for AIDS Relief (PEPFAR) focus districts in South Africa	
Mr Richard Machava	
TRACK 2	11
Abstract #1	11
Repurposing Novobiocin for activity against latency associated Mycobacterium tuberculosis drug target nicotinate-nucleotide adenyltransferase (Rv2421c)	
Dr. Ruben Cloete	
Abstract #33	12
Factors associated with latent tuberculosis infection among HIV positive adults in South Africa in 2016 - 2017: A cross-sectional study.	
Mrs. Galenda Jeniffer Nagudi	
Abstract #9	12
Peripheral blood kynurenine, tryptophan and Indoleamine 2, 3-dioxygenase expression for TB diagnosis, a nested case-control study in TB-infected households	
Dr Heena Ranchod	
Abstract #4	13
Conducting clinical trials in the COVID-19 era: Mitigating risks for staffs and participants without compromising the research agenda	
Dr Khatija Ahmed	
TRACK 3	14
Abstract #14	14

Tuberculosis care cascade among people living with HIV in the US President’s Emergency Plan for AIDS Relief (PEPFAR) supported districts in South Africa

Ms Katlego Motlhaoleng

Abstract #1115

Implementation of an integrated solution for monitoring and evaluation and computer assisted diagnostics software with chest x-ray for enhanced tuberculosis screening and reporting in five high TB burden provinces in South Africa

Mr Andries Vorster

Abstract #1616

Patient experiences of using medication monitors for supporting adherence to drug sensitive TB treatment

Dr Noriah Maraba

Abstract #2516

Describing the acceptability of AitaHealth, a mobile data collection application, for Tuberculosis (TB) contact tracing by outreach teams in South Africa

Don Mudzengi

Abstract #3517

The prevalence of COVID-19 for selected mines in South Africa: Phase 1 results

Don Mudzengi

Abstract #1318

Completeness and accuracy of tuberculosis data in South Africa’s routine electronic health information system

Joshua Murphy

Abstract #4219

Assessment of paediatric clinical records as a proxy for quality of care at a drug-resistant tuberculosis hospital in the Eastern Cape

Dr Razia Gaida

Abstract #3920

Effective and Sustainable Public Private Partnerships for TB Control - A South African Case Study from the Nelson Mandela Metro & OR Tambo District of the Eastern Cape.

Dr Siphon Nyathie

Abstract #4321

PPM AN OPPORTUNITY TO FIND MISSING CASES

Miss snenhlanhla Sibisi

Abstract #3121

Mapping of rifampicin-resistant tuberculosis case detection following the onset of COVID-19 in Khayelitsha, South Africa

Mrs Erika Mohr-Holland

Abstract #2222

What works to promote TB-IPC in primary care settings in the Western Cape Province, South Africa?

Prof. Christopher Colvin

Abstract #2923

Experiences and opportunities for HIV testing among household contacts during TB contact tracing in the Ekurhuleni district, Gauteng Province, South Africa – an exploratory study. Ms Fadzai Munedzimwe	
Abstract #32	24
Integrated management of rifampicin-resistant tuberculosis and diabetes mellitus in Khayeltisha, South Africa Ms Nandipha Mema	
TRACK 4.....	25
Abstract #3	25
Undiagnosed depression among tuberculosis patients in the Matjhabeng Sub-district, Free State Province, South Africa Dr Gladys Kigozi	
Abstract #7	25
Health-related quality of life among TB patients prior to TB treatment initiation – results from an observational cohort study in Johannesburg, South Africa Miss Tembeka Sineke	
Abstract #8	26
Age and not HIV status contributes to TB-related stigma among patients starting treatment for pulmonary tuberculosis in Johannesburg, South Africa Miss Tembeka Sineke	
Abstract #5	27
Socio-cultural and economic factors contributing to non-adherence to TB treatment among HIV positive rural women registered for TB treatment in Tshepong hospital. Dr Shumani Mulaudzi	
Abstract #45	28
Identifying contextual determinants of problems in tuberculosis care provision in a district South Africa to inform an integrated, person-centred approach Dr Robyn Curran	
Abstract #37	28
Reflecting on challenges in recruiting children to a multidrug-resistant tuberculosis prevention trial Dr Susan Purchase	
Abstract #47	29
An all-oral 6-month regimen for multidrug-resistant TB (the NExT study) Keertan Dheda	
Abstract #48	30
Impact of a scalable intervention package, including a point-of-care molecular diagnostic tool, on community-based active case finding for tuberculosis: a pragmatic randomised controlled trial Aliasgar Esmail	
POSTER PRESENTATIONS	31
Track 1.....	31

Abstract #20	31
End-of-treatment PET-CT clusters predicted with RNA-seq and multiplexed immuno-assay data measured in peripheral blood. Dr Elizna Maasdorp	
Abstract #37	32
CLINICAL, RADIOLOGICAL AND LABORATORY PREDICTORS OF POSITIVE URINE LIPOARABINOMANNAN IN SPUTUM SCARCE AND SPUTUM NEGATIVE PATIENTS WITH HIV ASSOCIATED TB IN TWO JOHANNESBURG HOSPITALS Dr Lior Chernick	
Abstract #18	32
Serum CA-125 in the diagnosis and therapeutic monitoring of tuberculosis Dr Kenneth Akwue	
TRACK 2.....	33
Abstract #10	33
Investigating the relation between persister formation and clinical outcome in Tuberculosis (TB) patients Mr Julian Coetzee	
TRACK 3.....	34
Abstract #17	34
Migration and Tuberculosis: Need for better monitoring Dr Khatija Ahmed	
Abstract #6	35
Organizational readiness for the implementation of a three-month short-course TB preventive therapy regimen (3HP) in four health facilities in Zimbabwe in 2020 Miss Dorothy Chisare	
Abstract #21	36
Health seeking behaviours and patient delays in accessing TB care in South Africa: a cross-sectional study Farzana Sathar	
Abstract #23	36
Social protection to mitigate the impact of COVID-19 on TB patients in South Africa. A qualitative study Ms Lieve Vanleeuw	
Abstract #15	37
Willingness of drug sensitive TB patients to enrol in a study using digital technologies to support adherence in South Africa. Mr Israel Rabothata	
Abstract #44	38
Artificial Intelligence and mHealth solution for TB case finding: Experience from Port Elizabeth, South Africa Mr Freck Dikgale	
Abstract #38	39

Engagement of private providers (PP) to improve TB care in Nelson Mandela Bay Metro (NMBM): contribution, practice and perception

Mr Freck Dikgale

Abstract #4039

Scaling up paediatric DR TB patient finding – implementation at Jose Pearson

Dr Limpho Ramangoela

ORAL PRESENTATIONS

Track 1

Abstract #26

Novel urine-based diagnostics for the diagnosis of active TB in minimally symptomatic HIV-positive ART-initiators in Cape Town, South Africa

Miss Gcobisa Ndlangalavu, Dr Byron Reeve, Mrs Zaida Palmer, Miss Selisha Naidoo, Prof Rob Warren, Prof Grant Theron

Background: Urine-based diagnostics are a promising alternative for TB in people living with HIV (PLHIV) who often cannot produce sputum. Alere Determine TB-LAM (TB-LAM) is an approved urine-based TB test for PLHIV, however, it is recommended only for critically ill patients. This study aimed to evaluate the diagnostic accuracy of urine Xpert MTB/RIF Ultra (Ultra) and Fujifilm SILVAMP TB-LAM (FujiLAM) in PLHIV initiating antiretroviral therapy (ART), irrespective of symptoms, versus a reference standard of two induced sputum cultures.

Methods: 25-100ml urine was collected from 934 patients and used as per manufacturers' recommendations for point-of-care TB-LAM, Fujilam, and urine-based Ultra, (done on unconcentrated and concentrated urine from up to 20ml). Three induced sputa were collected, two were used for MGIT960 liquid culture and the other sputum Ultra. A head-to-head analysis in 129 patients negative by TB-LAM on urine Ultra and FujiLAM was done.

Results: 40% (51/129) had TB. FujiLAM was more sensitive than urine Ultra [59% (30/51) vs 20% (10/51); $p < 0.001$] and specificities were similar [94% (72/77) vs 95% (73/77); $p = 0.731$] (concentrated and unconcentrated Urine Ultras combined). Sputum Ultra had a sensitivity and specificity of 71% (36/51) and 97% (74/77), respectively. The proportion of TB cases that were FujiLAM positive was significantly higher in symptomatic patients than asymptomatic patients [68% (27/40) vs 27% (3/11); $p = 0.016$], and similar for urine Ultra positives in symptomatic patients than asymptomatic patients [23% (9/40) vs 9% (1/11); $p = 0.321$]. FujiLAM detected more symptomatic cases than urine Ultra [68% (27/40) vs 23% (9/40); $p < 0.001$] and a similar number of asymptomatic cases [27% (3/11) vs 9% (1/11); $p = 0.269$].

Conclusions: FujiLAM has superior sensitivity when compared to urine-based Ultra in ART initiators. A greater proportion of symptomatic TB patients were detected by FujiLAM. FujiLAM promises to be a replacement for sputum-based molecular TB tests in this high risk group.

Abstract #27

Adherence to anti-TB drugs during hospitalization at drug-resistant TB treatment hospitals in South Africa

Dr Elize Pietersen, Dr Kim Anderson, Prof Helen Cox, Prof Keertan Dheda, Dr Bryan Shepherd, Prof Timothy Sterling, Dr Julian Te Riele, Prof Robin Warren, Prof Yuri van der Heijden

Background

The World Health Organization (WHO) prioritizes all-oral drug-resistant tuberculosis (DR-TB) regimens that exclude several poorly tolerated drugs. Non-adherence increases the risk of

relapse and death. We determined whether adherence to anti-TB drugs and reasons for their discontinuation varied in closely-monitored hospital settings.

Methods:

We collected retrospective data on adult South African patients selected for a primary study of acquired drug resistance who received directly observed treatment during hospitalization at specialized DR-TB hospitals in the Western Cape Province. We reviewed medical records (until mid-2017) of patients with microbiologically confirmed DR-TB between 2008 and 2015. Individual anti-TB drug hospital-based adherence was determined by comparing dosages prescribed versus received on medication charts, stratified by HIV status and DR-TB regimen. We applied a generalized mixed effects model.

Results:

Among 242 patients, 131 (54%) were male, 97 (40%) were living with HIV, 175 (72%) received second-line treatment prior to first hospitalization, and 191 (79%) died during the study period. At initial hospitalization, 134 (56%) patients had rifampicin and isoniazid resistant TB. Most patients (129 [53%]) had multiple hospitalizations. During a single treatment period 130 (54%) patients received kanamycin and capreomycin or para-aminosalicylic acid (PAS). Adherence to amikacin (82%), capreomycin (82%), PAS (83%) and kanamycin (84%) was significantly lower than other DR-TB drugs ($P < 0.001$), including ofloxacin (93%), ethionamide (92%), terizidone (93%), ethambutol (93%), and pyrazinamide (94%). PAS and second-line injectables (SLI) were stopped most frequently due to refusal and adverse events, respectively. Adherence did not differ according to HIV status or drug combinations.

Conclusion

Our findings support the shift to all-oral regimens given low adherence to poorly tolerated SLI, even in monitored, hospital settings. Adherence improvement interventions may be necessary in cases when 2020 WHO recommended Group C drugs, PAS or amikacin, are needed to avoid acquisition of resistance to anti-TB drugs and treatment failure

Abstract #28

3D micro- and nano-CT imaging of TB infected and SARS-Cov 2 infected lung.

Dr Gordon Wells, Prof. Joel Glasgow, Kievershen Nargan, Kapongo Lumamba, Dr Rajhmun Madansein, Dr Kameel Maharaj, Dr Leon Perumal, Dr Malcolm Matthew, Prof. Robert Hunter, Dr Mpumelelo Msimang, Dr Gamalenkosi Nhlonzi, Prof. Threnesan Naidoo, Stephan le Roux, Muofhe Tshibalanganda, Carlyn Wells, Prof. Anton du Plessis, Prof. Adrie Steyn

Our current understanding of the spectrum of human lung pathologies caused by *Mycobacterium tuberculosis* (Mtb) is limited by a reliance on destructive and labour-intensive two-dimensional histopathological analysis which provides detailed but limited examination of small samples. Hence, three-dimensional (3D) examination of large TB lung tissues exhibiting diverse pathological features will significantly improve our understanding of the spectrum of TB disease.

We compared high resolution computed tomography (HRCT), soft tissue X-ray (SXT) imaging, high-resolution micro-computed tomography (μ CT) and conventional histopathology to

examine resected human tuberculous lung tissues. We also applied μ CT to investigate a SARS-Cov 2 infected lung.

HRCT and STX can identify macroscopic features such as calcification, tubercles, and necrotic and cavitory lesions, whereas μ CT yields superior high-resolution images. μ CT accurately detects microscopic features such as septa, airways, vascular rearrangement, mycetomas, cavities, variations in size and shape of calcium deposits, granulomas, and lesions within paraffin-embedded tissues. 3D segmentation of histopathological anomalies within necrotic granulomas obliterated airways as a source of these abnormalities, a finding likely to be missed using conventional histopathology. We also show that TB granulomas exhibit complex morphologies.

Lastly, we could observe the macro-scale distribution of vascular and alveolar destruction in late stage COVID 19 in two lobes of a right lung. In this case, most destruction seems to be concentrated in the lobe centers, with some healthy tissue remaining on the periphery.

Conclusions: Micro-CT provides a new means by which to study infectious lung diseases, that can complement existing modalities such as medical CT and histopathology. Quantitative 3D imaging of TB lung tissues provides new insight into the spatial organization of human TB lesions in relation to airways and vasculature. Furthermore, micro-CT of TB infected and SARS-Cov 2 infected lung can also provide high-resolution organ-level 3D context compared to other methods.

Abstract #46

What is “subclinical” tuberculosis? A case series of clinic attendees with sputum culture-positive for *M. tuberculosis* in rural KwaZulu-Natal

Dr Indira Govender, Dr Aaron S Karat, Ms Kathy Baisley, Ms Silindile V Mthembu, Dr Peter Beckwith, Professor Alison Grant

Background

TB prevalence surveys uncover many people with subclinical TB, defined by detectable *M. tuberculosis* in sputum among individuals reporting no TB symptoms. Understanding the natural history of subclinical TB is important to guide case finding strategies. Our aim was to describe symptom history among individuals with culture-positive *Mtb* identified in a TB prevalence survey.

Methods

Case series of adult clinic attendees with sputum culture-positive *Mtb* in a TB prevalence survey in two primary healthcare clinics in rural KwaZulu-Natal, South Africa, 2018-2019.

Demographics, self-reported HIV status, reason for clinic attendance, and TB symptom (cough, fever, weight-loss, night sweats) status were collected at enrolment, and a single spontaneous sputum for culture was collected at the same time. A follow-up telephone interview was conducted by a trained research assistant to ascertain symptom history and contact with health services over 3 months prior to enrolment.

Results

Of 20 clinic survey participants with Mtb culture-positive sputum (11 [55%] female, 16 [80%] HIV positive [14/16 {87.5%} attending for antiretroviral therapy]), 14/20 (70%) reported being asymptomatic at enrolment. 16/20 completed follow-up interviews.

Among 12 participants reporting no symptoms at enrolment, seven reported that they were actually symptomatic at enrolment. Five confirmed that they were asymptomatic at enrolment, though 4/5 reported having symptoms in the 3 months prior to enrolment.

The symptoms most commonly reported during interviews were loss of weight (5/12) and loss of appetite/cough/night sweats (3 each/12).

10/16 interviewees reported seeking healthcare at least once for their symptoms prior to enrolment most commonly at a PHC clinic (9/16), district hospital (4/16) or private doctor (3/16).

Conclusion

Though limited by small numbers and possible recall bias, these data suggest that many people with “subclinical TB” either did not report their symptoms at enrolment or had fluctuating symptoms. Further work is needed to improve TB screening procedures.

Abstract #34

Tuberculosis (TB) treatment initiation among patients newly initiating Antiretroviral Therapy (ART) and already on ART in the 27 President’s Emergency Fund for AIDS Relief (PEPFAR) focus districts in South Africa

Mr Richard Machava, Mr Mduzuzi Ndlovu, Mrs Katlego Motlhaoleng, Mrs Sarah Porter, Mrs Cindy Dlamini, Dr Lindiwe Mvusi, Dr Kgomotso Vilakazi

Background: South Africa (SA) has an estimated 7.7 million people living with HIV (PLHIV), the highest tuberculosis (TB) incidence in the world (781 cases per 100,000 people), and 59% of patients newly diagnosed with TB are co-infected with HIV. We compared TB treatment initiation among people living with HIV (PLHIV) screening positive for TB who newly initiated antiretroviral therapy (ART) with those who previously initiated on ART at the time they screened positive for TB to identify program gaps and suggest improvements.

Methods: We analysed data reported in PEPFAR’s Data for Accountability, Transparency, and Impact Monitoring (DATIM) between October 2019-September 2020 in the 27 PEPFAR focus districts. We calculated the proportion of patients starting TB treatment among those who screened positive for TB in two groups: those who initiated ART in the same reporting quarter as screening positive for TB, and those who initiated ART in a reporting quarter prior to screening positive for TB. We used chi-square test to evaluate the difference in proportions.

Results: A total of 9,331 newly initiated on ART patients screened positive for TB and 8,027 (86%) started treatment; while 52,090 already on ART screened positive and 11,996 (23%) started treatment. TB Treatment initiation among those screening positive differed significantly between the two groups ($p < 0.001$).

Conclusions: We observed higher uptake of TB treatment among newly initiated patients compared to previously initiated patients. In both groups, a gap in initiation of TB treatment remained, especially among the previously initiated patients who may be in differentiated service delivery models and have less frequent clinic visits. PEPFAR, in collaboration with the Department of Health, should intensify efforts to improve uptake of TB treatment among previously initiated ART patients

TRACK 2

Abstract #1

Repurposing Novobiocin for activity against latency associated Mycobacterium tuberculosis drug target nicotinate-nucleotide adenylyltransferase (Rv2421c)

Dr. Ruben Cloete, Dr Mohd Shahbaaz, Dr Melanie Grobbelaar, Prof Samantha Sampson, Prof Alan Christoffels

Background

Drug resistant strains of Tuberculosis are on the rise warranting the urgent development of new drugs to combat this disease before it becomes an epidemic. Nicotinamide-nucleotide adenylyl transferase (Rv2421c) was selected as a potential drug target, because it has been shown, in vitro, to be essential for Mycobacterium tuberculosis (Mtb) growth. It is conserved between mycobacterium species, is up-regulated during dormancy, has a known 3D crystal structure and has no known human homologs. The aim of this study was to exploit the known active site of Rv2421c to identify novel inhibitors of Mtb using computational methods.

Methods

An energy minimized model of Rv2421c in complex with nicotinic acid adenine dinucleotide and magnesium ion was prepared and subjected to a virtual ligand screen against the Prestwick Chemical Library and the ZINC database, which yielded 155 potential hit molecules. Furthermore, 3D-QSAR studies using Discovery studio was performed using the 155 drug molecules and indicated five compounds with similar inhibitory efficiencies compared to known inhibitors of Rv2421c.

Results

Molecular dynamics simulation analysis of the five compounds indicated that the inhibitor molecules bind to Rv2421c with comparable efficiency as the substrate DND. Subsequent in vitro testing of the five compounds identified Novobiocin sodium salt with activity against Mycobacterium tuberculosis at 50 μ M, 25 μ M and weakly at 10 μ M concentrations. Novobiocin is known to target Mtb DNA gyrase B, but emerging resistance stimulated us to seek derivatives to target Rv2421c as alternatives for the treatment of Mycobacterium tuberculosis. Docking studies supported the higher binding affinities of Novobiocin derivatives to Rv2421c compared to DNA gyrase B.

Conclusion

This study provides data to suggest that Novobiocin derivatives can be considered for Rv2421c inhibition because they bind to Rv2421c with higher affinity. Future studies will involve testing these Novobiocin derivatives for activity against Mycobacterium tuberculosis.

Abstract #33

Factors associated with latent tuberculosis infection among HIV positive adults in South Africa in 2016 - 2017: A cross-sectional study.

Mrs. Galenda Jeniffer Nagudi, LeeAnne Masilela, Gavin Churchyard, Vicky Cardenas, Violet Chihota, Kathy Mngadi, Modulakgotla Sebe, William Brumskine, Neil Martinson, Alison D. Grant, Katherine Fielding, Salome Charalambous

Introduction: Latent tuberculosis infection (LTBI) is a major public health concern as it is one of the main sources of Tuberculosis (TB). Approximately 10% of individuals with LTBI will develop TB disease. HIV-infected individuals are among the populations at highest risk of LTBI and progressing to active TB disease. Understanding prevalence and risk factors of LTBI is important in guiding implementation of strategies such as TB preventive therapy (TPT) and vaccination. This study aimed to estimate factors associated with LTBI and CD8 T-cell response among HIV-positive adults in South Africa.

Methods: Secondary data analyses were conducted on baseline data of HIV-positive adults enrolled for the WHIP3 TB trial conducted in South Africa in 2016-2017. Participants' medical history, vital signs, CD4 count, and QuantiFERON-TB (QFT) results were collected through self-reporting, physical examination, medical records, and LTBI blood testing respectively. Descriptive statistics and logistic regression analysis using Stata 15[®] were used to describe the study population and determine factors associated with LTBI and CD8+ T-cell response.

Results: 1087 of 2511 study participants tested positive, giving a 43.3% LTBI prevalence. Higher LTBI prevalence was associated with increasing age (OR 1.01 [95%CI 1.0;1.03]), having a previous TB diagnosis (OR 1.34 [95%CI 1.10;1.63]) and having a CD4 count > 200cells/mL3 (OR 1.60 [95%CI 1.25;2.05]). CD8+ T-cell response was associated with having a previous TB diagnosis (OR 1.85 [95%CI 1.35;2.53]).

Conclusion: Given the high prevalence of LTBI among HIV infected adults in South Africa, findings of this study should guide implementation of TPT and facilitate planning of the vaccine trials.

Abstract #9

Peripheral blood kynurenine, tryptophan and indoleamine 2, 3-dioxygenase expression for TB diagnosis, a nested case-control study in TB-infected households

Dr Heena Ranchod, Dr Heather Hong*, Prof Neil Martinson, Dr Melinda Suchard

Current methods for diagnosing tuberculosis (TB) are limited in their sensitivity, specificity, ease of obtaining test specimens as well as the time taken to obtain results. Indoleamine 2, 3-dioxygenase (IDO) is the rate-limiting enzyme that plays a key role in the synthesis of immunoactive kynurenines (Kyn) from tryptophan (Tryp). Several cell types within the immune system express IDO, and changes in enzyme activity and metabolite levels have been detected in inflammatory and autoimmune diseases. IDO can be measured by determining the ratio of Kyn to Tryp concentrations by ELISA or Real-Time quantitative PCR (qPCR) in peripheral blood. The Kyn/Tryp ratio has been previously proposed as a TB biomarker.

Here we compared the Kyn/Tryp ratio measured by ELISA, and IDO gene expression measured by qPCR in comparison to Beta-actin (an internal control gene), in patients with active TB versus healthy household contacts from the South Africa - Hopkins TB (SoHoT) collaboration study. The SoHoT study had used culture and GeneXpert Ultra (Cepheid) for TB diagnosis.

In HIV-infected individuals, we found that both ELISA and qPCR displayed good potential for distinguishing between TB infected patients and healthy controls ($p = 0.008$ and $p < 0.0001$, respectively). In contrast, in HIV-infected individuals, there was a trend towards an elevated Kyn/Tryp ratio in patients with active TB compared to healthy controls ($p = 0.128$) when considering all Xpert Ultra and culture positive results as the gold standard, but no difference between the groups using qPCR. Interestingly, limiting analysis to TB culture-confirmed patients, in the HIV-infected group the Kyn/Tryp ratio was significantly higher in patients with confirmed TB compared with those without TB ($p = 0.032$).

Thus, measuring IDO activity by ELISA or qPCR may indicate mycobacterial load and severity of active tuberculosis, and warrants deeper exploration particularly for treatment monitor

Abstract #4

Conducting clinical trials in the COVID-19 era: Mitigating risks for staffs and participants without compromising the research agenda

Dr Khatija Ahmed, Dr Annah Pitsi, Dr Mookho Malahleha, Dr Nadeem Mohamed, Dr Athmanundh Dilraj

Background: COVID-19 challenges and protective measures implemented have been reported for large hospitals. However, management of clinical trial participants according to protocol are different to that from hospitals that manage patients. We describe the challenges and measures adopted at Setshaba Research Centre (SRC) in a densely-populated, under-resourced area of Soshanguve, Gauteng.

Methods: SRC responded to challenges of COVID-19 by implementing measures prior to the initial 21-day lockdown (level 5) and as lockdown eased:

- Non-pharmaceutical interventions: disposable personal protective equipment, sanitisers, reminder announcements, social distancing and screening people entering the site for COVID-19 symptoms;
- Provision of resources to staffs, especially those with co-morbidities, for remote working;
- Regulating number of participants on-site;
- Staggering staff to work shifts;
- Providing transport to avoid exposure to COVID-19 in public transport;
- Education and ongoing awareness messaging for employees/participants;
- Testing of staff with COVID-19 symptoms, and once-off testing for asymptomatic infections;
- Open waiting areas to ensure distancing and ventilation;
- Health and Safety marshals to ensure adherence;
- Symptomatic staff/participants not to report for work/scheduled visits. Study procedures and SARS-CoV-2 testing was done off-site.

Results: In Wave 1, 33/115 staff and 1/16 visitors, and in Wave 2, 17 staff and 1 visitor screened tested positive for COVID-19. Infections were mainly among nurses (12/21) and

community outreach team (9/13). The most common symptoms were sore throat (8) and cough (7); 27 cases were asymptomatic. Three reinfections and one death occurred in Wave 2.

Conclusion

Measures implemented as the pandemic evolved enabled SRC to contain the impact of COVID-19 that allowed the site to remain operational. While technological tools can reduce contact between staff and trial participants, face-to-face study visits are unavoidable and require particular attention. With an imminent third wave, research centres have to be innovative and diligent in practising measures, such as those we implemented, to reduce transmission.

TRACK 3

Abstract #14

Tuberculosis care cascade among people living with HIV in the US President's Emergency Plan for AIDS Relief (PEPFAR) supported districts in South Africa

Ms Katlego Motlhaoleng, Mr Mduduzi Ndlovu, Dr Erick Bunyasi, Dr Philippe Chiliade, Dr Kgomotso Nhlapo-Vilakazi, Dr Melissa Briggs-Hagen

Background and Objective: Tuberculosis (TB) remains a leading cause of death among people living with HIV (PLHIV). Interruption of TB transmission requires efforts to rapidly identify and treat patients with infectious TB and provide TB preventive therapy (TPT) to those at risk of progressing to active TB disease. We aimed to characterize the TB care cascade of screening, testing, treatment and TPT provision among PLHIV to identify program gaps and develop recommendations for improvement.

Method: We used descriptive statistics to analyze the TB/HIV program data reported in PEPFAR's Data for Accountability, Transparency and Impact Monitoring (DATIM) from October 2019 to September 2020 in 27 PEPFAR supported districts. The latter half of this period corresponded with the first wave of COVID-19 in South Africa.

Results: There were 3,796,750 patients on antiretroviral therapy (ART), 3,169,846 (83%) of whom were screened for TB at least once during the reporting period. Overall 112,140 (4%) patients had presumptive TB; 95,506 (83%) were tested for Xpert MTB/RIF and 38,199 (40%) had positive Xpert MTB/RIF results. A total of 48,252 (43%) patients were diagnosed with TB and started on treatment, based on laboratory results and clinical diagnoses. Pertaining to the TPT cascade, 868,597 ART patients were eligible for TPT; 534,325 (62%) were initiated on TPT and 336,468 (63%) completed therapy.

Conclusion: Insufficient TB screening coverage and low yield highlight the need for a health policy shift to improve and strengthen strategies to find the missing TB cases, especially during the COVID-19 pandemic. TPT implementation remains a challenge; however roll-out of shorter novel TPT regimens such as Isoniazid-Rifapentine (3HP) may increase uptake and increase completion rates. Health providers and support partners should implement corrective interventions to improve the quality of TB/HIV care offered to PLHIV, using a data-driven approach to strengthen supervision and ensure compliance with national guidelines.

Abstract #11

Implementation of an integrated solution for monitoring and evaluation and computer assisted diagnostics software with chest x-ray for enhanced tuberculosis screening and reporting in five high TB burden provinces in South Africa

Mr Andries Vorster, Ms. Alexandra Mumbauer, Dr Gerhard Ferreira, Mr. Werner Swanepoel, Mr. Gert van der Merwe, Mr. Hendri Pretorius, Ms. Alexandra Mumbauer

Background:

With one of the highest tuberculosis (TB) burdens in the world, South Africa requires innovative approaches for the screening, diagnosing and reporting of TB. This abstract describes the implementation of an integrated technological solution that includes using chest X-ray (CXR) and computer-assisted diagnosis (CAD) artificial intelligence (AI) combined with real-time clinical software and data reporting systems for use by community TB programmes in South Africa.

Methods:

The Lynx-HCF electronic clinical management system provides community-based TB programmes with a total solution for TB screening and reporting in a single platform. CXR screening and CAD AI technology are embedded within the system, which is also used for client registration, collection of relevant health information, and clinical workflow management. The CAD tool identifies up to ten abnormalities on the CXRs, including those suggestive of TB. Findings are summarised on a report generated by the system to guide clinical decision making. The clinical management system will be implemented at 16 sites across five high TB burden provinces and aims to reach >620,000 clients with CXR services over two years.

Results:

To date, the clinical management system with CXR and CAD functionality has been implemented at ten sites across five provinces, with six additional sites going live in April 2021. The system has reduced human errors and decreased the time required to perform a CXR screening in a community setting to approximately ten minutes, thereby increasing programme efficiency and reducing barriers to screening. Real-time screening data and automated reporting enhance time and resource allocation and enable improved management of clients with screening results suggestive of TB.

Conclusion:

Clinical management systems enable more efficient and comprehensive data-driven healthcare delivery. The integration of AI-assisted tools, tele-medicine support services, remote linkage to clinical specialists and real-time data facilitates better healthcare decisions and improved outcomes for more people.

Abstract #16

Patient experiences of using medication monitors for supporting adherence to drug sensitive TB treatment

Dr Noriah Maraba, Mr Israel Rabothata, Mrs Vuyelwa Mehloakulu, Ms Vumile Gumede, Mr Lihle Mchunu, Ms Dolphina Cogill, Mr Bongani Zondi, Prof Salome Charalambous

Introduction

Non-adherence to TB medication is a challenge in South Africa. Digital adherence technologies like evriMED device (monitor) are being evaluated to support patients taking TB treatment. We aim to describe experiences of drug-sensitive TB patients using the monitor to support taking treatment.

Methods

In an ongoing cluster-randomised trial conducted across 18 clinics in 3 provinces of South Africa (Gauteng, Kwa-Zulu Natal and Western Cape) amongst drug-sensitive TB patients, participants in intervention arm received a monitor that beeps daily to remind them to take their medication. participants also received a differentiated care response, consisting of escalated support from sms reminders to home visits, depending on the number of doses missed. Follow-up in the study was for 18 months post enrolment. Participants in the intervention arm, who were in different stages of treatment, were approached to participate in the survey while attending the clinics for routine monthly follow-up.

Results

A total of 166 participants were interviewed, 103(63%) were male, median age 36 (interquartile range 30-48) years and 123(74%) had high school education. Majority 109(66%) of those interviewed were on treatment between 4-6 months. A total of 95/159 (60%) self-reported missing a dose in the previous month and 36/95(38%) had missed 2-3 doses. Of those interviewed, 100 reported using the medication monitor, either alone or with another method to remind them to take their medication and 35 used alarms. 62 (37%) participants reported occurrences when medication was taken but not documented on the monitor; reasons for this discrepancy included poor connection (16/62; 26%), did not keep medication in monitor (13/62; 21%) and monitor not used while travelling (9/62; 15%).

Conclusion

Participants preferred using the medication monitor to remind them to take treatment although sometimes they did not keep the medication in the monitor or use it while traveling.

Abstract #25

Describing the acceptability of AitaHealth, a mobile data collection application, for Tuberculosis (TB) contact tracing by outreach teams in South Africa

Don Mudzengi, Mr Piotr Hippner, Dr Kavindhran Velen, Professor Alison Grant, Dr Richard Lessels, Professor Katherine Fielding, Professor Salome Charalambous, Dr Candice M Chetty-Makkan

Background

Tuberculosis (TB) contact tracing is an effective intervention for identifying undiagnosed TB. Routine implementation of contact tracing has however been suboptimal due to reliance on

inefficient paper-based data collection methods. We evaluated the acceptability of using a mobile health application (AitaHealth) to collect data within a contact tracing programme.

Methods

As part of a broader approach to optimising the efficiency of TB household contact tracing in three districts in South Africa, we conducted two focus group discussions and four in-depth interviews encompassing 24 outreach team members and four TB programme stakeholders, respectively. Data from only one district was included in the analysis. We used deductive thematic analysis focusing on the usability of AitaHealth.

Results

Outreach teams felt that using AitaHealth improved their efficiency by guiding them to document relevant contact tracing information. AitaHealth also allowed supervisors to monitor and evaluate outreach work daily through a dashboard. Outreach teams felt they were more accepted by the community because AitaHealth looked more professional. They, however, felt that using AitaHealth increased their workload and their limited experience with technology led to some working slower, consequently upsetting household members. AitaHealth was also reportedly misaligned with national reporting procedures and some reverted to paper for other reports. There were also concerns about the personal safety of outreach teams due to carrying electronic devices in crime endemic areas. Outreach teams experienced hardware and software challenges which limited the usability of AitaHealth.

Conclusions

Outreach teams performing routine TB contact tracing found AitaHealth to be acceptable in supporting their data collection activities, including enabling active monitoring and evaluation. There were some reported challenges that represent barriers to scale-up of the application. Further development of this technology is thus required, ideally incorporating ongoing end-user feedback to improve its use and value for supporting TB contact tracing.

Abstract #35

The prevalence of COVID-19 for selected mines in South Africa: Phase 1 results

Don Mudzengi, Dr Vukosi Banyini, Dr Thuthula Balfour, Dr Khanyile Baloyi, Professor Violet Chihota, Ms Samantha Naicker, Ms Monica Longwe, Dr Evans Muchiri, Professor Salome Charalambous

Introduction

COVID-19 seroprevalence estimates are important indicators to characterise the disease and quantify the true burden. These indicators are however scarce in the mining industry and South Africa in general. We are conducting a seroprevalence survey at two mines to estimate the prevalence of COVID-19 and identify risk factors for infection.

Methods

We conducted a repeated cross-sectional survey at two mines in three phases: six weeks apart targeting 400 randomly selected participants per mine. Research assistants interviewed consenting participants for risk factors using an electronic semi-structured questionnaire and qualified nurses collected blood. Serology testing was conducted at accredited laboratories using the SARS-CoV-2 Abbott IgG assay to test for the presence of COVID-19 antibodies. Results were sent to participants using text messages and data were analysed in Stata 16.

Results

We present results from phase 1 of the survey implemented from November to December 2020. We enrolled 720 participants at both mines finding an overall seroprevalence of 21%: (19% mine 1 vs 23% mine 2, $p=0.106$). Seropositivity was highest in those with previous PCR positive diagnosis either with symptoms (84.6%) and without symptoms (64%). Of those asymptomatic and never been diagnosed, seropositivity was 16%. Seropositivity was significantly higher among Black Africans (24.6%) than whites (14%) and coloureds (11.4%). Obesity (23.6%) and being overweight (19.1%) also showed significantly higher seropositivity compared to normal BMI (13.5%), $p=0.036$. Miners with comorbidities had significantly lower seropositivity (22.5% vs 14.2%, $p=0.049$). Seropositivity did not vary by age or by gender.

Conclusion

Seropositivity was found in the majority of participants who previously tested positive and had been symptomatic. A small proportion of those who never had disease was found to be seropositive. Stay-at-home measures can protect miners with comorbidities from infection. Results of the last two phases will be able to estimate changes in prevalence over time.

Abstract #13

Completeness and accuracy of tuberculosis data in South Africa's routine electronic health information system

Joshua Murphy, Ms Sharon Kgowedi, Ms Lezanie Coetzee, Mr Vongani Maluleke, Ms Constance Mongwenyana, Mr Daniel Letswalo, Dr Aneesa Moolla, Dr Denise Evans

Background:

There has been substantial progress on the recommendations of the 2014 "Joint Review of HIV, TB and PMTCT Programmes in South Africa." Specifically, the Tuberculosis (TB) Module in TIER.Net, the primary electronic register for HIV/TB patient management in South Africa, has gone from several pilot sites in 2015/16 to near-complete national roll-out. Integration of HIV and TB data is of high importance because the TB/HIV co-infection rate is above 60%. In order to evaluate the implementation of the TB module in TIER.net, we assessed the accuracy and completeness of key data elements.

Methods:

We reviewed 222 records for adults (>18 years) that received TB treatment at one of 15 facilities in Gauteng, Limpopo and North West provinces between Oct and Dec 2021. We linked data collected from paper-based patient clinic files to TIER.Net and use descriptive statistics to describe the accuracy and completeness of data in TIER.Net.

Results:

Patient demographics (e.g., name, sex, date of birth) were complete and accurate with close to 90% agreement between TIER.Net and the paper-based patient file. Agreement was lower for the folder number at 83%. Recording of TB treatment regimen and patient category (new) were more complete in TIER.Net (96%;213/222 and 95%;202/213) than in the patient clinical file (89%;198/222 and 93%;187/201). HIV-positive status was 137/219 (63%).

Of 80 Xpert MTB positive results reported in the patient files, 75 (94%) were also reported in the TB Module. Accuracy of standard TB treatment outcomes was adequate (>70%) and time to outcome was similar between sources (median 188 days IQR 180-231 in the patient file compared to 184.5 days IQR 167.5-215.5 in TIER.Net).

Conclusion:

These relatively high completeness and accuracy results suggest that data in the TB module is valid and reliable at the facility level.

Abstract #42

Assessment of paediatric clinical records as a proxy for quality of care at a drug-resistant tuberculosis hospital in the Eastern Cape

Dr Razia Gaida, Mr Freck Dikgale, Mrs Nonkululeko Mshweshwe, Dr Siphon Nyathie, Ms Snenhlanhla Sibisi, Mr Freck Dikgale

Background: Approximately 11% of TB cases reported in South Africa in 2019 were children under the age of 15 years, amounting to approximately 38 000. While case finding has improved and the number of children accessing treatment has increased, the quality of care provided to this vulnerable population is of interest. The aim of the project was to assess the completeness of clinical charts as a proxy for quality of care at a drug-resistant tuberculosis hospital in the Eastern Cape.

Methods: The clinical records of paediatric patients treated at the hospital for the years 2017 and 2018 were assessed for completeness.

Results: A total of 14 records were assessed. In terms of diagnostics and treatment, 35.7% (n = 5) of charts were incomplete. Electrocardiograms, audiology, height measurements and chest x-rays were unavailable and many patients (64.3%; n = 9) were not initiated within the recommended five days of diagnosis, rather commencing treatment several weeks later. Evidence of structured adverse event monitoring was lacking in 28.6% (n = 4) of charts. None of the children received a psychological assessment during care and there was no recorded evidence of occupational therapy with any child. Positively, contact tracing and testing were often completed (85.7%; n = 12) and recorded, weight at baseline and monthly weigh-ins were performed and recorded (85.7%; n = 12), patients were dosed according to their weight (92.9%; n = 13) and patients and caregivers were educated about drug-resistant tuberculosis (92.9%; n = 13).

Conclusion: While there were positive and negative findings in the clinical charts, considering the frequency of unavailable information in the various components of care, patients could be considered to have been inappropriately managed. Proper record keeping is imperative to demonstrate and monitor appropriate care, to detect complications that need to be corrected and indicate gaps in resources.

Abstract #39

Effective and Sustainable Public Private Partnerships for TB Control - A South African Case Study from the Nelson Mandela Metro & OR Tambo District of the Eastern Cape.

Dr Siphon Nyathie

AQUITY Innovations and NEXT2PEOPLE were awarded the TB REACH grant to implement a Public Private Mix TB Control Programme in the Nelson Mandela Metro and the OR Tambo District. Objectives:

- Demonstrate feasibility of outsourced PPM model in South African setting for TB management;
- Implement PPM model to achieve targets on TB screening, testing, case identification, treatment initiation and completion;
- Explore and demonstrate steps for scale up.
- Explore the feasibility and practical steps for the PPM approach as a sustainable delivery model within the NHI

Method

Service delivery combined Private GPs, Nurses and CHCWs in a community-based approach: CHCWS screen households. Onsite sputum collection of presumptive people. Linkage of identified TB patients to GPs

Samples to NHLS

GeneXpert – first line diagnostic tool

Electronic notification – labtrak application

GPs evaluate and initiate patients/refer for extrapulmonary assessment

Free TB medicines – from public health facility

Reporting to health facility

Retention

GPs see patients monthly

CHWs provide adherence support /follow up missed appointments

Results

In Nelson Mandela Metro, the intervention screened 188,000 individuals, rates of 10% presumptive, 99% tested, 8% positivity and 96% treatment initiation. In OR Tambo District, the intervention and achieved rates of 100% screened (162,000 individuals), 18% presumptive, 89% tested, 6% positivity and 90% treatment initiation.

As the programmes developed (and received extension funding) additional private GPs joined the initiatives and actively engaged in identifying how to successfully and sustainably incorporate the PPM approach into the NHI.

Conclusion

This novel approach to active case finding of presumptive TB cases showed that it is possible for the Public and Private sectors to partner together towards a common goal with DoH primary care clinics supported by NHLS GeneXpert laboratories. The Eastern Cape experience has also developed an approach for the incorporation of the PPM model into the NHI.

Abstract #43

PPM AN OPPORTUNITY TO FIND MISSING CASES

Miss snenhlanhla Sibisi, Dr Siphon Nyathi, Mr Freck Dikgale, Ms Betty Ncanywa, DR Refiloe Matji

There is a two-tier healthcare system in South Africa with a large subsidized public sector and a small, but very highly skilled private sector. According to the NHI white paper a lot of patients will access health care in the private sector before going to public sector. Tuberculosis management is freely available in the public sector, is not currently managed in the private sector, a missed opportunity as the country embarks on finding the missing TB cases.

We conducted an intervention of unique pilot of private-public mix in a South African context. Which engaged 13 private sector health providers in Nelson Mandela Bay District. This GP consortium was trained on TB management with the project providing mentorship and data support. The district provided the GPs with free TB medication, and reporting of the GPs was linked to the catchment public health facility. We allocated two CHWs to each GP in sub-district C our intervention site. The intervention had to achieve targets on TB screening, testing, case identification, treatment initiation, and treatment completion. The project used contact tracing to improve case finding and introduce technology-based AI engine one of the primary goals of the digital data collection tools is the creation of a closed loop between the patient screening efforts, the active case finding activities and the AI model indicating areas with high risk and TB burden.

From October 2018 to March 2021, we screened 349,514; tested 28,846 people, identified 2,382 patients and 2268 (95%) of identified patients were managed by the GP consortium. Patients were started on treatment within 3 days of getting a positive result. The project identified 179 DR TB patients and referred for management.

There is a clear need for more sustainable PPM intervention as it assists to find missing cases, treatment adherence and significantly reduce treatment defaulting.

Abstract #31

Mapping of rifampicin-resistant tuberculosis case detection following the onset of COVID-19 in Khayelitsha, South Africa

Mrs Erika Mohr-Holland, Mr Damian Hacking, Mr Johnny Daniels, Dr Vera Scott, Dr Vanessa Mudaly, Dr Jennifer Furin, Dr Colin Pfaff, Dr Anja Reuter

Background: The novel coronavirus-2019 (COVID-19) has had a grave impact on preventative and curative TB services, reducing TB testing by 50% in South Africa.

Methods: A retrospective analysis of monthly RR-TB case detection in Khayelitsha from January 2018 to February 2021 was conducted; COVID-19 control measures and health care system adaptations were mapped to better understand how these impacted RR-TB diagnostic services.

Results: Six-hundred-and-eight patients were diagnosed with RR-TB over the study period. Marked drops in monthly diagnosis were observed in 2020, notably in April 2020. In quarters

2 and 3 of 2020, diagnosis dropped by 21% when compared to the same quarters in 2019 (32 versus 42 and 44 versus 56 cases, respectively); in quarter 4 of 2020, diagnosis was similar to that of quarter 4 in 2019 (48 versus 46 cases). The initial decrease in RR-TB diagnosis corresponds to the primary health care (PHC) de-escalation of services and the initial restrictive 'lockdown'. Upon the shift to a less restrictive 'lockdown' in May, the DoH recommended integrated TB/COVID-19 screening of PHC attendees: a slight increase in RR-TB diagnosis was noted. However, diagnosis remained low until August 2020 when the 'lockdown' became even less restrictive and the provincial DoH released TB recovery plans. In September 2020, the country moved to the lowest 'lockdown' level, however diagnosis only started increasing in November, around which time the second wave of COVID-19 began. In January and February of 2021, diagnosis was again dropped by 24% when compared to the same months in 2020 (28 versus 37 cases).

Conclusions: COVID-19 has had a sustained and concerning impact on the RR-TB programme in Khayelitsha which has not been fully addressed by integrated TB/COVID-19 screening or the TB recovery plans. There is a need for rapid and concerted action and innovative thinking in this area.

Abstract #22

What works to promote TB-IPC in primary care settings in the Western Cape Province, South Africa?

Prof. Christopher Colvin, Dr Alison Swartz, Dr Idriss Kallon, Dr Hayleyq MacGregor, Dr Karina Kielmann, Prof Alison Grant

Background and Objectives

The literature on TB infection prevention and control (TB-IPC) identifies a wide range of barriers to the implementation of IPC policies. The literature also reports generally poor adherence to IPC policies and practice, especially in primary care settings. We know much less, however, about the factors that promote effective TB-IPC practice in these settings. This study examined what works to promote TB-IPC in primary care settings in the Western Cape, South Africa.

Method

This qualitative research study included key informant interviews with policy actors, interviews with healthcare workers and staff, and ethnographic observation at six clinics in the Western Cape. Data analysis was iterative and triangulated across multiple data sources.

Results

Our study identified a number of critical success factors in primary care clinics where TB-IPC practices were being effectively implemented. These included the presence of strong champions and role modeling, either individuals or management teams at subdistrict or district level, clear guidelines and ongoing supportive reinforcement and supervision, as well as time, consistency and focused effort in TB-IPC support interventions. Budgeting (or lack thereof) for TB-IPC-related costs as well as the appointment and support of clinic-level staff responsible for TB-IPC were seen as clear indications by staff of management commitment to and support of TB-IPC practice.

Conclusion

Our findings clearly demonstrate that effective TB-IPC practice is less a matter of individual training and motivation among healthcare staff but rather the product of concerted and ongoing effort at the facility, subdistrict and district levels of management. Clear policies and guidelines, along with a clear mandate, from provincial and national levels of management are in turn critical in promoting and supporting effective management at these lower levels.

Abstract #29

Experiences and opportunities for HIV testing among household contacts during TB contact tracing in the Ekurhuleni district, Gauteng Province, South Africa – an exploratory study.

Ms Fadzai Munedzimwe, Dr Mari Armstrong-Hough, Dr Lucian Davis, Dr Salome Charalambous, Dr Kavindhra Velen

BACKGROUND: Tuberculosis (TB) household contact tracing (HHCT) serves as an ideal conduit for increasing access and uptake of HIV testing services (HTS). Little is known about how home testing is received in the context of HHCT. We piloted HHCT with oral HIV testing and explored the experiences of household contacts (HHCs) receiving these services.

METHODS: We recruited households in the Ekurhuleni district, Gauteng Province who received HHCT and offered oral HIV testing. We selected households with at least two HHCs aged at least 15 years. We conducted in-depth interviews with purposively selected HHCs who had been offered the oral HIV test including those who accepted and declined the test. A semi-structured interview guide was used to explore how HHCs decided to test and felt about oral HIV testing in the household. An inductive approach was used to reveal emerging themes from the interviews.

RESULTS: Between September 2020 and February 2021, 20 HHCs aged between 16 and 59 years were interviewed of whom 11(55%) were female. HHCs preferred to be tested for HIV at home. HHCs who accepted the test (62%) cited a desire to: 1) know about their health or a known HIV exposure; and 2) novelty and ease of an oral HIV test as reasons for testing. HHCs who declined the test (38%) were afraid of knowing their HIV status. In addition, concerns about HIV/TB stigma in the community were raised, however most HHCs felt that their families were supportive.

CONCLUSION: Household-based HIV testing using oral HIV tests was welcomed by HHCs because they valued privacy and were surrounded by supportive family in the household. To improve access to HIV testing among HHCs, health programs can consider integrating HIV testing into HHCT. Future research must examine strategies to improve the appeal of home HIV tests and increase their uptake.

Abstract #32

Integrated management of rifampicin-resistant tuberculosis and diabetes mellitus in Khayelitsha, South Africa

Ms Nandipha Mema, Dr Anja Reuter, Dr Shaheed Mathee, Mr Lwando Cengani, Mrs Erika Hollard-Mohr, Mr Goodman Makhanda, Mr Johnny Daniels, Dr Jennifer Furin

Background

South Africa has high burdens of diabetes mellitus (DM) and rifampicin-resistant tuberculosis (RR-TB), both of which are associated with morbidity and mortality. Management of and care for these diseases is rarely integrated. We describe the lessons learnt from the implementation of an integrated service for RR-TB patients with DM in Khayelitsha.

Methods

In November 2020 an integrated service for RR-TB patients with DM was established at a primary health care facility within Khayelitsha to mitigate the risk of mortality among these patients during the COVID-19 pandemic. Set-up of this service entailed the development of a multidisciplinary team (including a Medical officer, Professional nurse, counselors, dietician and health promotions officer) providing services including the provision of glucometers to all patients, monitoring of HbA1C, screening for renal impairment, optic and peripheral neuropathy, the provision of diabetic diaries for patients to self-monitor glucose, healthy eating and health promotion activities, focused on DM. Monthly follow-ups and telephonic support was provided for patients requiring extra care.

Results

Since the start of the clinic 10 patients have received care, five of whom are HIV-positive. Other comorbid conditions included Hypertension (n=2), Epilepsy (n=1), Asthma (n=1), and chronic kidney disease (n=1). The average HBA1C at start of clinic was 8.5% (NGSP).

Since inception the following successes/challenges have been experienced:

Successes

- o Improved glucose control.
- o Interest in attending health promotion sessions
- o Better understanding of diabetes and RR-TB.
- o Fewer patient visits for health services

Challenges

- o Space constraints challenging socially distanced health promotion sessions
- o Time constraints, due to medication preparation and dispensing by the pharmacy.
- o Multiple folders requiring duplicate recording

Conclusion

Integrated RR-TB/DM care requires fewer patient visits to the health care facilities and allows for improved co-management of these conditions. This clinic was well accepted, emphasizing the need for more integrated services.

TRACK 4

Abstract #3

Undiagnosed depression among tuberculosis patients in the Matjhabeng Sub-district, Free State Province, South Africa

Dr Gladys Kigozi, Prof Christo Heunis, Prof Michelle Engelbrecht, Dr Raymond Tweheyo, Dr André Janse van Rensburg, Dr Perpetual Chikobvu

Background: There is increasing evidence of co-morbidity between tuberculosis (TB) and depression. This study examined the prevalence of probable depression among TB patients in the Matjhabeng Sub-District in the Free State Province.

Methods: A pilot study was conducted during November-December 2019. The study population was 208 drug-susceptible TB patients conveniently selected from 10 primary health care (PHC) facilities in Matjhabeng. Trained fieldworkers conducted face-to-face interviews with TB patients using a structured questionnaire. Probable depression was assessed using the Patient Health Questionnaire-9. Logistic regression was used to determine factors associated with probable depression. Statistical significance was considered at $p < 0.05$ and 95% confidence interval (CI).

Results: Almost half ($n = 96$) patients had probable depression — 22.6%, 18.8%, and 4.8% with mild, moderate, and severe symptoms respectively. Patients' sex and anti-retroviral treatment (ART) status were independently significantly ($p < 0.05$) associated with probable depression. When adjusted for potential confounding variables, the odds of probable depression for females were three times higher than the odds for males (adjusted odds ratio [AOR]: 3.0; 95%CI: 1.33-6.60; $p = 0.008$). Probable depression was 3.6 times more likely among pulmonary TB (PTB) compared to extra-PTB patients (AOR: 3.6; 95%CI: 1.10-11.41 $p = 0.034$). HIV co-infected patients who were not receiving ART were 2.4 times more likely to experience symptoms of depression compared to their counterparts who were receiving ART (AOR: 2.4; 95%CI: 1.08-5.16; $p = 0.026$). TB treatment duration was a protective factor (AOR: 0.81; 95%CI: 0.67-0.97; $p = 0.032$) against probable depression.

Conclusion: Results add to the growing evidence of TB and depression comorbidity. Given that TB and HIV treatment adherence seem to provide a degree of protection against depressive symptoms, more support is warranted within this part of the care cascade. The Matjhabeng TB programme should strengthen the screening, diagnosis, and treatment of depression among TB patients.

Abstract #7

Health-related quality of life among TB patients prior to TB treatment initiation – results from an observational cohort study in Johannesburg, South Africa

Miss Tembeka Sineke, Dr Denise Evans, Mr Kamban Hirasen, Dr Olena Ivanova, Mr Abhishek Bakuli, Dr Andrew Rachow, Mr Salome Charalambous, Dr Lawrence Long, Mr Knut Lönnroth, Prof Ianne Sanne, Group TB Sequel Consortium TB Sequel Consortium

BACKGROUND: Because poor health-related quality of life (HRQoL) and untreated depression in individuals with TB can negatively affect treatment outcomes, identifying those at risk for greater mental health disability is important for achieving TB program goals. We describe HRQoL, psychological distress, and impairment in the four weeks preceding TB treatment initiation.

SETTING: Ongoing observational study (n=359) in Johannesburg, South Africa of a cohort receiving treatment for pulmonary TB through the South African national TB program.

METHODS: Adult outpatients were recruited at TB treatment initiation between 09/2017-01/2020 and administered 1) the Medical Outcomes Short Form-36 (SF-36) for HRQoL (higher norm-based score indicates better HRQoL); 2) the Kessler Psychological Distress Scale for depression or anxiety; and 3) the Sheehan Disability Scale for health status impairment associated with TB, with responses pertaining to the previous 4 weeks.

RESULTS: 343 patients were included in the analysis (median age 37 years [IQR 30-45], 37% female, 67% HIV-positive, 81.9% smear-positive). 60.9% of patients indicated that TB disrupted their work, 44.1% their social life, and 38.7% their family life; 14.7%, 10.0%, and 9.0% of patients reported mild, moderate, and severe forms of depression or anxiety, respectively. Patients reported a lower physical component summary score (PCS; mean 42.9 SD10.1) than mental component summary score (MCS; mean 44.4 SD11.1) (p=0.03) and both were lower than those for healthy adults in the same setting (PCS mean 57.6 SD5.1; MCS mean 50.3 SD10.3). No differences in SF-36 domains were observed by gender or HIV status.

CONCLUSION: In the weeks preceding TB treatment, patients reported poorer physical and mental quality of life scores and more than a third suffered some degree of depression or anxiety. A majority reported that their illness disrupted their work. Offering counseling and other forms of support at TB treatment initiation may be important to improving treatment outcomes.

Abstract #8

Age and not HIV status contributes to TB-related stigma among patients starting treatment for pulmonary tuberculosis in Johannesburg, South Africa

Miss Tembeka Sineke, Dr Denise Evans, Mr Kamban Hirasen, Dr Olena Ivanova, Mr Abhishek Bakuli, Dr Andrew Rachow, Mr Salome Charalambous, Dr Lawrence Long, Mr Knut Lönnroth, Mr Mohammed Rassool, Prof Ian Sanne, Prof Sydney Rosen, Group TB Sequel Consortium TB Sequel Consortium

Background: In settings with a high burden of tuberculosis (TB) and HIV like South Africa, fear of HIV/AIDS can amplify stigma surrounding TB. We explore factors associated with an increased level of perceived (anticipated) stigma among patients initiating treatment for pulmonary TB through a national TB program in Johannesburg, South Africa.

Methods: Data were collected at study entry as part of an ongoing observational cohort study that enrolled adults (≥ 18 years) with drug-susceptible TB (DS-TB) recruited between 07/2017-09/2019. We used Van Rie et al's (2008) comprehensive TB stigma assessment scale, with 12 items for self-perceived stigma and 11 items for TB stigma at the community level. Items were

summed to create final scales and means and standard deviations reported (Cronbach's alpha 0.83 for self-perceived stigma and 0.877 for community stigma). We identified factors associated with stigma at the start of TB treatment (>mean vs. ≤ mean) using log binomial regression and report crude relative risk (RR) and 95% confidence intervals.

Results: 189 patients were included in the analysis (median age 37 years IQR 30-45, 32% female, 60% HIV-positive, 83% smear-positive). Self-perceived stigma (mean 32.9 SD 6.1) was higher than community stigma (mean 28.9 SD 7.5). HIV status, gender, employment status, marital status, current substance use (smoking or alcohol), and history of TB were not associated with stigma. Older adults (≥50 vs. 18-30 years) were more likely to report community stigma (RR1.9 95% CI 1.2-2.9) whereas adults 30-49 years (RR1.8 95% CI 1.1-3.1) and older adults (RR1.9 95% CI 1.1-3.3) were more likely to report self-perceived stigma.

Conclusion: Age, rather than HIV status or other personal characteristics, is the major determinant of self- and community-perceived stigma for TB patients in South Africa. Understanding what is driving perception of stigma may help improve treatment outcomes and reduce social impacts.

Abstract #5

Socio-cultural and economic factors contributing to non-adherence to TB treatment among HIV positive rural women registered for TB treatment in Tshepong hospital.

Dr Shumani Mulaudzi

TB is one of the deadliest diseases in the world, in 2017, 1.6 million people around the world died of tuberculosis (TB) which persists as the globe's top infectious disease killer, despite being preventable and curable. Deaths are down slightly from the 1.7 million in 2016, but the disease still claims 4 000 lives every day. The situation is worse in developing countries where HIV has fuelled an already serious situation. An estimated 10 million people fell ill with TB in 2017, just under the 2016 figure: 10.4 million. Two thirds of these new cases were found in just eight countries, including South Africa. South Africa has the largest share of people living with both HIV and TB (39%), but is one of only eight countries that achieved over 50% in terms of access to HIV medication for patients with both conditions. The number of new cases is falling by an average of 2% a year, which is not nearly enough to meet the global target of ending TB by 2030.

The study aimed to explore how socio-cultural, economic and related factors contribute to non-adherence to TB treatment among HIV positive rural women registered for TB treatment in the North-West province .A qualitative-cohort, exploratory study was conducted and purposive sampling method was used to select 20 participants. An interview guide was used to carry out in-depth interviews. The study was conducted over a period of 6 months. The study found that stigma and discrimination were still the main contributory factors to patients not adhering to TB treatment. Participants who had support of their family members and friends were more likely to adhere to TB and HIV treatment than those who did not disclose their status or lacked support. Acceptance of the illness versus Denial played a very important role.

Abstract #45

Identifying contextual determinants of problems in tuberculosis care provision in a district South Africa to inform an integrated, person-centred approach

Dr Robyn Curran, Dr Jamie Murdoch, Dr Andre J Van Rensburg, Dr Ajibola Awotiwon, Professor Max Bachmann, Professor Inge Petersen, Professor Lara Fairall

Background

South Africa remains among the top ten high-burden tuberculosis countries globally. There has been little theoretical development of how the healthcare system interacts with people's lives to produce poor service delivery and poor outcomes for patients. We investigated the contextual determinants of problems in TB care in one district in South Africa to inform intervention development to reduce TB deaths and incidence whilst ensuring the delivery of quality integrated, person-centred care.

Method

Theory-building case study design using the Context and Implementation of Complex Interventions (CICI) framework. Between February and November 2019, we used mixed methods in six public-sector primary healthcare facilities and one public-sector hospital serving impoverished urban and rural communities in the Amajuba district of KwaZulu-Natal province, South Africa. Qualitative data included stakeholder interviews (TB service users, health workers, community health workers, and managers), observations and documentary analysis. Quantitative data included routine data on sputum testing and TB deaths.

Results

Delayed diagnosis was caused by interactions between fragmented healthcare provision; limited resources; verticalised care; poor TB screening, sputum collection and record-keeping. One nurse responsible for TB care, with limited integration of TB with other conditions, and policy focused on treatment adherence contributed to staff stress and limited consideration of patients' psychosocial needs. Patients were lost to follow up due to discontinuity of information, poverty, employment restrictions and limited support for treatment side-effects.

Conclusion

Strengthening the quality and processes for screening, testing and diagnosing patients within primary healthcare facilities are essential but need to be supported by policy that resolves tensions between treating TB as a population-based epidemic and TB as an individually-experienced social problem. Structuring TB care as a collective endeavour may promote person-centred support for healthcare professionals and patients.

Abstract #37

Reflecting on challenges in recruiting children to a multidrug-resistant tuberculosis prevention trial

Dr Susan Purchase

Background and objectives

Recruitment to randomised clinical trials can be challenging, and slow recruitment has serious consequences. This study aimed to summarise and reflect on the challenges in enrolling young children to a multidrug-resistant tuberculosis (MDR-TB) prevention trial in South Africa.

Methods

TB-CHAMP is a randomised placebo-controlled trial to assess the efficacy of fluoroquinolone preventive therapy in young children exposed to an adult with MDR-TB. Recruitment to TB-CHAMP is tracked using an electronic recruiting platform, which was used to generate a recruiting flow diagram. Structured personnel questionnaires, meeting minutes and workshop notes were thematically analysed to elucidate recruitment barriers and solutions.

Result

4,317 adult index cases were identified between September 2017 and July 2019. Of 3,682 (85.3%) adult MDR-TB index cases with pre-screening outcomes, 1597 (43.4%) reported having no children under 5 years in the household and 562 (15.3%) were rifampicin mono-resistant. More than nine index cases were pre-screened for each child enrolled. Numerous barriers to recruitment were identified. Thorough recruitment planning, customized tracking data systems, a dedicated recruiting team with strong leadership, adequate resources to recruit across large geographic areas, and excellent relationships with routine TB services emerged as key factors to ensure successful recruitment.

Conclusion

Recruitment of children into MDR-TB prevention trials can be very difficult. Several MDR-TB prevention trials are underway, and lessons learnt from TB-CHAMP will be relevant to these and other TB prevention studies.

Abstract #47

An all-oral 6-month regimen for multidrug-resistant TB (the NExT study)

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Background: Improving treatment outcomes, reducing drug toxicity, eliminating injectable agents, and shortening the treatment duration to 6-months (the same as rifampicin-susceptible tuberculosis) remains an aspirational goal for the treatment of multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB).

Methods: We conducted a multicentre randomised controlled trial in adults with MDR/RR-TB (i.e. without resistance to fluoroquinolones or aminoglycosides). Participants were randomly assigned (1:1 ratio) to a ~6-month all-oral regimen that included levofloxacin, bedaquiline and linezolid, or the standard-of-care \geq 9-month WHO-approved injectable-based regimen. The primary endpoint was a favourable WHO-defined treatment outcome 24 months after treatment initiation.

Results: 93 of 112 participants randomised were included in the modified intention-to-treat analysis; 51 (55%) were HIV co-infected (median CD4 count 158 cells/mL). Participants in the intervention arm were 2.2 times more likely to experience a favourable 24-month outcome than participants in the standard-of-care arm [RR 2.2 (1.2-4.1); $p=0.006$]. Toxicity-related drug substitution occurred more frequently in the standard-of-care arm [(65.9% (29/44) versus 36.7% (18/49), $p=0.001$)]; 52.3% (23/44) due to kanamycin-induced hearing loss (replaced by

bedaquiline) in the standard-of-care arm, and 30.6% (15/49) due to linezolid (mainly anaemia) in the intervention arm. Culture conversion was significantly better in the intervention arm [HR 2.6 (1.4-4.9); $p=0.0015$] after censoring those with bedaquiline replacement in the standard-of-care arm.

Conclusion: An all-oral 6-month levofloxacin, bedaquiline and linezolid-containing MDR/RR-TB regimen was associated with significantly improved 24-month treatment outcomes compared with

Abstract #48

Impact of a scalable intervention package, including a point-of-care molecular diagnostic tool, on community-based active case finding for tuberculosis: a pragmatic randomised controlled trial

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ABSTRACT

Introduction: There are ~3 million undiagnosed or unreported TB cases globally, the majority of whom reside in peri-urban informal settlements. Feasibility and optimisation of mobile low-cost active case finding (ACF) models using portable molecular tools are urgently required.

Methods: We undertook community-based ACF in peri-urban townships of Cape Town, South Africa, using a mobile clinic-based scalable intervention package incorporating a low-cost minivan and portable battery-operated Gene-Xpert-MTB/RIF. Rapid non-targeted questionnaire-based screening in 5247 individuals identified 608 participants with at least one TB symptom and/or HIV co-infection who underwent randomisation to either point-of-care sputum Xpert ($n=302$) or same-day smear-microscopy ($n=306$). The primary endpoint was time-to-treatment of culture-positive TB patients initiating therapy within 60 days of diagnostic testing. Cough aerosol sampling was used to quantify infectiousness.

Results: 61/608 (10%) participants who underwent targeted screening had culture confirmed TB. Overall time-to-treatment initiation within 60-days was proportionally significantly better in the Xpert versus the smear-microscopy arm ($p=0.01$). When specifically excluding culture-only-based treatment initiation, Xpert performed better than smear-microscopy at 60 days [17/33 (51.5%) versus 7/28 (25%), $p=0.04$; intergroup difference (95% CI) of 26.5% (9-50%; $p=0.0047$); 70.8% more patients initiated treatment in the Xpert versus the smear-microscopy arm]. Xpert detected almost all likely infectious cases (17/18 [94.4%] smear-positive and/or cough aerosol culture-positive and/or with cavitary disease).

Interpretation: Community-based ACF using a scalable mobile health intervention package incorporating portable molecular diagnostics is feasible and detects the majority of community-based infectious TB cases. These data inform community-based ACF strategies in TB endemic settings.

Track 1

Abstract #20

End-of-treatment PET-CT clusters predicted with RNA-seq and multiplexed immuno-assay data measured in peripheral blood.

Dr Elizna Maasdorp, Dr Stephanus Malherbe, Prof Novel Chegou, Prof Gerhard Walzl, Prof Gerard Tromp, The Catalysis TB Biomarker Consortium

Monitoring of tuberculosis (TB) treatment response relies on month 2 sputum culture, which is a poor predictor of treatment failure and recurrent disease and has a long turnaround time. A better biomarker of treatment response will benefit both TB patient care and research. PET-CT provides complementary information to microbiology at the end of treatment, but is expensive and not widely available. It would be most practical to replace PET-CT with a blood-based biomarker.

We derived outcome groups for predictive modelling, from quantitative end-of-treatment PET-CT scan variables, as an alternative to microbiological treatment outcome groups, to investigate replacing PET-CT with multiplexed immuno-assay data, gene expression data, or both in combination.

Methods

Ninety-nine participants with sputum culture positive TB were followed-up during treatment until 2 years after treatment completion. PET-CT scans, multiplexed immuno-assay (Luminex) and RNA-sequencing data were available at the diagnosis, week 4 and week 24 time points.

Unsupervised hierarchical clustering of selected quantitative end-of-treatment PET-CT variables produced two outcome groups for predictive modelling.

Results

One PET-CT cluster consisted of 23 participants with a predominantly inflammatory lung picture, and included seven of eight participants who failed treatment. The second consisted of 76 participants with a less inflammatory or resolved lung picture and 88% of these participants displayed durable cure during study follow-up. Both gene expression and Luminex data models could predict cluster membership and achieved cross-validation areas-under-the-curve that ranged from 0.74 to 0.90 at all time points. Combining gene expression and Luminex data in classification models did not improve on the classification accuracy of the separate models.

Conclusion

At the end of TB treatment, PET-CT provides complementary information to microbiological treatment outcomes. Gene expression or protein measured in peripheral blood could potentially replace PET-CT, but accuracy should be improved and validated in independent data sets.

Abstract #37

CLINICAL, RADIOLOGICAL AND LABORATORY PREDICTORS OF POSITIVE URINE LIPOARABINOMANNAN IN SPUTUM SCARCE AND SPUTUM NEGATIVE PATIENTS WITH HIV ASSOCIATED TB IN TWO JOHANNESBURG HOSPITALS

Dr Lior Chernick, Dr Ismail Kalla, Dr Michelle Venter

Tuberculosis is a major cause of mortality in HIV-infected patients. The diagnosis of TB in patients with low CD4 counts using sputum-based diagnostics is hampered by paucibacillary disease, patients often being sputum negative or sputum scarce. Urine lipoarabinomannan (LAM) has shown promise in point of care detection of TB in this patient subset but it lacks sensitivity.

This multicentre retrospective record review compared the clinical, radiological and laboratory characteristics of sputum scarce or sputum negative HIV infected patients in two hospitals who underwent urine LAM testing.

Over a third of patients (35%) had a positive LAM, with a higher yield in sputum scarce patients (42 vs 30%, $p = 0.0141$). These patients were more likely to have delirium (OR 2.2, 95% CI 1.2 - 3.7), a higher median heart rate ($p=0.0135$) and a qSOFA score ≥ 2 (OR 3.5, 95% CI 1.6 – 7.6). A positive LAM was significantly associated with the presence of disseminated TB ($p < 0.0001$). It was also associated with a clinical diagnosis of TB immune reconstitution syndrome ($p=0.0035$) and abdominal TB ($p<0.0001$). Laboratory predictors of a positive LAM included renal dysfunction ($p=0.044$), severe anaemia ($p = 0.0116$) and a higher median C-Reactive protein ($p=0.0131$). Positive LAM results were also noted in 75% of patients with disseminated non-tuberculous mycobacterial infections ($p=0.0053$).

Urine LAM had significant diagnostic utility in HIV infected inpatients that were sputum scarce or sputum negative. A positive LAM was associated with disseminated disease, several markers of severe illness, and the diagnosis of TB IRIS. Disseminated non-tuberculous mycobacterial infection may result in positive urine LAM results. Select use in these patient subsets could maximise yield and improve predictive value, in addition to improving the time to diagnosis.

Abstract #18

Serum CA-125 in the diagnosis and therapeutic monitoring of tuberculosis

Dr Kenneth Akwue

Background: The diagnosis of active tuberculosis (TB) in patients with human immunodeficiency virus (HIV) co-infection is challenging, and few biomarkers are available to aid diagnosis. Serum CA-125 is a host biomarker elevated in pulmonary and extra-pulmonary TB in HIV-uninfected individuals. We investigated the use of serum CA-125 in the diagnosis of active TB with HIV co-infection.

Methods: We conducted a retrospective, case-control analysis of CA-125 in 109 stored serum samples of individuals with active TB disease compared to TB-uninfected controls, with or without HIV co-infection. Samples were collected from February to September 2009 by the

Perinatal HIV Research Unit, South Africa. Kruskal-Wallis with Dunn's post-test was used for multiple groups and Wilcoxon matched-pairs signed-rank test for pre and post-treatment values.

Results: In HIV-uninfected individuals, pre-treatment measured serum CA-125 was significantly higher in the TB group compared to healthy controls (Figure). Using a receiver operating characteristic (ROC) curve, CA-125 had a sensitivity 82%, specificity 95%, positive predictive value (PPV) 93%, and negative predictive value (NPV) 86% at a threshold value of 27 U/mL (area under the curve, AUC = 0.96) (Figure, dotted blue line). Two months post-treatment measured serum CA-125 declined significantly ($P < 0.0017$).

HIV-infected individuals showed no significant difference in measured serum CA-125 between those with and without active TB (Figure). At a threshold of 28 U/mL, CA-125 had sensitivity 56%, specificity 72%, PPV 56% and NPV 72% (AUC = 0.59). Following two months of TB treatment, measured serum CA-125 was not statistically different from pre-treatment levels.

Conclusion: Serum CA-125 level has potential for the diagnosis and therapeutic monitoring of TB in HIV-uninfected patients with the advantage of being a blood-based assay.

TRACK 2

Abstract #10

Investigating the relation between persister formation and clinical outcome in Tuberculosis (TB) patients

Mr Julian Coetzee

Tuberculosis (TB) is one of the top ten causes of death worldwide. Despite the availability of multiple anti-TB drugs, TB still claims ~2 million lives annually. Statistics indicate that 80% of the South African population (~46 million) has latent TB. Latent TB is partly attributed to a phenomenon known as bacterial persistence. Factors that trigger the entry into, survival in, and exit from a persistent state is largely unknown. However, the successfully adapted and validated fluorescence dilution (FD) technology provides a tool to investigate viable, but non-replicating (VBNR) persister bacteria. Previously it was shown that patients' sputum and bronchoalveolar lavage samples have remaining lesion activity and *M. tuberculosis* mRNA post TB treatment, suggestive of difficult-to-culture bacteria indicative of persisters. The aim of this study is to determine whether *M. tuberculosis* strains from TB patients who were considered cured, but have relapsed, or failed treatment, will be more likely to be predisposed to persister formation than those who remained "cured".

Methods: Flow cytometry and FD have been exploited to assess whether persister proportions in clinical *M. tuberculosis* isolates (taken at baseline) from both cured and failed/recurrent patient groups correlate with clinical outcome. Comparative next-generation sequencing, using a reference guided approach, were used to determine whether the clinical isolates were genetically predisposed to form persister populations.

Results and Discussion: At baseline all bacterial isolates possessed a level of heterogeneous replication dynamics both in vitro and intracellularly. Furthermore, isolates from the cured

patient group showed low persister proportions compared to isolates from the failed/recurrent patient group. However, no underlying unique variants that could possibly clarify the phenotypic observations were present.

Conclusion: Our work suggests that persisters play a role in the unfavourable TB disease outcome.

TRACK 3

Abstract #17

Migration and Tuberculosis: Need for better monitoring

Dr Khatija Ahmed, Dr Sherman Padayachee, Ms Zaheerah Carrim, Ms Kagiso Mothwa, Mr Ross Malamatscho, Mr Peter Silwimba, Mr Mpho Moshime, Mr Jane Maluleke, Dr Athmanundh Dilraj, Dr Mookho Malahleha

Background

Interrupting transmission of tuberculosis (TB) is critical in controlling the epidemic. Delays in diagnosis or starting treatment, treatment interruption and movement of infectious individuals all play a role in transmission of the disease. We aimed to investigate the extent of transfers and treatment outcomes in migrating TB patients.

Methods

This study was a retrospective analysis of confirmed drug-sensitive TB cases registered in 2017–2018, retrieved from TIER.Net, an Electronic Patient Management System, from a random sample of seven clinics in sub-district 1 (Soshanguve), Tshwane. We only looked at transfers in and out of sub-district 1 from/to other sub-districts within Tshwane, other areas within Gauteng, or other provinces/countries.

Results

Of 3336 TB cases registered, there were 320 (9.6%) transfers, of which 180 (56.3%) were male. Of the 320 transfers, 123 (38.4%) were transferred in and 197 (61.6%) transferred out. Seventy-five (61%) transferred in and 121 (61%) transferred out occurred within Gauteng, whereas 18/123 (15%) and 59/197 (30%) were transferred in from or out to other provinces/countries, respectively. Of 191 with transferred-out dates, 51 (26.7%) transfers occurred within the first month of treatment initiation and 94 (49.3%) by 3 months. The cure/treatment completion rate for transfers in was 51.2%, slightly lower than for patients not transferred/moved in/out (54.4%). No outcomes were recorded for transfers out.

Conclusions

Data demonstrated that 10% of registered cases migrated in/out. As no outcomes data were captured for transfers out, we cannot confirm cure/treatment completion. Thus, migration of patients between different facilities has an impact on monitoring and control of TB transmission. TIER.Net provides a good base for capturing relevant data; however, in isolation it compromises evaluation of treatment outcomes of transferred patients. Interventions to track migrating populations and improvement in data sharing between facilities are needed. Transfers out need closer follow-up to determine the final treatment outcome.

Abstract #6

Organizational readiness for the implementation of a three-month short-course TB preventive therapy regimen (3HP) in four health facilities in Zimbabwe in 2020

Miss Dorothy Chisare, Prof Rutendo Gutsire, Prof Charles Chasela

Background: Zimbabwe plans to roll-out the three-month short-course Tuberculosis preventive therapy (TPT) regimen (3HP) to address the implementation lag and poor uptake of the 6-9-month regimens. The study aimed to measure the level of organizational readiness while identifying barriers and facilitators to implementing 3HP in four health facilities in Zimbabwe.

Methodology: The study used a convergent parallel mixed-methods approach to collect data from four primary health clinics in Bulawayo and Harare Metropolitan provinces, Zimbabwe. Twenty healthcare providers completed a self-administered questionnaire; nine of whom further took part in semi-structured key-informant interviews in addition to five TB program managers from the Ministry of Health and implementing partners. Median scores with interquartile ranges were calculated to determine levels of organizational readiness. Qualitative data on barriers and facilitators were transcribed and analyzed using a framework approach.

Results: The overall readiness to implement 3HP across the four facilities was positive with a median score of 3.8(IQR 3.3 – 4.1). The findings, however, presented varied facility scores($p=0.039$). One facility did not meet the readiness threshold of 3.3 at 3.2(IQR 2.7 – 3.3) because of low contextual 2.5(IQR 2.0 -3.3), task demands 2.6(IQR 2.3 – 2.9), and resource availability 2.1(IQR 1.5 – 2.5) scores. Key organizational readiness facilitators included healthcare provider and management buy-in; community willingness to generate demand for 3HP; strong collective capability through task-shifting, alignment with existing primary healthcare programs, perceived benefits, and need for 3HP. Barriers were negative past TPT experiences, suboptimal programmatic monitoring, inconsistent health provider remuneration, inadequate staffing, added workload, and an erratic supply chain across facilities. The organizational communication gap prompts the slow program implementation culture.

Conclusions: The varied scores between facilities suggest distinct underlying organizational conditions for readiness to implement 3HP. Less ready facilities may require more flexibility to reach the intended program merits. Proactive improvements are needed to further strengthen the 3HP implementation strategy.

Abstract #21

Health seeking behaviours and patient delays in accessing TB care in South Africa: a cross-sectional study

Farzana Sathar, Violet Chihota, Denise Evans, Mohammed Rassool, Olena Ivanova, Knut Lönnroth, Salome Charalambous

Background: Undiagnosed TB is a reservoir for TB transmission. Passive TB case finding, a widely used approach, could result in a delayed diagnosis. Our study aimed to describe health seeking behaviour and patient delay among TB symptomatic individuals.

Methods: We enrolled 359 patients (≥ 18 years) with pulmonary TB at TB treatment initiation in Johannesburg from September 2017 to December 2019 (TB Sequel). We used structured questionnaires to collect data on the presence and duration of TB symptoms and patterns of health seeking behaviour.

Results: There were 138 (38.4%) females and 221 (61.6%) males. The mean age was 38.4 years. More than half (51.8%) were single and 80 (22.3%) married. 277 (77.2%) completed high school and 247 (69.0%) were HIV positive. Common TB symptoms were; cough [331, (93.5%)], night sweats [267 (75.4%)] and weight loss [314 (89.7%)], with majority [136 (37.9%)] experiencing a sum of two TB symptoms. Patients went to various healthcare providers for their first visit; primary healthcare clinic [247 (70.6%)], pharmacy [50 (14.3%)], private practitioner [29 (8.3%)], public hospital [23 (6.6%)], and a traditional practitioner [1 (0.3%)]. 101 (28.8%) patients visited ≥ 2 healthcare providers prior to being diagnosed. Since the start of their first TB symptom, patients delayed accessing TB care (patient delay: median=5 weeks, mean=9.1 weeks). 153 (43.7%) delayed accessing care for ≥ 6 weeks.

Conclusions: Our study found that a considerable delay exists between the onset of TB symptoms and accessing TB care. A contribution to this delay stems from patients visiting multiple healthcare providers in order to treat their symptoms. Thus, the opportunity to diagnose TB early at the initial visit may have been missed. Delayed diagnosis increases TB transmission in the community and leads to poorer patient outcomes. Future research should explore the patient and healthcare perspective for reasons of delayed health care seeking.

Abstract #23

Social protection to mitigate the impact of COVID-19 on TB patients in South Africa. A qualitative study

Ms Lieve Vanleeuw, Dr Wanga Zembe, Dr Salla Atkins

Background

The COVID-19 pandemic and its subsequent response has had severe consequences on TB services, with lockdowns and limitations on diagnosis and treatment services. In response, the South African government expanded social assistance programmes by topping up existing grants and the creation of the COVID-19 Social Relief of Distress grant (SRD grant). This qualitative study explored how the COVID-19 epidemic and response have affected the social, economic, and health situation of TB patients, as well as access and receipt of the SRD grant.

Methods

We interviewed 15 TB patients and 5 healthcare workers at a health facility in Cape Town.

Findings

Preliminary results found that participants associated COVID-19 with TB and this affected their health-seeking behaviour. Participants mainly fell into two camps -those who delayed care for fear of catching COVID at the health facility (majority), and those who confused their symptoms with COVID-19. Once they arrived at the clinic, however, they were given priority. Few participants reported losing income because of COVID-19 as many were already unemployed before the pandemic struck; however, several reported household members on whom they depended, losing income which significantly affected the household budget and therefore the food available for them to eat. Several participants reported that the household ran out of money for food before the end of the month and having to skip meals. Despite considerable pressure on the household budget and food supply due to COVID-19, few participants received the SRD grant.

Conclusion

Our study found that the pandemic increased pressure on TB patients' households due to loss of income leading to increased food insecurity. Despite this increased pressure, few participants received the SRD grant. Further research is needed on the impact of COVID-19 on TB patients and their households, as well as the role of social protection for TB patients.

Abstract #15

Willingness of drug sensitive TB patients to enrol in a study using digital technologies to support adherence in South Africa.

Mr Israel Rabothata, Mr Lihle Mchunu, Mr Thulani Mbatha, Mrs Catherine Orrell, Mrs Katherine Fielding, Mrs Rachel Mukora, Mr Kavindhran Velen, Mrs Lauren Jennings, Mrs Salome Charalambous, Mrs Noriah Maraba

Introduction: South Africa remains a high TB burden country. The reported treatment success rate among drug-sensitive TB (DS-TB) patients is 81%. Despite the availability of treatment and other support, adherence still remains a challenge. Electronic pill boxes with real time electronic adherence monitoring system could improve medication adherence; success has been demonstrated in other countries. We aim to look at the willingness of DS-TB patients to enroll into a trial using digital technologies to support adherence.

Methods: We report screening and enrolment data from an ongoing cluster-randomised trial. Adults and children (aged ≥ 2 years) with DS-TB disease, meeting the following criteria were eligible to enrol: initiated on DS-TB treatment within 14 days; agree to use the electronic pill box; able to give informed consent/assent; have access to a working mobile phone; can read text messages on the mobile phone and intending to remain in study area for 18 months. Screening data were collected on all the patients invited to participate. We report on screening data collected between May 2019 to December 2020.

Results: 3028 persons were screened, 2726 (90%) participants were enrolled with median age of 36 years (interquartile range: 27-45) and 62% (1694) male. A total of 302/3028 (10%) participants were screened out: 120 (40%) were not interested in the study; 72 (24%) had

started treatment >14 days ago; 23 (8%) enrolled in another TB study; 29 (10%) did not have access to a phone; 13 (4%) refused to use the electronic pill box; 22 (7%) were diagnosed with drug resistance TB/ referred to hospital for treatment 16 (5%) did not live in the study catchment area/planning to move away and 7(2%) mentioned other reasons.

Conclusion: Although the conditions of the trial may have affected this, the willingness to use a technological adherence support system seemed high in our study.

Abstract #44

Artificial Intelligence and mHealth solution for TB case finding: Experience from Port Elizabeth, South Africa

Mr Freck Dikgale, Ms Sumbul Hashmi, Dr Siphon Nyathi, Mr Freck Dikgale, Ms Snehlanihla Sibisi, Mrs Betty Ncanywa

Background: AQUITY Innovations has been driving TB screening and care in the Eastern Cape under the support and supervision of TB Reach, the Global Fund and NDOH. South Africa, with an estimated TB prevalence of 737/100.000 (2018 TB Prevalence Survey) and more in particular the Eastern Cape is considered one of the high burden provinces in South Africa. There was a need to scale up TB case finding with innovative technologies.

Method: In 2020, Aquity Innovations engaged ECPON to collaborate on the introduction of AI steered intervention planning and SMART screening tools, enabling a more effective deployment of resources and a higher yield in the detection of TB cases. Environmental and contextual real-world data in combination with program output and evidence was used to develop a model for defining high resolution burden estimates. The model uses Bayesian learning and reasoning methods and incrementally learns as new data becomes available. SMART screening tools allow for efficient data capturing and a 360° coordinated response between public and private providers. The output is generated and displayed using detailed maps for the region and near real-time dashboards for continuous monitoring.

Results: Prior to the introduction of the model the team executed approx. 56,300 screening at random locations yielding 105 (0,2%) case notifications. When contact tracing was introduced the yield was increased with 0,6%, resulting in 643 case notifications over a period of 6 months. After the introduction of the platform and screening tools, the performance of the team increased with yield 0.9% resulting in screening of 90,616 individuals over 6 months and a total of 884 diagnosed with TB.

Conclusion: Use of SMART screening tools driven by artificial intelligence for TB case finding is feasible and can help to estimate disease burden, planning subnational interventions and maximizing the yield of interventions.

Abstract #38

Engagement of private providers (PP) to improve TB care in Nelson Mandela Bay Metro (NMBM): contribution, practice and perception

Mr Freck Dikgale

Background: Tuberculosis (TB) remains a huge problem in the Eastern Cape. World Health Organization has called for collaboration between public and private healthcare providers to maximize integration of TB/HIV services and minimize costs.

In 2018, AQUITY Innovations, in partnership with NEXT2PEOPLE, were awarded the TB REACH wave 6 grant to implement in Nelson Mandela Bay, sub-district C. Part of the objective was to demonstrate feasibility of outsourced public-private model in the South African setting for TB management. The project was implemented between October 2018 and December 2020, using the PDSA model of quality improvement. The purpose of this paper is to examine evidence on the use of PP in the provision of TB care services, data practice and perception.

Methods: A review of programme data and reports (2018-2020) were collected and managed by AQUITY under the TB REACH grant.

Results: People screened for TB increased from 56,300 (October 2018–April 2019) to 187,535 (Jan 2020–March 2021). This has yielded 1640 (from 105 cases) diagnosed with all forms of TB at the testing rate of 99%. 1363 (98%) of the patients were initiated on treatment. Treatment success rate was 98% (n=447) for the January-June 2020 cohort.

Data Quality Assessments conducted in two PPs shows that the TB registers were available and had been utilised (100%). However, the DHIMS policy and monthly summaries were missing (0%). Poor recording on patient return dates (80%) was noted.

Post implementation survey findings shows that 90% (n=9) of PPs were very satisfied with the partnership and interactions. They saw value in engaging with the Department of Health (DOH), access to DoH commodities, monitoring of TB patients treatment, and easy follow up of patient through support from community healthcare workers.

Conclusion: PPs can be engaged to provide TB care conforming to national reporting guides and improving the outcomes.

Abstract #40

Scaling up paediatric DR TB patient finding – implementation at Jose Pearson

Dr Limpho Ramangoela, Dr. Siphon Nyathie

Paediatric DR TB is difficult to diagnose and requires multiple diagnostic tools to make a diagnosis resulting in high proportion of missing cases amongst this population group. Referral pathways are also quite complex and frequently children are lost while making the diagnostic journey.

The project conducted a baseline assessment of paediatric DR TB case finding activities in Jose Pearson Hospital, being on the only site providing paediatric DR TB in Nelson Mandela Metro. The district notified 11 patients in 2017, 27 in 2018, and 23 in 2019. There was no prophylaxis

being offered prior to project implementation. The project engaged a community based organisation to conduct contact management in the community based on list of index DR TB patients drawn from patients being managed at the hospital. The project also conducted a needs assessment and procured diagnostic equipment – for gastric lavage, sputum induction, and patient monitoring stands (temp, saturation, and weight). An additional paediatric nurse was also placed at the hospital to assist with anticipated increase in diagnostic services. All under 5 patients screened in the community were all referred to Jose Pearson for evaluation on paediatric clinic days – Tuesdays and Thursdays, with over 5yrs relying on symptom screening.

From June 2020 to March 2021, 105 index cases were drawn with 406 contacts being screened in the community. 265 under 5 patients were evaluated with 18 being diagnosed and 18 initiated on treatment. A total of 28 patients under 15years were diagnosed. The yield on this project is 6.9 %. To date 63 patients have been started on DR TB prophylaxis.

There is a need for increased community screening to identify more paediatric DR TB cases, with contact management being a feasible strategy.