Abstracts

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Abstracts for Oral Presentation

How is the COVID-19 Pandemic Affecting Tuberculosis Surveillance in the United States?

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Chest X-Rays Analyzed by Artificial Intelligence-Based Software as Triage Tests for Pulmonary Analysis of Diagnostic Accuracy for Detection of Microbiologically-Confirmed Disease ®

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Depression Risk Trends Before and After TB Treatment: Longitudinal Analysis of a South African TB Patient Cohort

Sarah Weber, BS
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Primary Care Providers Knowledge, Attitudes, and Skills Regarding Latent Tuberculosis Infection Testing and Treatment in Rhode Island, USA

Daria Szkwarko, DO, MPH
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Spatial Characterization of Pediatric Tuberculosis in Ukraine Using Geographic Information System

Michal Rajski, BA
The Warren Alpert Medical School of Brown University, Providence, RI, USA

Gene Expression Profile of Individuals Recently Infected with Mycobacterium Tuberculosis

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Poster Session 1

A. TALKING TB

A1. MOBILIZING TB STORIES: THE DEVELOPMENT AND EVALUATION OF A DIGITAL STORYTELLING PRODUCT FOR TB ELIMINATION IN NORTHERN FIRST NATIONS

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BACKGROUND
In First Nations communities, storytelling is foundational for holistic learning, relationships, and knowledge transfer across generations. In the field of public health knowledge translation, increasingly innovative approaches such as digital storytelling have been used to mobilize knowledge into policy and practice. In partnership with the Northern Inter-Tribal Health Authority (NITHA) and the National Collaborating Centre for Indigenous Health (NCCIH), the National Collaborating Centre for Infectious Diseases (NCCID) developed, disseminated, and evaluated a podcast documentary series following the lived experiences of TB survivors and front line TB program staff during a Dec2018-Jun2019 outbreak in a northern First Nation community in Saskatchewan, Canada.

INTERVENTION/RESPONSE
Four 20 minute podcast episodes were produced following a site visit and orientation to the First Nations community, including 6 in-person interviews. The information was directed at, and disseminated to, a wide audience of health professionals and community stakeholders. A process and outcome evaluation of the development and dissemination of the episodes was undertaken. The process, products, and evaluative methods were designed in collaboration with NITHA and NCCIH.

RESULTS
Preliminary feedback regarding the method, products and early outcomes of the initiative has been positive. Partners reflected the process to be engaging and culturally appropriate, and the products as high quality and reflective of community experiences. Reach, uptake and KT outcomes will be evaluated for 1 year following product dissemination in November 2020.

CONCLUSION
Digital storytelling products are a promising medium for sharing lived experiences among public health professionals and other community stakeholders to support TB elimination in northern First Nations communities.

A2. **"[YOUNG PEOPLE] CAN BE THE BEST TEACHERS FOR OTHERS" - HEALTHCARE WORKER PERSPECTIVES ON MAKING BOTSWANA'S TB SERVICES ADOLESCENT-FRIENDLY**

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BACKGROUND

Adolescents and young adults (AYA, ages 10-24 years) are at risk for tuberculosis (TB) and for adverse outcomes, particularly from TB/HIV co-infection. TB services have not been tailored to AYA needs. We examined healthcare worker (HCW) perspectives on needed adaptations for adolescent-friendly TB care.

METHODS

In-depth interviews were conducted with HCW managing AYA with TB at high-volume public clinics in Gaborone, Botswana. Thematic analysis by multiple researchers examined HCW perspectives on needed strategies for adolescent-friendly TB care, using the WHO framework for quality adolescent-friendly services (AFS) to categorize statements related to acceptability, effectiveness, accessibility, equitability, and appropriateness.

RESULTS

Sixteen interviews were conducted with HCW at nine clinics. HCW discussed themes in all dimensions of AFS. Unmet needs for acceptable care included: timely care at convenient hours, adolescent-dedicated clinic times or spaces, and peer support models. Needs to improve effectiveness included: training and expertise in adolescent-friendly care; dedicated guidelines for AYA TB care; adequate HCW staffing to allow sufficient time for AYA, particularly for psychosocial complexities of TB/HIV; and resources for making home visits. Further, accessibility could be enhanced through strengthening community-based TB care models and addressing TB and HIV stigma. Equitable care required meeting the needs of vulnerable AYA, such as those with limited social or family support. Appropriateness of care required meeting a range of adolescent needs, most acutely for accessing HIV care and support to achieve successful treatment outcomes.

CONCLUSION

Innovative strategies are needed to provide quality AFS to AYA with TB and TB/HIV, to address AYA needs and improve outcomes.

A3. **THE ROLE OF COUNSELLING IN TUBERCULOSIS DIAGNOSTIC EVALUATION AND CONTACT TRACING: A SCOPING REVIEW OF CURRENT KNOWLEDGE AND IDENTIFIED RESEARCH GAPS**

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BACKGROUND

Although there is a new emphasis on the importance of person-centered tuberculosis (TB) care, its precise definition remains uncertain. Experience with HIV has taught us that counselling at the point of screening increases the likelihood that an individual will complete diagnostic evaluation. While counselling is often assumed as being as a core component of TB care, little is known about its specific role within TB diagnostic evaluation.

METHODS

We conducted a scoping review to examine evidence regarding the use of counselling at the point of TB diagnosis and for contact tracing. Using search terms for TB, diagnosis and counselling, we searched PubMed, EMBASE and Web of Science. Two reviewers (IF and AS) screened all abstracts, full-texts and extracted data. We used thematic analysis to identify common themes based on the review of data.

RESULTS

After screening 1784 articles, we extracted data from 21 studies. Studies were conducted across 12 countries and varied healthcare settings including pharmacies, primary health centers and clinics. Only four studies included counselling as part of an intervention being evaluated. Although the impact of counselling was not directly assessed, counselling was hypothesized to play an important role in improving the uptake of diagnostic testing and contact tracing. Barriers to counselling included the time taken and dedicated personnel needed.

CONCLUSION

Data on the use and impact of counselling to improve TB case detection are limited. Further research is needed to understand how to operationalize and evaluate counselling as part of efforts to strengthen the TB care cascade.

A4. **“WE NEED AN INUK WHO KNOWS ABOUT TB”: A QUALITATIVE EVALUATION OF A TB SCREENING CAMPAIGN IN A NORTHERN NUNAVIK VILLAGE**

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BACKGROUND
In Canada, the incidence of active tuberculosis (TB) among the Inuit is over 400 times higher than among the non-Indigenous Canadian-born population. Community-wide screening campaigns to detect undiagnosed latent and active TB have been conducted in several Inuit villages seeking to eliminate TB. As part of a quality assessment program, we qualitatively evaluated the acceptability, feasibility, and implementation of one screening campaign that took place between October and December 2019 in a village in Nunavik, Quebec.

METHODS
We conducted in-depth and focus group interviews with a purposive sample (n=35) of: screening staff; TB nurses and doctors; individuals who attended the screening; individuals who refused screening; and individuals newly diagnosed with latent or active TB. We thematically analyzed field observation and interview notes to identify emergent themes.

RESULTS
Analysis revealed themes under three categories: implementation, engagement, and retention-in-care. Overall, interviewees were satisfied with the campaign, particularly its convenience and nondisruptiveness. Community members often spoke of a social responsibility to be screened. However, a few harboured scepticisms primarily due to a perceived over-testing of the population. Many interviewees stressed the importance of ongoing engagement with local leaders and elders, and the need to train and empower community members to lead education and mobilization strategies within screening campaigns.

CONCLUSION
We identified several suggestions for improvements to inform future campaigns. Key recommendations include: training local workers to take on more responsibilities before and during the campaign, and developing Inuit-led TB education strategies to improve engagement and retention-in-care.

A5. THINKING INSIDE THE CIRCLE: THEMES OF COMMUNITY ENGAGEMENT AND TUBERCULOSIS IN INDIGENOUS RESEARCH

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BACKGROUND

In 2017, of the 313 TB cases reported among the Indigenous Peoples, 154 were First Nations, 142 were Inuit and 17 were Métis. Fifty-two of the First Nations cases occurred in Saskatchewan where the incidence rate among First Nations was 40.3 per 100,000 people compared to a rate of 0.6 per 100,000 people and five total cases among the Canadian-born non-Indigenous group. Reinfection TB indicates ongoing transmission and requires an urgent public health response which differs from the response appropriate for relapse TB.

METHODS

A collaboration of community stakeholders and a university team engaged in a Traditional Sharing Circle on May 8th, 2019 to explore the themes of TB knowledge that surfaced with specific reference to Indigenous communities. The gathering was held in Prince Albert, Saskatchewan and was open to the public. An Integrated Research Team evolved out of the egalitarian process wherein diverse approaches to TB were discussed within an ethical space of mutual respect and reciprocity.

RESULTS

The participants experienced TB disease in a cascade of lived experience, prevention, diagnosis, management and appropriate policy development. Most of the themes were on the physical dislocation from the TB patient's home to the TB sanatoriums which were likened to residential schools or jails.

CONCLUSION

The Traditional Sharing Circle is a model for initiating conversation and establishing relationships upon which policies can be built. The community specific context is the heart of the process and is an ideal vehicle to promote dialogue around TB transmission and elimination.

A6. **IDENTIFICATION OF BARRIERS AND FACILITATORS FOR OPERATION OF THE EPIDEMIOLOGICAL SURVEILLANCE SYSTEM OF PULMONARY TUBERCULOSIS IN SAN CRISTÓBAL PROVINCE, VALDESIA REGION I, DOMINICAN REPUBLIC, 2018: A CASE STUDY IN IMPLEMENTATION RESEARCH.**

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BACKGROUND
Tuberculosis (TB) control and prevention require accurate epidemiological information. In the Dominican Republic's province of San Cristóbal the TB surveillance system differences between data found in the Operational and Epidemiological Information System Registry (SIOE), the National Epidemiological Surveillance System (SINAVE) and data collected by laboratories were detected. Due to the inconsistencies detected, an investigation was performed aiming to describe the operation of this surveillance system and evaluate its attributes. The main goal was to identify barriers and facilitators that would indicate how the system's performance could be improved.

METHODS
Case study in implementation research using mixed methods. Databases were created from TB laboratory's and control program cards. The latter were used as reference standard to estimate the system's sensitivity and positive predictive values. Agreement, data quality, timeliness, flexibility, and acceptability were also assessed. Semi-structured interviews and a focus group were performed to evaluate the last two attributes.

RESULTS
The sensitivity of SIOE and SINAVE were 60.7% and 74.1%, respectively. Agreement between these sources of information was low (Kappa =0,21). Mistakes in registration of dates for initial identification and health care were found for 26.4% of cases. Some actors felt committed to their jobs and some expressed discomfort with the the system's lack of articulation.

CONCLUSION
Low sensitivity, agreement, and articulation are barriers that require collegiate work bodies to monitor and analyse this systems' performance and thus be able to meet TB control goals on time in the Dominican Republic.

A7. PRIMARY CARE PROVIDERS' KNOWLEDGE, ATTITUDES, AND SKILLS REGARDING LATENT TUBERCULOSIS INFECTION TESTING AND TREATMENT IN RHODE ISLAND, USA

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BACKGROUND
United States Preventive Services Taskforce(USPSTF) guidelines recommend that primary care providers(PCPs) conduct latent tuberculosis infection(LTBI) testing and treatment for high risk populations in primary care(PC). Historically, LTBI management has been handled by specialists as PC training rarely includes LTBI management. Task shifting of LTBI management to PC is an important strategy towards TB elimination, yet it is unknown if PCPs have the knowledge, attitudes, and skills(KAS) to rapidly engage.

METHODS
Qualitative interview study. Key informant interviews(KIIs) were conducted with PCPs in Rhode Island(RI) to assess KAS regarding LTBI management. KIIs were conducted using a semi-structured interview guide, audio-recorded, and professionally transcribed. A codebook was created, tested, refined, and used for line-by-line coding in NVivo. Data were categorized into topical and/or thematic segments to reach final interpretation.

RESULTS
21 KIIs were conducted with PCPs. Participants' knowledge declined as the LTBI care cascade progressed – they expressed more knowledge and comfort with LTBI testing than with treatment/follow up. The majority had never treated LTBI. One stated, "I would say primarily the barrier to treating people…is that providers feel TB is such a specific and special thing. But they don't feel equipped and knowledgeable enough." Several interviewees admitted that patients do not make it to specialists given transportation barriers, and expressed interest in learning to treat LTBI.

CONCLUSION
Despite recent guidelines for LTBI management to shift into PC, RI PCPs lack critical knowledge and confidence regarding LTBI treatment. Our study suggests that training and support is needed for PCPs to confidently assume LTBI management.

A8. **BUILDING AN ONLINE COMMUNITY OF PRACTICE TO ENGAGE PRIVATE PROVIDERS IN TB CARE**

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BACKGROUND

More than 60% of people with TB who were not notified in 2019 were from seven countries ("Big Seven"): Bangladesh, India, Indonesia, Myanmar, Nigeria, Pakistan and Philippines. The private health sector dominates service-delivery in these countries. Since the initiation of the public private mix (PPM), the notification rate in private sector has tripled.[1] Despite this increase in notification, evidence suggests that the quality of care in private sector falls short of international standards.[2]

METHODS

To enhance cross learning and information exchange, a vibrant online community was launched in October 2019. The TBPPM Learning Network (TBPPM LN) facilitates interaction amongst key stakeholders. At the end of first year with a rapid growth to over 1300 members, a voluntary online survey was conducted to assess the benefits and identify the gaps in the learning network.

RESULTS

Respondents indicated they learnt about practical steps to engage private sector and about the impact of COVID19 on TB. Most respondents interacted on a weekly basis with the platform (62%). They indicated that TBPPM lessons and information are forwarded to colleagues and used in daily work (57 and 61 on scale of 100). Overall, 78% respondents concluded that the TBPPM LN is worth their time.

CONCLUSION

In times of COVID-19 with rapidly increased online interaction, the TBPPM learning network has proven to be an effective platform for knowledge exchange toward the End TB goals.

A9. SUPPORTING PATIENTS WHO ARE FOREIGN-BORN AND THEIR FAMILY MEMBERS EXPERIENCING INFECTIOUS TB THROUGH CLINICAL COMMUNICATION

Bedingfield N, Lashewicz B, Fisher D, King-Shier K. Cumming School of Medicine, University of Calgary, Canada

BACKGROUND
In countries with low TB incidence, linguistic and cultural dissonance between families experiencing infectious TB and TB health care providers (TB HCPs) is an important barrier to effective communication and successful treatment outcomes. Thus, the purpose of this research was to explore infectious TB education and counselling from the perspective of patients and family members who are foreign-born.

METHODS
This research represents one component of a multiphase, ecologically-framed, qualitative case study underway in a major city in western Canada. Data were collected primarily through semi-structured interviews and analyzed thematically. Eight families were represented amongst participants who included 6 patients and 13 family members who are foreign-born, recently experiencing infectious TB.

RESULTS
Participants learned about TB from many sources and shared learnings with others. Receiving consistent, reassuring messages helped participants feel less afraid and increase confidence with new information. Participants trusted information received from TB HCPs and expressed satisfaction with counselling received. Despite participant satisfaction, there were indications that communication problems with TB HCPs had occurred. During research interviews, participants often asked questions of the interviewer, expressed areas of lingering confusion, and shared TB-related health behaviours incongruent with current medical understanding.

CONCLUSION
Patient and family member experience can be negatively impacted by gaps in infectious TB counselling. Counselling for patients and family members who are foreign-born can be improved by intentionally using multiple modes of communication, proactively addressing common misperceptions, and using translated materials. Such improvements will empower families to better manage their own wellbeing and to share accurate TB knowledge with their communities.

A10. SUPPORTIVE SYSTEMS FOR PEOPLE WHO ARE FOREIGN-BORN AND THEIR FAMILY MEMBERS EXPERIENCING INFECTIOUS TUBERCULOSIS

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BACKGROUND
Adverse social determinants of health for people who are foreign-born are key drivers of tuberculosis (TB) disparity in countries with low rates of TB. Patients diagnosed with infectious TB experience psychosocial challenges which can deepen pre-existing health inequity. Family members of patients who are foreign-born are also likely to be significantly affected, but little is known about their experience. Thus, the aim of this study was to explore the infectious TB experience of patients and family members who are foreign-born.

METHODS
This study formed one component of a multiphase, ecologically-framed, qualitative case study underway in a major western Canadian city. Data were collected primarily through semistructured interviews with 6 patients and 13 family members who were foreign-born, representing eight families. Data were analyzed thematically.

RESULTS
Many patients and family members experienced high levels of fear and stress for months following the patient's diagnosis, though there was considerable variation in family experience. Isolation was pervasive and multifaceted for both patients and family members. Intra-family support was critical for managing during early stages when the situation was most challenging. Support from outside the family was not prominent and attempts to obtain assistance from government programs were mostly unsuccessful.

CONCLUSION
Responding to isolation caused by the intersection of TB stigma, language barriers, and poor access to government programs is critical for patients and family members who are foreign-born experiencing infectious TB. TB programs alone cannot fully meet family needs and systems of support should be created through collaboration with government institutions and organizations serving ethnocultural communities.

C. EPIDEMIOLOGY

C1. **RECURRENT TB POPULATION IN ALBERTA AND SASKATCHEWAN: DESCRIPTIVE CHARACTERISTICS**

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BACKGROUND

The contribution of relapse and reinfection to recurrent TB in Canada is unknown. We are examining four jurisdictions with whole genome sequencing and epidemiologic data.

METHODS

A descriptive analysis was conducted to ascertain the characteristics of dual culture positive recurrent TB separated by one year in Saskatchewan and Alberta. Age, gender, ethnicity, domicile and comorbidity data were compared. Chi square and t tests were used for comparison between provinces.

RESULTS

Table 1: Demographic and Comorbidity Data for persons with recurrent TB in Saskatchewan and Alberta

Data	Alberta	Saskatchewan	Chi sq/t test (p)
n	19	68	
Gender f/m	9/10	32/36	X2=.001805, p=.966
Age (years): mean, SD			
1st epidsode	52.31, 19.1	28.6, 16.36	t=-4.92612, p=<.00001
2nd episode	58.6. 18.78	37.3, 15.1	t=-5.14914, p=<.00001
Interval between two episodes (years): mean, SD	6.29, 6.56	8.7, 2.06	t=2.66675, p=.009168
Ethnicity			
Indigenous	6	67	
Non-indigenous	1	1	
Not Can born	12	0	X2=92.36, p=<.00001
Domicile			
Rural	4	58	
Urban	14	11	
Comorbidity			
HIV*	0	4	
Cancer	0	1	
Diabetes	6	3	
Renal failure	0	1	
Fibronodular CXR	4	0	
Recent infection	2	14	
Unknown	10	45	

*Not all were tested

CONCLUSION

We found important differences with respect to age, ethnicity, country of origin and recent infection of recurrent cases in Alberta and Saskatchewan. HIV coinfection was seen in Saskatchewan as a potential driver of recurrence. The relationship of these factors to relapse versus reinfection will be explored.

C2. **TUBERCULOSIS AND DRUG USE IN CALIFORNIA, 2008-2018**

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BACKGROUND

California has the largest population of persons who use drugs (PWUD) and the most TB cases in the United States. Little is known about concurrent TB disease and drug use in California.

METHODS

We determined annual TB incidence among PWUD using population-based estimates of drug use for persons ≥18 years in California from 2008–2018 and described changes in concurrent TB/drug use over time. We attributed recent transmission among PWUD using a plausible source-case algorithm based on TB genotypes.

RESULTS

Concurrent TB/drug-use cases (comprising 22% of total US-born cases and 3% of non–US-born cases) fell 36% from 2008–2018 while non-PWUD TB cases declined 19% in the same period. Average annual TB disease incidence per 100,000 person-years during 2014–2018 was 4.0 among PWUD, compared to 6.9 among non-PWUD. From 2008–2013 to 2014–2018, the number of TB cases with concurrent drug use decreased 34% in Northern California (north of San Luis Obispo, Kern, and San Bernardino Counties); in Southern California, the same proportion increased slightly (2%). TB cases among PWUD were more frequently attributed to recent transmission (15%) than cases among non-PWUD (6%) (X^2 $p < 0.001$).

CONCLUSION

Unstratified TB disease incidence among PWUD was lower than among non-PWUD in California, probably related to differences in drug use by country of origin. TB cases with concurrent drug use increased 2% in Southern California amidst overall declines in PWUD and non-PWUD TB cases statewide. Better understanding geographic patterns could help interrupt TB transmission in PWUD.

C3. **TUBERCULOSIS AMONGST INDIGENOUS PEOPLES IN CANADA**

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BACKGROUND
In Canada, colonization has sought out to disconnect Indigenous peoples from their very systems of knowledge. Early medical interventions introduced by western society often supplanted traditional forms of medicine and healing practices. Today, Indigenous peoples account for more than 50% of the Canadian-born TB cases, yet they represent only 5% of the Canadian-born population. As well, social determinants of health, including level of education, food insecurity, insufficient housing and inadequate access to health care contribute to the burden of TB disease.

METHODS
This paper aims to inform health providers, decision makers and policy analysts regarding the unique context of TB among Indigenous peoples in Canada. A critical review of the health literature surrounding TB rates related to Indigenous peoples in Canada was completed.

RESULTS
The literature illustrates the need for TB programs that include culturally safe services, community engagement to inform best practice, culturally relevant resources and education, and routine community screening programs. These practices are integral to a relevant health care approach committed to the reduction and elimination of TB in a culturally appropriate and supportive context. Additionally, equitable access to diagnostic services and treatment options are necessary to ensure a comprehensive program for TB prevention and treatment.

CONCLUSION
It is critical that health professionals recognize the limitations of western health practices in addressing persistent rates of TB among Indigenous peoples. I propose that Indigenous people should be a part of the planning of locally relevant and responsive health practices that also reflect the values and perspectives of those impacted by TB.

C4. **FACTORS ASSOCIATED WITH NOT SEEKING MEDICAL CARE AMONG INDIVIDUALS WITH TUBERCULOSIS SYMPTOMS IN INDIA: A SYSTEMATIC REVIEW OF TWO DECADES OF STUDIES**

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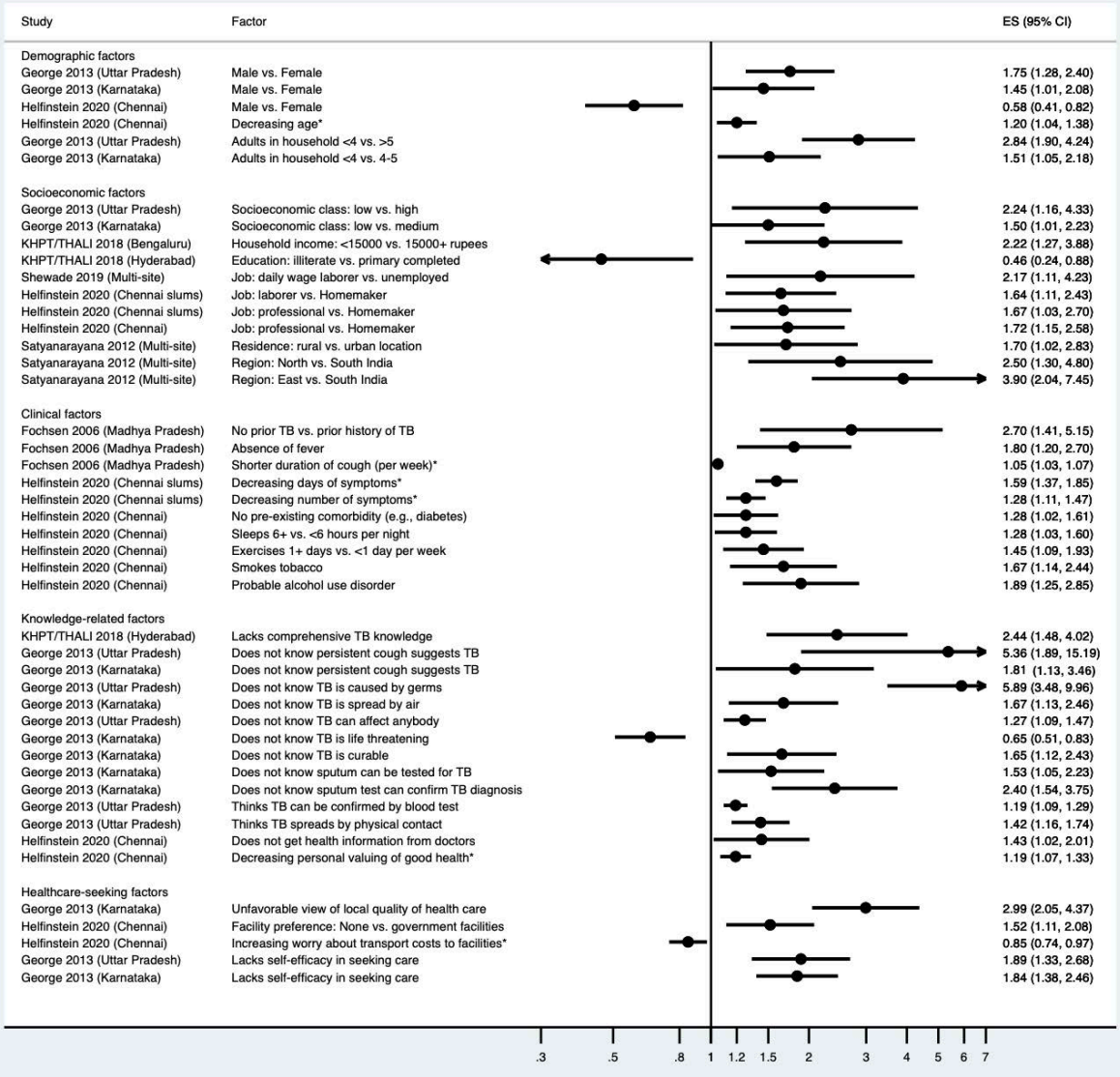
BACKGROUND
India has the highest burden of active tuberculosis (TB), accounting for one-quarter of patients and one-third of deaths globally. We conducted a systematic review to identify factors associated with individuals with TB symptoms in the population not seeking medical evaluation, as this is a major gap in India's TB care cascade.

METHODS
We searched PubMed, Embase, and Web of Science and queried experts to find studies published between January 1, 2000 and July 31, 2020 using search terms and related variants for TB, TB symptoms, India, and healthcare-seeking behavior. Two independent reviewers found population-based studies surveying individuals with TB symptoms and extracted adjusted odds ratios on factors associated with not seeking care.

RESULTS
Out of 4,776 abstracts identified by systematic search, six studies were included in the review. Factors significantly associated with higher adjusted odds of not seeking care included: male sex, lower age (demographic factors); lower socioeconomic status (SES), daily wage labor, rural (vs. urban) residence, residence in poorer northern or eastern (vs. southern) regions of India (socioeconomic factors); less severe symptoms, lack of comorbidities, smoking, alcohol use (clinical factors); lower TB knowledge (knowledge-related factors); unfavorable view of local health care, and lower self-efficacy in seeking care (healthcare-seeking factors) (Figure).

CONCLUSION
Not seeking care is associated with social vulnerability, lower symptom severity, lower TB knowledge, and lower self-efficacy in seeking care. Together, these findings suggest that educational outreach to vulnerable populations—to improve knowledge and motivation to seek care early—may improve outcomes in India's TB care cascade.


Study
Factor
ES (95% CI)
Demographic factors
George 2013 (Uttar Pradesh) Male vs. Female 1.75 (1.28, 2.40)
George 2013 (Karnataka) Male vs. Female 1.45 (1.01, 2.08)
Helfinstein 2020 (Chennai) Male vs. Female 0.58 (0.41, 0.82)
Helfinstein 2020 (Chennai) Decreasing age* 1.20 (1.04, 1.38)
George 2013 (Uttar Pradesh) Adults in household <4 vs. >5 2.84 (1.90, 4.24)
George 2013 (Karnataka) Adults in household <4 vs. 4-5 1.51 (1.05, 2.18)
Socioeconomic factors
George 2013 (Uttar Pradesh) Socioeconomic class: low vs. high 2.24 (1.16, 4.33)
George 2013 (Karnataka) Socioeconomic class: low vs. medium 1.50 (1.01, 2.23)
KHPT/THALI 2018 (Bengaluru) Household income: <15000 vs. 15000+ rupees 2.22 (1.27, 3.88)
KHPT/THALI 2018 (Hyderabad) Education: illiterate vs. primary completed 0.46 (0.24, 0.88)
Shewade 2019 (Multi-site) Job: daily wage laborer vs. unemployed 2.17 (1.11, 4.23)
Helfinstein 2020 (Chennai slums) Job: laborer vs. Homemaker 1.64 (1.11, 2.43)
Helfinstein 2020 (Chennai slums) Job: professional vs. Homemaker 1.67 (1.03, 2.70)
Helfinstein 2020 (Chennai) Job: professional vs. Homemaker 1.72 (1.15, 2.58)
Satyanarayana 2012 (Multi-site) Residence: rural vs. urban location 1.70 (1.02, 2.83)
Satyanarayana 2012 (Multi-site) Region: North vs. South India 2.50 (1.30, 4.80)
Satyanarayana 2012 (Multi-site) Region: East vs. South India 3.90 (2.04, 7.45)
Clinical factors
Fochsen 2006 (Madhya Pradesh) No prior TB vs. prior history of TB 2.70 (1.41, 5.15)
Fochsen 2006 (Madhya Pradesh) Absence of fever 1.80 (1.20, 2.70)
Fochsen 2006 (Madhya Pradesh) Shorter duration of cough (per week)* 1.05 (1.03, 1.07)
Helfinstein 2020 (Chennai slums) Decreasing days of symptoms* 1.59 (1.37, 1.85)
Helfinstein 2020 (Chennai slums) Decreasing number of symptoms* 1.28 (1.11, 1.47)
Helfinstein 2020 (Chennai) No pre-existing comorbidity (e.g., diabetes) 1.28 (1.02, 1.61)
Helfinstein 2020 (Chennai) Sleeps 6+ vs. <6 hours per night 1.28 (1.03, 1.60)
Helfinstein 2020 (Chennai) Exercises 1+ days vs. <1 day per week 1.45 (1.09, 1.93)
Helfinstein 2020 (Chennai) Smokes tobacco 1.67 (1.14, 2.44)
Helfinstein 2020 (Chennai) Probable alcohol use disorder 1.89 (1.25, 2.85)
Knowledge-related factors
KHPT/THALI 2018 (Hyderabad) Lacks comprehensive TB knowledge 2.44 (1.48, 4.02)
George 2013 (Uttar Pradesh) Does not know persistent cough suggests TB 5.36 (1.89, 15.19)
George 2013 (Karnataka) Does not know persistent cough suggests TB 1.81 (1.13, 3.46)
George 2013 (Uttar Pradesh) Does not know TB is caused by germs 5.89 (3.48, 9.96)
George 2013 (Karnataka) Does not know TB is spread by air 1.67 (1.13, 2.46)
George 2013 (Uttar Pradesh) Does not know TB can affect anybody 1.27 (1.09, 1.47)
George 2013 (Karnataka) Does not know TB is life threatening 0.65 (0.51, 0.83)
George 2013 (Karnataka) Does not know TB is curable 1.65 (1.12, 2.43)
George 2013 (Karnataka) Does not know sputum can be tested for TB 1.53 (1.05, 2.23)
George 2013 (Karnataka) Does not know sputum test can confirm TB diagnosis 2.40 (1.54, 3.75)
George 2013 (Uttar Pradesh) Thinks TB can be confirmed by blood test 1.19 (1.09, 1.29)
George 2013 (Uttar Pradesh) Thinks TB spreads by physical contact 1.42 (1.16, 1.74)
Helfinstein 2020 (Chennai) Does not get health information from doctors 1.43 (1.02, 2.01)
Helfinstein 2020 (Chennai) Decreasing personal valuing of good health* 1.19 (1.07, 1.33)
Healthcare-seeking factors
George 2013 (Karnataka) Unfavorable view of local quality of health care 2.99 (2.05, 4.37)
Helfinstein 2020 (Chennai) Facility preference: None vs. government facilities 1.52 (1.11, 2.08)
Helfinstein 2020 (Chennai) Increasing worry about transport costs to facilities* 0.85 (0.74, 0.97)
George 2013 (Uttar Pradesh) Lacks self-efficacy in seeking care 1.89 (1.33, 2.68)
George 2013 (Karnataka) Lacks self-efficacy in seeking care 1.84 (1.38, 2.46)
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C6. **ONGOING ZOONOTIC TUBERCULOSIS TRANSMISSION FROM DEER TO HUMANS: TWO NEW CASES IN MICHIGAN**

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BACKGROUND

Spillover of Mycobacterium bovis infection from wildlife to humans is uncommon, but in northern lower Michigan (United States) free-ranging white-tailed deer have been a source of disease for other wildlife, cattle, and even humans. Since M. bovis was first detected in the deer of this region in 1994, the Michigan Department of Natural Resources has conducted TB surveillance and archived M. bovis isolates. M. bovis infection was previously identified in three humans (2002, 2004, 2017), all associated with deer hunting-related activities. This report describes two additional M. bovis infections identified in humans in Michigan.

METHODS

In both cases, after the patients' cultures revealed M. bovis infection, an in-depth case investigation with whole-genome sequencing was performed.

RESULTS

Patient 1, a taxidermist, presented in 2019 with a chronic finger abscess; M. bovis was isolated from the wound. The patient recalled preparing deer from northern lower Michigan. Patient 2 presented in 2020 with pulmonary disease; M. bovis was isolated from respiratory specimens. The patient recalled hand-feeding deer in northern lower Michigan several years prior. In both cases, the whole genome sequences shared very recent common ancestors with isolates recovered in the region, indicating spillover into these humans.

CONCLUSION

This report demonstrates ongoing spillover of M. bovis infection from deer to humans in Michigan. The previously described cases associated with hunting activities resulted in targeted efforts to educate hunters about prevention strategies. This current report demonstrates that the risk of M. bovis extends beyond hunters, suggesting the need for a broader educational approach in the endemic region.

C7. DEVELOPING A RISK PREDICTION MODEL FOR USE AS A TOOL TO SCREEN MIGRANTS IN A LOW TB INCIDENCE COUNTRY

Puyat JH, Shulha H, Johnston J

BACKGROUND
There are tools to estimate risk of active TB among those who were TST-/IGRA-tested, but none is available for estimating pre-test risk. Pre-test TB models would be valuable to help risk stratify patients, particularly given the low predictive value of TST and IGRAs. We propose a risk prediction model for use as a pre-test screening tool among migrants in a low TB incidence country.

METHODS
We examined linked health and TB registry data from individuals who migrated to British Columbia, Canada from 1996-2013. We tested extended proportional hazard models containing combinations of time-invariant (age at index date, sex, refugee status, TB incidence from country of origin) and time-varying variables (TB contact history, comorbidities, and use of immune suppressants). The models' predictive performance was assessed using discrimination and calibration statistics and calibration plots, generated using cross-validations and bootstraps.

RESULTS
A total of 715,537 individuals, including 1407 with active TB, were included in the cohort. The cross-validated models yielded discrimination index ranging from 0.65 to 0.68, calibration-in-the-large ranging from -0.0007 to -0.0005, and calibration slopes between 0.9672 and 0.9845. All tested models perform equally well, but the most stable was the simplest model containing only categorical variables without interaction terms. Calibration plots of this model indicate very good correspondence between predicted and observed risks. Plots of cumulative incidence by risk quartiles indicate good separation of groups with varying risk levels.

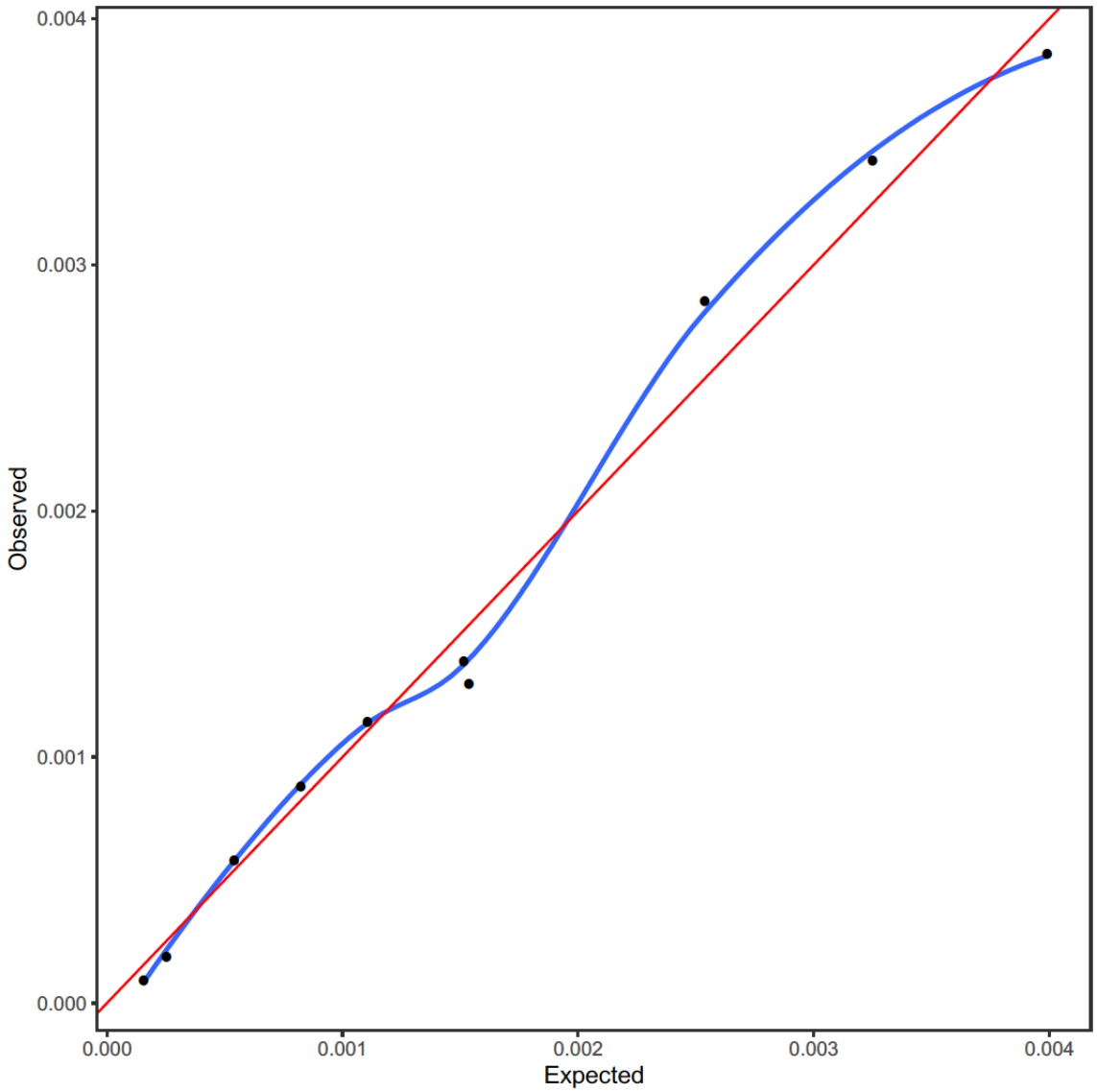
CONCLUSION
The risk prediction models developed and tested appear to have adequate discrimination and calibration properties. Further work is needed to externally validate this model and maximize its use as a screening tool in the clinical setting.

Discrimination and calibration statistics obtained from 20 x 10-fold cross validation

Models	Discrimination	Calibration-in-the-large	Calibration slope
Model 1: Age and TB incidence from country of origin modeled as numeric variables	0.7820	-0.0005	0.9822
Model 2: Age and TB incidence from country of origin modeled as numeric variables, plus age X TB incidence interaction	0.7804	-0.0007	0.9665
Model 3: Age and TB incidence from country of origin modeled as categorical variables	0.7804	-0.0005	0.9841
Model 4: Age and TB incidence from country of origin modeled as categorical variables, plus age X TB incidence interaction	0.779	-0.007	0.9749
Model 5: Stratified by TB incidence from country of origin	0.7265	-0.0007	0.9826

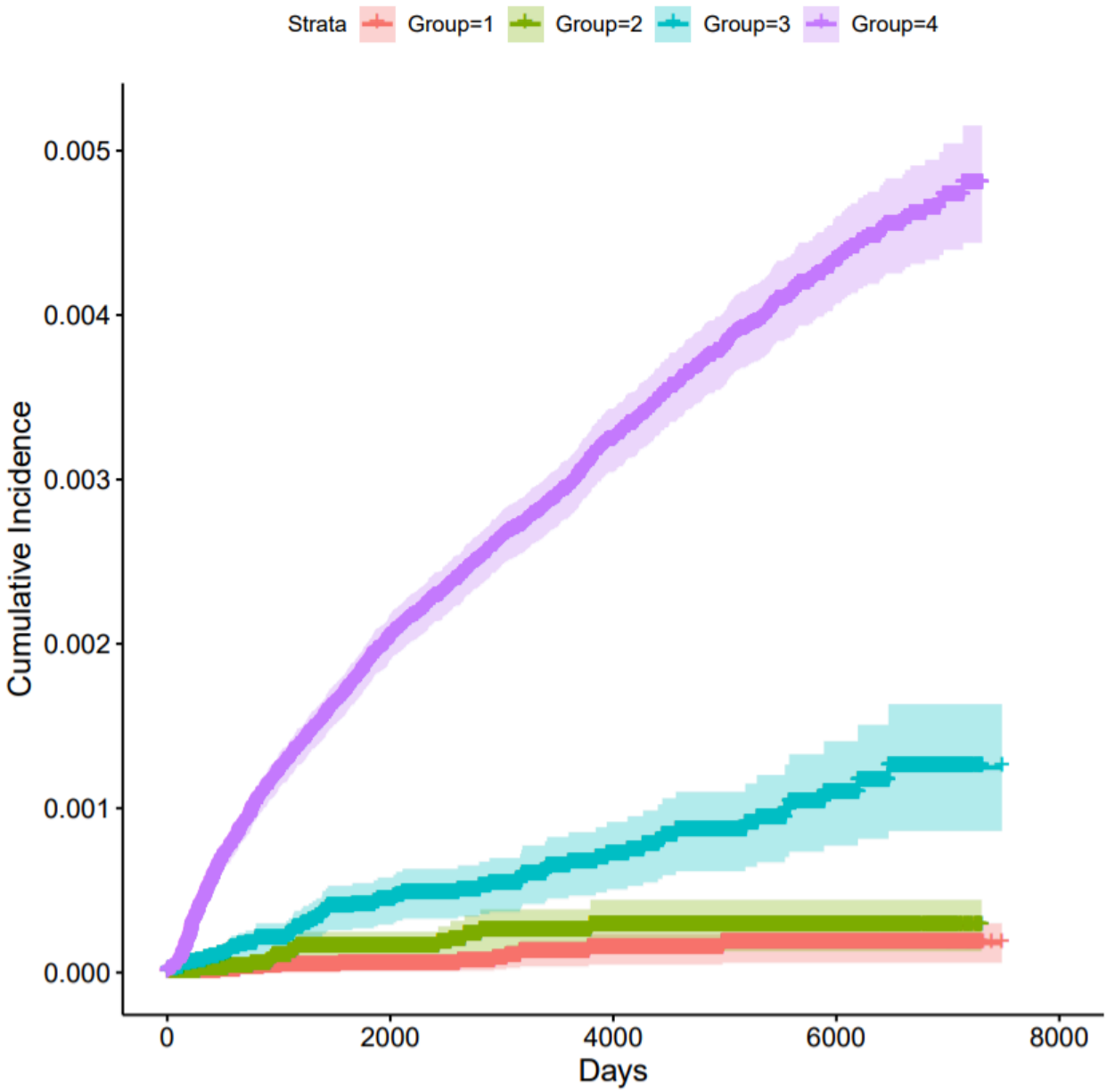
Discrimination was assessed using Harrel's concordance index while calibration-in-the-large and calibration slope were calculated following Crowson's model-based calibration procedure.16 A c-index equal to or near 1 indicates perfect discrimination. Calibration-in-the-large equal to zero indicate that there is no difference between the overall observed and predicted risks (no over or underestimation). Calibration slope measures the spread or variation in the predicted risk across observed risk; a value of 1 indicates perfect calibration whereas values less than 1 suggest overfitting and values over 1 suggest underfitting. Models 1 through 5 contain the following predictors: (time-invariant) age at index date, sex, refugee status, TB incidence from country of origin (time invariant); (time-varying) contact history, diabetes, HIV, chronic kidney disease, cancer, solid organ transplant, TNF inhibitors, steroids, biologic, cytotoxic, disease modifying anti-rheumatic drugs, high (DMARDH), DMARDL. The five models differ in terms of whether a) age at index and TB incidence at country of origin were entered as continuous vs categorical variables, b) interaction terms were included, and c) stratification by TB incidence from country of origin was used.

Mean observed risk (y-axis), grouped by deciles, plotted against the mean risk (x-axis) predicted by the model



The risk prediction model contains the time-invariant variables age at index date (categorical), sex, refugee status, TB incidence from country of origin (categorical); and the following time-varying variables: contact history, diabetes, HIV, chronic kidney disease, cancer, solid organ transplant, TNF inhibitors, steroids, biologic, cytotoxic, disease modifying anti-rheumatic drugs, high (DMARDH) and DMARDL.

Incident TB risk across quartiles derived from the risk prediction model



The risk prediction model contains the following time-invariant variables age at index date (categorical), sex, refugee status, TB incidence from country of origin (categorical); and the following time-varying variables: contact history, diabetes, HIV, chronic kidney disease, cancer, solid organ transplant, TNF inhibitors, steroids, cytotoxic, disease modifying anti-rheumatic drugs, high (DMARDH) and DMARDL.

C8. SPATIAL CHARACTERIZATION OF PEDIATRIC TUBERCULOSIS IN UKRAINE USING GEOGRAPHIC INFORMATION SYSTEM

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BACKGROUND

The incidence of tuberculosis in Ukraine is the second highest in Europe, but increasingly affected pediatric populations have received relatively little attention. In 2015, the Ukrainian government mandated universal reporting of TB using the "e-TB Manager" database. Our aim is to analyze the geographic distribution of pediatric tuberculosis patients using Geographic Information System (GIS) to identify hotspots in Ukraine.

METHODS

We identified all children <15 years old treated for tuberculosis between January 1, 2015 and December 31, 2018 in Ukraine (n=2324). Pediatric TB incidence was estimated in all 136 Ukrainian "District" administrative subdivisions based on location of initial patient presentation. Using GIS technology, we also determined the locations and relative treatment burdens of TB treatment centers in the country.

RESULTS

Our assessment of the spatial distributions of pediatric tuberculosis cases has revealed significant heterogeneity, including several areas of notably increased incidence. These population-densityadjusted clusters include Ukraine's central-southern districts, with the exception of the capital of Kyiv. The strikingly low disease burdens in several eastern districts overlap with areas of inconsistent national government control and raise suspicion for lack of reporting in separatist controlled regions.

CONCLUSION

Owing to now universal reporting of pediatric tuberculosis cases in Ukraine, GIS technology may be a useful tool for identifying specific areas of high rates of transmission. We believe that determining which areas are at increased risk for future outbreaks will allow for effective, targeted interventions that may decrease morbidity and mortality in vulnerable pediatric populations.

C9. **TBDATA4ACTION: USING LOCAL DATA TO IMPROVE THE QUALITY OF CARE IN TB PROGRAMS IN KENYA**

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BACKGROUND

TB Programs routinely collect data regarding notifications, age, gender, treatment outcomes, HIV indicators, and drug resistance. Data is passed upwards through the health system ultimately reporting to WHO. To date, this locally generated data has rarely been utilized to inform program implementation.

METHODS

TBData4Action is an approach, developed by the Zimbabwe National TB Program and The Union, of local staff utilizing their own data coupled with support supervision to improve TB indicators, patient management and programmatic performance. Key element is data conversion into rates per 100,000 population or percentages allowing for comparison over time (usually, a quarter or year) and between facilities, sub-counties and counties. In 2017 the Kenya National TB Program, the Centre for Health Solutions, and The Union introducedTBData4Action throughout Kenya.

RESULTS

Over 3 years, through 11 trainings, >300 coordinators were trained. Trainings consisted of 7-day curriculum for TB care and prevention. One day was devoted to TBData4Action training followed by 2 days of field practicums where teams visited 3 health facilities to perform support supervision using facility data. On the final day each sub-county team utilizes their data to develop action plans to address programmatic gaps.

CONCLUSION

Locally collected data is underutilized in day-to-day operations in most TB programs. TBData4Action is an approach for clinicians and TB coordinators using their own data for finding 'missing' people with TB and strengthening quality of services. The approach is integrated into support supervision and performance review meetings. Ongoing analysis is required to determine TBData4Action's longer impact on programmatic indicators.

B. COVID

B1. HOW IS THE COVID-19 PANDEMIC AFFECTING TUBERCULOSIS SURVEILLANCE IN THE UNITED STATES?

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BACKGROUND
The COVID-19 pandemic has led to widespread disruptions to health department routines as work duties are reassigned to prioritize COVID-related activities. We explored the pandemic's effects on the National Tuberculosis Surveillance System (NTSS).

METHODS
We compared the tuberculosis (TB) case count reported to NTSS during January 1–July 31, 2020, with the average count during the same 7 months in 2016–2019, at both national and state levels. We reviewed information shared from 52 TB programs (50 states, New York City, and Washington DC) regarding how the COVID-19 pandemic is affecting TB prevention activities and surveillance.

RESULTS
The number of verified TB cases reported to NTSS as of July 31, 2020, was 14.7% lower than the average number reported during the equivalent period in 2016–2019. For individual states, relative changes in reported cases ranged from −100% to +113%. Most programs reported difficulties maintaining core TB services, including contact tracing, because of staff reassignments and community fears of COVID-19 exposure. Some programs anecdotally reported delays in case reporting and ascertainment; programs also reported receiving fewer notifications that post-arrival screenings were needed for newly arrived immigrants and refugees.

CONCLUSION
Even with an average annual decline of <1% in recent years, reported TB cases to date are dramatically lower in 2020. Multiple factors have likely contributed to this decline. This decline may represent underascertainment/underreporting or reflect a true decline in U.S. TB incidence. Further evaluation of NTSS and complementary data sources is needed to understand the root causes of this decline in TB case reporting.

B2. RAPID SCALE-UP OF TELEHEALTH FOR TUBERCULOSIS PATIENTS IN NEW YORK CITY DURING THE COVID-19 PANDEMIC

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BACKGROUND

New York City Bureau of Tuberculosis Control (BTBC) operates four tuberculosis (TB) clinics. In response to the COVID-19 pandemic, BTBC temporarily closed three TB clinics and quickly expanded telehealth coverage to minimize patient travel and direct provider-patient interaction.

METHODS

Providers reviewed medical records and screened patients with TB and latent TB infection (LTBI) for telehealth eligibility. Patients were eligible for telehealth visits if they were medically stable, not requiring in-person supervision for clinical improvement, and additionally demonstrated ability in using a video-enabled device. At telehealth visits, providers called patients with audio- and/or videoconferencing and assessed treatment progress. BTBC delivered medications to patients' homes by mail or in-person.

RESULTS

Between March 1 and September 1, 2020, 615 patients completed 2,152 (84%) of 2,575 scheduled telehealth appointments. In March and April, at the height of the COVID-19 pandemic in NYC, the median daily number of telehealth visits increased from 1 (IQR 0-4.75) to 24.5 (IQR 22-33.8). Of 615 patients, 196 (32%) received treatment for active TB disease, 338 (55%) for LTBI, and 81 (13%) other patients were evaluated for TB or LTBI. A small proportion (15/2,152, < 1%) of telehealth visits were conducted with video, because of initial challenges in implementing new technologies.

CONCLUSION

BTBC scaled up its telehealth program to provide continuity of TB care during the pandemic, while minimizing the healthcare-associated risk of COVID-19 exposure. Further evaluation is needed to assess provider acceptance, patient satisfaction, and treatment outcomes with telehealth.

B3. **IMPACT OF COVID-19 PANDEMIC ON LATENT AND ACTIVE TUBERCULOSIS TREATMENT REGISTRATIONS IN MONTRÉAL, CANADA: A RETROSPECTIVE STUDY AT THE MONTRÉAL CHEST INSTITUTE**

Geric C*[1, 2], Saroufim M*[1], Mannix S[3], Tchabo Fosso A[3], Francis D[3], Boitor O[3], Richard J[3], Benedetti A[1,2], Ahmad Khan F[1,3], *co-first authors. [1]McGill International TB Centre, Research Institute of the McGill University Health Centre, Montreal, Canada; [2]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada; [3]Montreal Chest Institute, McGill University Health Centre, Montreal, Canada

BACKGROUND

We sought to assess the effect of the COVID-19 pandemic on registrations for treatment of latent tuberculosis infection (LTBI) or active tuberculosis at the Montreal Chest Institute (MCI), since Montreal is the city with the highest number of COVID-19 cases and deaths in Canada.

METHODS

We used data from the MCI Tuberculosis Clinic E-Chart, which included all registered patients with LTBI or active tuberculosis since November 26, 2005. Separately for LTBI and active tuberculosis, we compared the number of registrations per week since the Quebec government declared a public health emergency ("COVID era" as Week 11, 2020 and after) to the number per week prior to this ("pre-COVID" era). Using Poisson regression, we estimated rate ratios comparing the number registered per week in the COVID and pre-COVID eras, adjusting for year, and week of the year.

RESULTS

Between November 26, 2005, and June 23, 2020, we registered 6849 patients for LTBI treatment (6801 pre-COVID, 48 COVID era) and 902 for active TB treatment (890 pre-COVID, 12 COVID era). Figure 1(a) shows the average number of LTBI treatment registrations per week in the pre-COVID (blue) and COVID (red) eras, and Figure 1(b) shows this for active TB. Compared to pre-COVID, there was a 59% reduction in the registration rate for LTBI treatment during the COVID era (rate ratio=0.41 $p<0.0001$), and a 24% reduction for active TB treatment (rate ratio=0.76, $p=0.37$).

CONCLUSION

The COVID-19 pandemic has negatively affected LTBI and active TB management in Montreal and strategies to mitigate this need to be implemented.

B4. **COVID-19 AMONG PATIENTS WITH TUBERCULOSIS IN NEW YORK CITY**

Easton AV, Salerno M, Macaraig M, Humphrey E, Trieu L, Nilsen D, Burzynski J.

BACKGROUND
Patients with tuberculosis (TB) and COVID-19 may be at high risk for poor health outcomes. We examined the demographics, clinical characteristics, and health outcomes of TB patients with COVID-19 in New York City (NYC).

METHODS
Patients who were under care for TB disease in NYC between March 1 and November 10, 2020 were deterministically matched to COVID-19 surveillance data based on demographic identifiers, including name, birthdate, and address. Case managers documented patients' clinical status throughout TB care. Chi-squared and Wilcoxon rank sum tests were used to determine statistical differences between TB patients coinfected with COVID-19 and patients with TB-only.

RESULTS
Of 703 TB patients, 39 (6%) were matched with a positive COVID-19 test result. Five (13%) tested positive for COVID-19 within one week of TB diagnosis, 24 (62%) were already under care for TB when they got COVID-19, and ten (26%) were diagnosed with TB over a week after a positive COVID-19 test. Compared to patients with TB-only, coinfected patients were older (median 62 vs 50 years, $p<0.01$), and more likely to have diabetes mellitus (36% vs 21%, $p=0.045$). Similar proportions were female (44% vs 39%, $p=0.67$) and non-U.S.-born (87% vs 85%, $p=0.84$). Ultimately, a higher proportion of coinfected patients died (28% vs. 4%, $p<0.01$) as of November 10.

CONCLUSION
Mortality was higher among persons coinfected with TB and COVID-19 than among those with TB alone. Further analysis is needed to assess the impact of COVID-19 on the clinical course of patients with TB and to find effective ways to support their care.

B5. **RISK FACTORS FOR SEVERITY OF COVID-19 IN HOSPITAL PATIENTS AGE 18-30 YEARS**

Sandoval M, Nguyen DT, Graviss EA.

BACKGROUND
Since February 2020, over 1 million Texans have been diagnosed with COVID-19, and 20% are young adults at risk for SARS-CoV-2 exposure at work, academic, and social settings.

METHODS
A retrospective chart review was conducted investigating demographic and clinical risk factors for severity for all patients aged 18-30 who tested positive for COVID-19 at the Houston Methodist Hospital, Texas, USA.

RESULTS
In the cohort of 1,649 young adult COVID-19 patients, the median age was 24 years (IQR 21, 27), 1,027 (62%) were women, including 204 pregnant women, and 713 (43%) were Hispanic. Although 78% scored 0 on the Charlson Comorbidity Index (CCI), 206 (13%) had asthma or COPD, and 667 (40%) were obese. In total, 72 (4.4%) and 53 (3.2%) reported history of cholecystectomy and appendectomy, respectively, while 737 (60%) were symptomatic, and 620 (38%) reported exposure to a sick contact. Within the diagnostic encounter, 234 (14%) patients were diagnosed with pneumonia, and 189 (11%) required supplemental oxygen, ventilation assistance, or ECMO. Most, 1,592 (97%) of these young adults were discharged home, but 285 (17%) returned to the hospital within 30 days. In multivariable logistic regression analyses, increasing age (aOR: 1.1, p-value: <0.001), male gender (2.1, <0.001), Hispanic ethnicity (1.7, 0.021), class 3 obesity (2.3, <0.001), cerebrovascular disease (4.0, 0.035) and increasing CCI score: score 1-2 (2.3, <0.001, 3-4 (4.9, 0.018), >4 (9.0, 0.004) were predictive of respiratory interventions.

CONCLUSION
Health authorities must emphasize COVID-19 awareness and prevention in young adults and continue investigating risk factors for severe disease, readmission and long-term sequalae.

E. TREATMENT

E1. **TRENDS IN MAGNITUDE AND TREATMENT OUTCOMES OF TUBERCULOSIS PATIENTS IN SOUTHERN ZONE OF TIGRAY REGION, NORTHERN ETHIOPIA: A FIVE-YEAR RETROSPECTIVE STUDY**

Embaye GK, Gezihegn AD, Gebrekidan MG.

BACKGROUND
Tuberculosis (TB) is one of the world's most pressing health challenges and one of the top ten causes of death – yet it is a treatable and curable disease. Ethiopia had 200,000 new cases and ranked 10th globally and 4th in Africa.We analyzed the trends in magnitude and treatment outcomes of TB in Southern zone of Tigray region, Ethiopia, from 2012-2016.

METHODS
We conducted retrospective secondary data review from (2012-2016) in March 2017. Data were extracted from Health Management Information System data base of eight district health offices reported on a quarterly basis using the WHO reporting format and analyzed using Microsoft Excel 2010.

RESULTS
A total of 8,804 all forms TB cases and 198 (3.8%) deaths were reported, of which 4,938(56%) were males and 7,687 (87.3%) were in adults >15 years. The average incidence and prevalence of all forms of TB was 259/100,000 and 410/100,000 population. Eleven percent of the TB cases were co-infected with HIV. Half, 1,050 (49%) of TB patients were cured and the overall treatment success rate was 94.8%.

CONCLUSION
TB is more prevalent in males and those aged >15 years. Majority of the cases were smear negative pulmonary TB. Even though, the incidence and prevalence rate of all forms of TB seems to be decreasing, intensified efforts are needed to decrease the disease burden to the national target which is 200/100,000 population. In the current study, the rate of successful TB treatment outcome was acceptable. This rate should be maintained and further improved by designing appropriate monitoring strategies.

E2. TB PREVENTATIVE TREATMENT (TPT) FOR DRUG SUSCEPTIBLE TB PATIENTS IN LANDHI AND KORANGI TOWNS IN KARACHI, PAKISTAN

Malik AA[1,2,3], Jaswal M[2], Farooq S[2], Safdar N[2], Khan AJ[3], Keshavjee S[4], Becerra MC[4], Hussain H[3]. [1]Yale Institute for Global Health, New Haven, USA; [2]Global Health Directorate, Indus Health Network, Karachi, Pakistan; [3]Interactive Research and Development (IRD) Global, Singapore; [4]Harvard Medical School, Boston, USA

BACKGROUND

There are many barriers to TPT including long duration of treatment. Recently, WHO has recommended a shorter regimen, 3HP for treating household contacts.

METHODS

A prospective study of systematic contact screening and TB preventive treatment for household contacts of TB patients was conducted from October 2016 to September 2017. All household contacts were invited to enroll in the study and were verbally screened for TB symptoms. These household contacts were evaluated for TB disease with clinical evaluation, chest x-ray and sputum examination using MTB/RIF assay if able to provide a sputum sample. Contacts free of active TB disease were offered treatment with either 6 month of isoniazid (INH) or 3HP (if > 2 years of age). Contacts were followed up regularly at the clinic and over the phone.

RESULTS

A total of 6,767 household contacts of 2,004 index patients consented to participate of which 5,876 (82%) were screened verbally for TB symptoms. 3,254 (55%) of screened contacts completed disease evaluation of which 59 (1.8%) were diagnosed with TB disease. 864 and 1475 contacts initiated treatment with INH and 3HP, respectively. 404 (47%) of the INH group and 968 (66%) of the 3HP group completed treatment. Age and sex adjusted OR for treatment completion for 3HP vs INH was 2.2 (95%CI: 1.8-2.6).

CONCLUSION

This was the first time where TB preventive treatment was offered for the whole household in Pakistan in a program setting with 3HP showing better completion. Results are encouraging for other low-income settings for implementation.

E3. **ADHERENCE TO TUBERCULOSIS PREVENTATIVE THERAPY IN A NOVEL COMMUNITY-BASED DIFFERENTIATED CONTACT MANAGEMENT PROGRAM IN ESWATINI**

Sandoval M, Mtetwa G, Dube G, Devezin T, Sibanda J, Mandalakas AM, Kay A.

BACKGROUND
Eswatini is a high TB/HIV burden country; with 65% coinfection rate , and the prevention of TB disease in child contacts of TB cases and people living with HIV is a public health priority. In April 2019, we implemented Vikela Ekhaya, a community-based TB contact management program.

METHODS
Vikela Ekhaya offered differentiated TB and HIV testing and care for household contacts of TB cases, by utilizing mobile contact management teams to screen contacts, assess their eligibility for TB preventive therapy (TPT), initiate and then monitor TPT adherence in participants' homes. Pill counts, self-reported missed doses, measures of drug acceptability, and caregiver beliefs about TPT and TB were collected to supplement adherence monitoring.

RESULTS
949 contacts from 235 households were screened for TB symptoms. 321 (98%) of eligible asymptomatic household contacts initiated TPT; 248 children under 15 initiated 3HR, while 74 children and adults living with HIV initiated 6H (standard of care). 305 (95%) of participants completed TPT, with facility-based care and low household income emerging as risk factors for discontinuing treatment. 45 (11%) of participants reported missing at least one dose; in household-clustered logistic regression analysis, low household income, unknown HIV status, and urban setting were associated with increased risk of missing at least one dose (aORs: 2.1, 3.1, 3.8; P-values: 0.041, 0.004, <0.001).

CONCLUSION
The findings support implementation of differentiated community-based care, the use of 3HR in children at risk for TB and identified risk factors for missed TPT doses. This model of care needs further study in high HIV/TB burden settings.

E4. **UNDERSTANDING NON-ADHERENCE TO TUBERCULOSIS MEDICATIONS IN INDIA USING URINE METABOLITE TESTING: A COHORT STUDY**

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¶These authors contributed equally to this work

BACKGROUND

Suboptimal adherence to tuberculosis (TB) therapy is associated with increased risk of death, disease recurrence, and development of drug resistance. In India, little research has been conducted to understand factors contributing to non-adherence, particularly using rigorous measures, such as testing for medication metabolites.

METHODS

We enrolled adult drug-susceptible TB patients in Chennai, Vellore, and Mumbai. We conducted an unannounced home visit (i.e., without prior notice) to assess reasons for non-adherence and collect a urine sample that was tested for isoniazid content. We used multivariable logistic regression to identify factors associated with non-adherence (negative urine test).

RESULTS

Out of 650 patients in the cohort, 77 (11.8%) had a negative urine isoniazid test result. In the regression model, age 25-34 (aOR 3.0, CI: 1.3—7.0), daily wage labor (aOR 3.1, CI: 1.3—7.5), smearpositive pulmonary disease (aOR 2.1, CI: 1.1—1.4), spending >=60 minutes getting to the clinic to pick up medications (aOR 9.2, CI: 1.9—45.7), and alcohol use disorder (aOR 2.5, CI: 1.2—5.4) were significantly associated with non-adherence (Table). Of 167 patients who reported missing doses, the most common reasons reported were traveling away from home, forgetting, feeling depressed, and running out of pills, reported by 67 (40%), 50 (30%), 39 (23%), and 35 (21%) patients, respectively.

CONCLUSION

Challenges in picking up medication refills, traveling away from home, alcohol use disorder, and feelings of depression were major contributors to non-adherence. Addressing these structural and psychosocial barriers will be critical to improve adherence and TB treatment outcomes in India.

Covariates	Multivariable findings	
	Adjusted odds ratio (confidence interval)	p-value
Gender		
Female	Ref	
Male	0.8 (0.4—1.6)	0.50
Age		
18-24	Ref	
25-34	3.0 (1.3—7.0)	0.01*
35-44	0.8 (0.3—2.1)	0.68
≥45	0.6 (0.2—1.7)	0.37
Income quartiles		
<5,000	Ref	
5000—9,999	0.7 (0.3—1.4)	0.27
10,000—14,999	1.1 (0.5—2.6)	0.76
>=15,000	0.6 (0.2—1.5)	0.26
Occupation		
Self employed	Ref	
Government/private employment	1.8 (0.8—4.3)	0.16
Laborer on daily wages	3.1 (1.3—7.5)	0.01*
Unemployed	1.9 (0.8—4.5)	0.13
Housewife or student	1.0 (0.3—2.9)	0.99
Phase of Therapy		
Intensive phase	Ref	
Continuation phase	1.5 (0.9—2.6)	0.15
Category of TB		
Category I	Ref	
Category II	1.6 (0.9—2.9)	0.11
Type of TB		
Extrapulmonary	Ref	
Smear-negative pulmonary	2.0 (0.8—4.9)	0.5
Smear-positive pulmonary	2.1 (1.1—4.1)	0.02*
HIV co-infection		
No	Ref	
Yes	1.5 (0.6—3.8)	0.38
Time Spent to Collect Medication		
<30 minutes	Ref	
30 to 59 minutes	6.2 (1.4—28.1)	0.02*
>=60 minutes	9.2 (1.9—45.7)	0.01*
Alcohol use disorder		
No use or non-hazardous use	Ref	
Hazardous alcohol use	2.5 (1.2—5.4)	0.02*

E5. **THE EFFECTS OF ISONIAZID PREVENTATIVE THERAPY ON SUBCLINICAL TUBERCULOSIS**

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BACKGROUND

Preventive therapy is recommended for people with latent tuberculosis infection (LTBI) but have not developed active tuberculosis. Recent research has demonstrated that incipient and subclinical tuberculosis are the two additional clinical stages between LTBI and active tuberculosis. The effect of preventive therapy on these two stages remain unknown.

METHODS

In a prospective cohort study conducted between 2009 and 2012 in Lima, Peru, we enrolled 14,044 household contacts (HHCs) of incident tuberculosis patients and followed them for incident tuberculosis. We defined HHCs as having subclinical tuberculosis at enrollment if they had abnormal chest X-ray but had not developed tuberculosis symptoms. We evaluated the effect of isoniazid preventive therapy (IPT) on incident tuberculosis among the child contacts (age≤19) who had subclinical tuberculosis. We further examined whether the effect of IPT varied by the isoniazid resistance profile.

RESULTS

Among 52 child contacts with subclinical tuberculosis, 24(46%) received IPT at enrollment. Child contacts who received IPT were less likely to develop active tuberculosis by 6-month follow-up than those who did not (adjusted risk ratio[95%CI]=0.19[0.04-0.84]). The efficacy of IPT against tuberculosis progression remained strong among HHCs exposed to isoniazidresistant Mycobacterium tuberculosis (0.17[0.02-0.94]).

CONCLUSION

IPT protected the child contacts with subclinical tuberculosis from progressive tuberculosis, even when they had been exposed to isoniazid-resistant Mycobacterium tuberculosis. Besides the bactericidal effect, IPT may remedy TB through other unknown mechanisms.

E6. EVALUATION OF VIDEO-DIRECTLY OBSERVED THERAPY IMPLMENTATION UNDER ROUTINE CONDITIONS IN A BUSY URBAN TB PROGRAM

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BACKGROUND

Directly observed therapy (DOT) is commonly used for tuberculosis (TB) treatment support and adherence monitoring in the US. Video-DOT was proposed to increase flexibility and meet patient-specific needs. Alameda, California introduced video-DOT in a pilot program (2017) and for routine use (2018). We report on the reach and effectiveness of video-DOT implementation (2018-2020) during routine conditions.

METHODS

We prospectively evaluated video-DOT implementation at Alameda's TB program. We abstracted routinely-collected data to estimate 1) Reach (proportion of patients initiated on video-DOT versus in-person DOT) and 2) Effectiveness (proportion of prescribed doses with verified administration by video-DOT versus in-person DOT).

RESULTS

Among 163 TB patients, 94 (58%) utilized video-DOT during treatment, of whom 54 (57%) received exclusively video-DOT. Individuals receiving video-DOT were, on average, younger (46 years) than those receiving in-person therapy (61; $p<0.001$). Among individuals receiving video-DOT, median time from treatment start to video-DOT initiation was 2.2 weeks (IQR 1.1-10.0); patients were monitored for a median of 27.6 (IQR 24.6-31.9) weeks. Video-DOT led to higher proportions of prescribed doses verified by observation (68%) than in-person DOT (54% ; $p<0.001$). Unobserved self-administration commonly occurred for all patients on weekends (including video-DOT, based on clinic instructions), but a larger proportion of prescribed doses were self-administered using in-person DOT (45%) than video-DOT (24%; $p<0.001$). Patients were guided to intake non-observed, self-administered medications on weekends.

CONCLUSION

A busy TB program successfully implemented and maintained video-DOT over two years under routine conditions, independent of research activities, reaching the majority of patients and achieving greater medication verification than in-person DOT.

Poster Session 2

D. EPIDEMIOLOGY (2)

D1. **ECONOMIC EVALUATIONS OF ACTIVE CASE FINDING FOR TUBERCULOSIS AMONG HIGH-RISK GROUPS: A SYSTEMATIC REVIEW**

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BACKGROUND
Active case finding (ACF) is a strategy which requires the health system to seek out individuals in a community for screening and diagnosis of TB. Critical high-risk populations for targeted ACF include: people living with HIV (PLHIV) and persons with clinical or structural risk factors (i.e. diabetes, homeless, prisoners, and miners).

METHODS
We conducted a systematic review of the literature on economic evaluations of ACF for active TB. We searched three databases for studies published between 2010-2020. To be considered an economic evaluation, data about cost and health utility must have been reported.

RESULTS
A total of 27 articles were included in our review, the majority of which were conducted in Sub-Saharan Africa (54%). The most common ACF screening strategies included door-to-door visits and mobile CXR. ACF was shown to be cost-effective in 12/14 (86%) studies among PLHIV, with incremental cost-effectiveness ratios (ICERs) ranging from US$56-$2809 per disability-adjusted life year (DALY) averted using willingness-to-pay thresholds determined by study authors. There was significant heterogeneity in screening algorithms and unit costs included (table 1).

CONCLUSION
Studies reported here showed that cost-effectiveness is most likely in high TB prevalence settings and that programmatic costs such as additional staffing and transportation costs for door-to-door screening activities are key drivers of cost-effectiveness. Limited economic evidence was available for persons with clinical or structural risk factors.

Table 1: TB Screening Algorithm Costs in High-Risk Populations

Countries	Number of Studies	Screening Algorithm		Type of Unit Costs						Average Cost[1] of Screening Per Person	Average Cost[1] of Diagnosis Per Person
		Screening Tools Used	Diagnostic Tests	Staff	Equipment	Consumables	Overhead	Transport	TB Treatment		
People Living with HIV (PLHIV)											
Uganda, South Africa, Russia, Ethiopia, Vietnam, Mozambique, Malawi, Sub-Saharan Africa	13	WHO 4SS, CXR, LF-LAM, Xpert MTB/RIF	SSM, CXR, Xpert MTB/RIF	✓	✓	✓	✓	✓	✓	$2-$164 per person screened	$56-$2,809 per DALY averted
Elderly (55+)											
Cambodia, China	3	Symptom screen	Xpert, SSM, CXR	✓	✓	✓	✓	✓		$0.63-$1.82 per person screened	$72-$963 per person diagnosed
Workers with silica exposure (miners)											
Zimbabwe	1	WHO 4SS, CXR	Xpert MTB/RIF	✓		✓				$14 per person screened	$397 per person diagnosed
Prisoners											
Zimbabwe, Belgium, Former Soviet Union, South Africa	4	WHO 4SS, CXR, sputum smear	Xpert MTB/RIF	✓	✓	✓	✓		✓	$2.16-$35 per person screened	$451-€11,603 per person diagnosed; $543 per QALY gained
Persons with clinical risk factors (respiratory disease, GI, steroid use, fibrotic chest lesions, diabetes mellitus)											
China, Russia, Zimbabwe	3	CXR; WHO 4SS then CXR	SSM	✓	✓	✓		✓		$1.21 per person screened	$2,151-$101,879 per person diagnosed; $287.84 per DALY averted
Persons with structural risk factors (migrants/refugees, homeless, intravenous drug users, persons living in slums or remote areas, indigenous persons)											
Belgium, Russia, Uganda, Peru, United Kingdom, Cambodia, India, Papua New Guinea	9	Mobile or mass CXR screening; door-to-door visits; WHO 4SS	SSM; SSM and CXR; Xpert MTB/RIF	✓	✓	✓	✓	✓	✓	$0.42-$33 per person screened	$77- €418,359 per person diagnosed; £6400 per QALY gained; $3347 per DALY averted

Abbreviations: ACF, active case finding; CXR, chest x-ray; SSM, sputum smear microscopy; WHO 4SS, WHO four symptom screen; Xpert MTB/RIF, GeneXpert
[1]Costs in USD unless stated otherwise; '✓' indicates cost component was explicitly included in unit cost calculation

D2. ECONOMIC EVALUATIONS OF ACTIVE CASE FINDING FOR TUBERCULOSIS: CHILDREN, CONTACTS AND GENERAL POPULATION SCREENING; A SYSTEMATIC REVIEW

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BACKGROUND

Active case finding (ACF) has the potential to reduce the delay between symptom onset and when symptomatic individuals are diagnosed and treated, potentially decreasing community spread. We conducted a systematic review of economic evaluations of ACF for tuberculosis and have reported our results for the general population, children and household contacts of individuals with tuberculosis.

METHODS

We searched Embase, Ovid and SCOPUS databases for studies that were published within the past ten years. Studies had to include both costs and outcome data (in effectiveness or utility measures).

RESULTS

Twenty studies were identified among these specific subpopulations. The actual ACF intervention varied between studies and included door to door screening, screening of clinic attendees or inpatients and targeted screening of high risk subgroups. All studies were conducted in low or middle income countries. Most studies presented their outcomes as cost effectiveness estimates (cost per case diagnosed, 14/20).

Cost effectiveness of ACF among the general population ranged from 31-1626 USD per case detected, cost effectiveness for children ranged from 18-28 USD per case detected and cost effectiveness for household contacts ranged from 36-2693 USD per case detected. Key drivers of cost-effectiveness were underlying tuberculosis prevalence, false positive screen rates, downstream treatment costs and the inclusion of programmatic costs. The majority of studies (19/20) concluded that ACF was cost effective based on their pre-defined willingness to pay threshold, but there was significant heterogeneity among the diagnostic algorithm and costs included.

CONCLUSION

ACF was found to be cost effective in many subgroups but this depends on contextspecific factors and the underlying tuberculosis prevalence of the population.

D3. **POST-TUBERCULOSIS AIRWAY DISEASE: A POPULATION-BASED COHORT STUDY OF PEOPLE IMMIGRATING TO BRITISH COLUMBIA, CANADA, 1985-2015**

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BACKGROUND

Post-TB airway disease prevalence is estimated between 10-80%, although evidence is largely cross-sectional and derived from high-TB burden settings. We conducted the first cohort study of post-TB airway disease in low-TB-incidence setting. Aims: (1) analyze the risk of airway disease by TB status, (2) assess potential unmeasured confounding, and (3) investigate effect modification.

METHODS

We used a population-based cohort design to analyze administrative data for people immigrating to British Columbia (BC), Canada, from 1985-2015. Airway disease was defined as chronic airway disease, asthma, chronic bronchitis, or emphysema. Respiratory TB was defined from diagnostic and treatment data. Cox proportional hazards regression was used in primary analyses. To assess potential unmeasured confounding, we calculated e-values and used a hybrid of high-dimensional propensity score (hdPS) and LASSO.

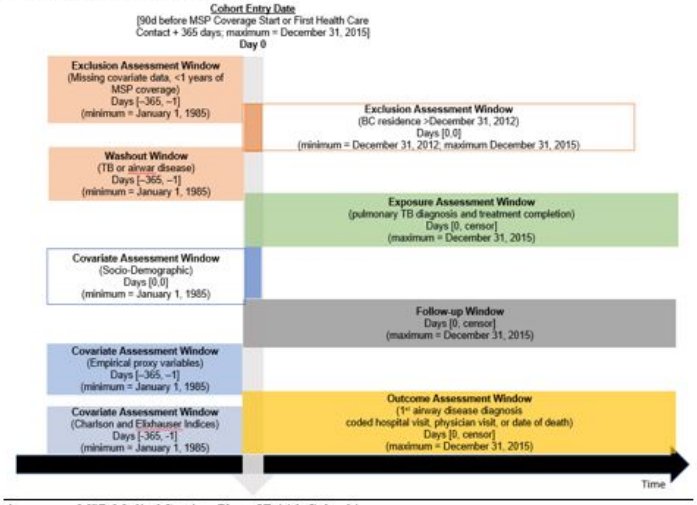
RESULTS

In our cohort (N=1,005,328), 116,840 people were diagnosed with airway disease during follow-up, producing a cumulative incidence of 42.5% among respiratory TB patients experiencing compared with 11.6% among non-TB controls. We observed a covariate-adjusted hazard ratio (aHR) of 1.66 (95% CI: 1.61-1.93). An unmeasured confounder with aHR>2.7 would be required to eliminate this effect based on the e-value for our primary analysis. The hybrid hdPS-LASSO analysis produced aHR=2.19 (95% CI: 2.00-2.39). People with fewer comorbidities experienced greater aHR for airway disease (aHR=2.13) than people with more comorbidities (aHR=1.49).

CONCLUSION

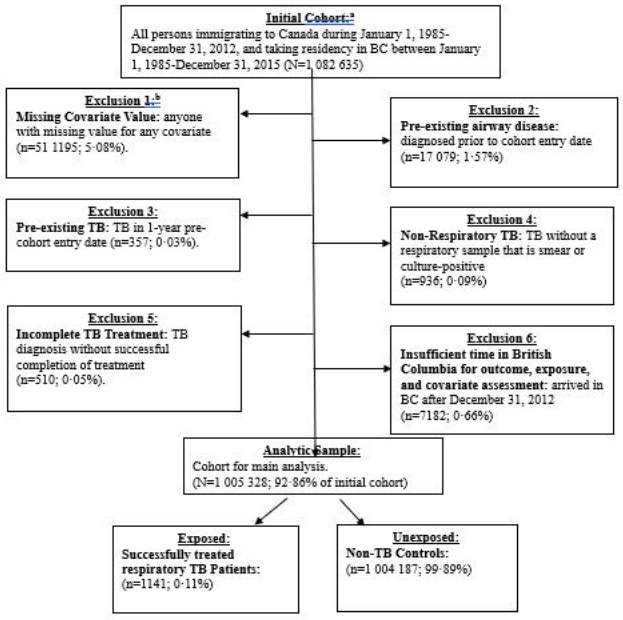
Post-TB airway disease is a concern in low-TB-incidence settings, with a 66% increased risk among people immigrating to BC and diagnosed with respiratory TB, compared with non-TB controls. Unmeasured confounding is unlikely to explain this elevated risk.

Figure 1. Design of retrospective cohort study of post-tuberculosis airway disease among immigrants to British Columbia, Canada, 1985-2015.



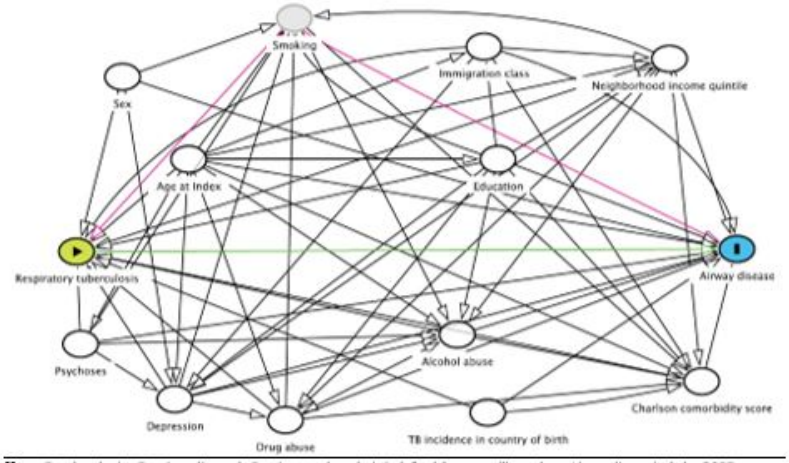
Acronyms: MSP, Medical Services Plan of British Columbia.
Notes: The MSP is a population-wide provincial health insurance registry that provides a reliable population-based denominator for the province of British Columbia.

Figure 2. Flow chart: analytic sample for post-tuberculosis airway disease among people immigrating to British Columbia, Canada, 1985-2015.



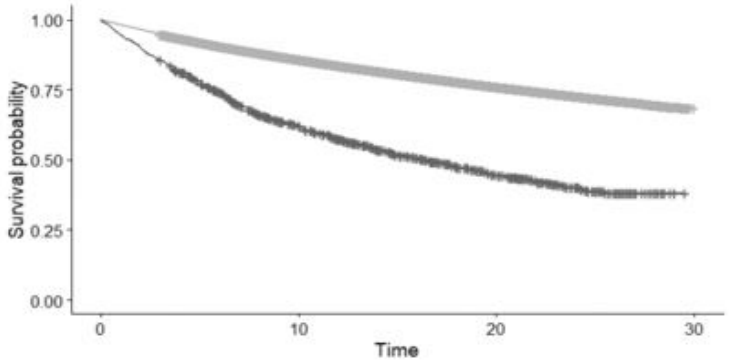
Notes: [a]Ascertained from IRCC permanent resident database. Residency in BC defined by acquisition of provincial health insurance (MSP) registration minus 90 days, or first healthcare contact, whichever occurred first. [b]Covariates for which people with a missing value were excluded were age, sex, income quintile, country of birth, immigration class, educational qualification, Charlson comorbidity index, or index year. Most people excluded in Exclusion 3 were due to missing value for income quintile. **Legend:** BC = British Columbia, BCCDC = British Columbia Centre for Disease Control, IRCC = Immigration, Refugees, and Citizenship Canada, TB = tuberculosis.

Figure 3. Directed acyclic graph (DAG) for post-tuberculosis airway disease among people immigrating to British Columbia, Canada, 1985-2015.



Notes: Developed using Daggity online tool. Respiratory tuberculosis is defined from surveillance data. Airway disease includes COPD, asthma, chronic bronchitis, bronchiolitis, and emphysema. **Legend:** TB = tuberculosis.

Figure 4. Kaplan-Meier plot for airway disease among people immigrating to British Columbia, Canada 1985-2015: tuberculosis survivors (black) vs non-tuberculosis controls (grey)



Time (years)	0	10	20	30
Number at-risk				
Respiratory TB	1141	644	244	*
Controls	1 004 187	487 329	147 470	*
Number events				
Respiratory TB	0	78 734	32 279	5342
Controls	0	333	132	20

Notes: *suppressed due to cell count <6. **Legend:** Black = Respiratory TB; Grey = non-TB controls.

Table 1. Cohort characteristics stratified by outcome (airway disease or censored) among people immigrating to British Columbia, Canada, 1985-2015

Characteristic	Censored N (%)	Airway disease N (%)	Hazard Ratio
Total	888 488	11 6840	-
Successfully treated respiratory tuberculosis	656 (0·074)	485 (0·42)	3·24*
Time-at-risk (mean (SD))	11·56 (7·36)	7·97 (6·02)	-
Sex = Male	432 751 (48·7)	54 592 (46·7)	0·95*
Age, years (mean (SD))	32·41 (16·33)	35·04 (18·81)	1·01*
Neighbourhood income quintile			
Highest 20%	133 301 (15·0)	13 468 (11·5)	-
Middle-High 20%	128 939 (14·5)	15 001 (12·8)	1·14*
Middle 20%	161 746 (18·2)	21 343 (18·3)	1·28*
Low-Middle 20%	201 033 (22·6)	29 692 (25·4)	1·40*
Lowest 20%	263 469 (29·7)	37 336 (32·0)	1·37*
Education level			
None/Unknown	109 282 (12·3)	18 657 (16·0)	-
Secondary or less	374 619 (42·2)	57 554 (49·3)	0·76*
Trade/diploma	164 367 (18·5)	20 595 (17·6)	0·65*
University degree	240 220 (27·0)	20 034 (17·1)	0·54*
Immigration class			
Economic	544 098 (61·2)	50 362 (43·1)	-
Family	253 158 (28·5)	50 522 (43·2)	1·86*
Other	23 900 (2·7)	3957 (3·4)	1·49*
Refugee	67 332 (7·6)	11 999 (10·3)	1·52*
TB incidence rate in country of origin at time of immigration			
<100 per 100 000 pop·	381 530 (42·9)	36 967 (31·6)	-
200 to <300 per 100 000 pop·	112 878 (12·7)	30 077 (25·7)	2·01*
100 to <200 per 100 000 pop·	292 116 (32·9)	35 552 (30·4)	1·02*
300+ per 100 000 pop.	101 964 (11·5)	14 244 (12·2)	1·23*
Year of arrival in BC (mean (SD))	15·16 (7·01)	10·21 (6·16)	0·96*
Charlson comorbidity score (mean (SD))	0·05 (0·33)	0·22 (0·65)	1·38*
Alcohol treatment	157 (0·018)	51 (0·044)	1·84*
Drug treatment	129 (0·015)	37 (0·032)	1·70*
Psychosis	174 (0·020)	29 (0·025)	1·03
Depression	4682 (0·53)	1037 (0·89)	1·42*
Personal health risk proxy variable	62 307 (7·0)	15 309 (13·1)	1·83*

Notes: Univariable Cox proportional hazards regression was used for hazard ratios for airway disease by each covariate. *significant at α=0·05

Table 2. Cox proportional hazards regression analyses: time-to-airway disease by respiratory TB status among people immigrating to British Columbia, Canada, 1985-2015

Statistical Analysis	*N*	aHR	95% CI
Aim 1: analyzing post-TB airway disease risk			
Covariate-adjusted (main analysis)	1 005 328	1·66	1·52 – 1·82
Sensitivity analyses			
Non-respiratory TB with covariate adjustment	1 004 733	1·00	0·88 – 1·13
Covariate-adjusted (removed ETOH, drugs, and psychoses)	1 005 328	1·66	1·52 – 1·82
Covariate-adjusted (replaced weighted Charlson comorbidity score with van Walraven weighted Elixhauser comorbidity score, dropping depression, ETOH, and psychoses)	1 005 328	2·14	1·95 – 2·34
Bronchiectasis added to the airway disease definition	1 005 283	1·72	1·58 – 1·88
Aim 2: addressing potential unmeasured confounding			
PS analysis using investigator-specified covariates	1 005 328	2·16	1·98 – 2·37
hdPS analysis using investigator-specified covariates + proxy variables from hybrid high-dimensional propensity score	1 005 328	2·22	2·03 – 2·42
hdPS analysis using investigator-specified covariates + proxy variables from hybrid high-dimensional propensity score and LASSO	1 005 328	2·19	2·00 – 2·39
Subdata analysis with non-missing tobacco use variable from BCCDC TB Registry	31 063	1·34	1·18 – 1·49
Covariate-adjusted + personal health risk proxy variable	1 005 328	1·64	1·50 – 1·79
Aim 3: investigating effect measure modification			
Age group			
<40 years	681 049	1·83	1·57 – 2·13
40+ years	324 279	1·82	1·62 – 2·03
Sex			
Male	487 343	1·68	1·49 – 1·89
Female	517 985	1·64	1·43 – 1·88
Immigration class			
Economic	594 460	2·11	1·76 – 2·53
Family	303 680	1·54	1·37 – 1·74
Refugee	27 857	1·39	1·05 – 1·83
Other	79 331	2·54	1·48 – 3·07
Education level			
None/unknown	127 939	1·25	1·02 – 1·53
Secondary or less	432 173	1·74	1·54 – 1·96
Trade/diploma	184 962	2·03	1·57 – 2·61
University degree	260 254	1·95	1·50 – 2·54
Neighbourhood income quintile			
Lowest	300 805	1·40	1·20 – 1·63
Low-middle	230 725	1·71	1·44 – 2·03
Middle	183 089	1·82	1·48 – 2·23
Middle-upper	143 940	2·42	1·89 – 3·10
Upper	146 769	1·65	1·18 – 2·33
TB incidence in country of birth			
<100 per 100 000	418 497	1·91	1·63 – 2·69
100-200 per 100 000	142 955	2·25	1·94 – 2·60
200-300 per 100 000	327 688	1·52	1·33 – 1·75
300+ per 100 000	116 208	1·13	0·90 – 1·43
Weighted Charlson comorbidity score			
<1	958 168	2·13	1·88 – 2·40
1-2	36 247	1·49	1·25 – 1·76
2+	10 913	1·07	0·86 – 1·32
Depression			
No	999 609	1·31	1·23 – 1·39
Yes	5719	0·31	0·08 – 1·24
Personal health risk proxy variable			
No	927 712	1·35	1·10 – 1·66
Yes	77 616	1·72	1·56 – 1·90

Notes: Covariates included: age at index, sex, income quintile at index, educational qualification upon immigration, immigration class, TB incidence in country of birth, weighted Charlson comorbidity score, year of arrival in BC, alcohol abuse, drug abuse, psychoses, and depression. **Acronyms:** aHR = covariate-adjusted hazard ratio; BC = British Columbia; BCCDC = British Columbia Centre for Disease Control; CI = confidence interval; hdPS = high-dimensional propensity score; ETOH = ethanol use disorder; LASSO = least absolute shrinkage and selection operator; N = analytic sample; PS = propensity score; TB = tuberculosis.

D4. REVIEW OF TUBERCULOSIS MANAGEMENT WITHIN FIRST NATIONS ON-RESERVE COMMUNITIES IN NORTHWESTERN ONTARIO

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BACKGROUND

TB rates amongst First Nations Peoples in Canada remain 4.4 times higher than non-Indigenous rates despite transfer of health services to First Nations. The aim of this study was to examine TB outcomes in Sioux Lookout Zone in Northwestern Ontario and compare with Canadian TB Standards and First Nations and Inuit Health Branch guidelines.

METHODS

Sioux Lookout First Nations Health Authority (SLFNHA) records from 2013 – 2015 were reviewed for diagnostic, treatment, and contact trace outcomes. SLFNHA TB nurses, an administrator and community physicians were interviewed regarding roles, lines of communication, and barriers to care.

RESULTS

Six case records were reviewed. Two patients died, four were sputum smear positive, and two completed treatment. Comparison with guidelines could not be completed due to missing data elements in all records. Decisions and communication came through SLFNHA and Provincial Public Health Units. Duties were vaguely defined. Access to TB expert capacity was reported to decrease compared to pre-transfer. Community staff turnover was frequent.

CONCLUSION

The transfer of health care to First Nations focused on administrative aspects of patient care. Outcomes could not be fully assessed due to data gaps. Community staff had minimal authority, additional administrative duties, incomplete access to patient data, and less expert support. To improve patient outcomes a Pilot Project is recommended where the community has the assigned authority, becomes the hub of communication, and has the necessary resources.

D5. OPTIMIZING APPROACHES FOR TB SCREENING - PRIORITIZING PEOPLE WITH A PRIOR HISTORY OF TB

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BACKGROUND

The optimal approach to tuberculosis (TB) screening in patients presenting to hospitals in TB endemic countries is not known. There is an urgent need for a rapid, accurate, low-cost nonsputum based TB triage test. We evaluated different approaches to identifying patients with infectious TB as part of the FAST (Find cases Actively, Separate safely and Treat effectively) transmission prevention strategy in Lima, Peru.

METHODS

We screened patients admitted to Hospital Nacional Hipolito Unanue in Lima between June 2017 and December 2019 and enrolled patients reporting cough of any duration, contact with TB or a prior history of TB. All enrolled patients underwent sputum smear microscopy, Xpert MTB/RIF and mycobacterial culture.

RESULTS

Of the 952 enrolled patients with complete data for Xpert MTB/RIF and culture results, 139 (14.6%) were culture positive. Almost one third of enrolled patients (32.8%) had a history of prior TB, which was higher in those with culture confirmed TB (43.2% versus 32%, p=0.01). When adjusted for age, sex, HIV, diabetes, and prior incarceration, those with prior TB had 2.27 times the odds (CI: 1.35-3.80, p=0.002) of being TB culture positive as compared to those who were TB culture negative (Table).

CONCLUSION

Active case finding in patients at a hospital in Lima identified a high frequency of patients with microbiologically confirmed TB, almost one third of whom had a prior history of TB. Given their greater than two-fold increased odds of being diagnosed with TB again, hospitalized patients with prior TB should be prioritized for TB testing.

Table: Unadjusted and Adjusted Logistic Regression Models evaluating the association between Prior TB and Culture-Diagnosed TB

	Univariate regression (Outcome= positive TB culture) N= 837			**Multivariate regression (Outcome= positive TB culture) N= 837**		
Variables	**Odds Ratio**	**95% CI**	**P-value**	**Odds Ratio**	**95% CI**	**P-value**
Prior TB *No* *Yes*	*Referent* *1.63*	- (1.12, 2.37)	- **0.010***	*Referent* 2.27	- (1.35, 3.80)	- **0.002***
Prison *No* *Yes*				*Referent* 2.25	- (1.36, 3.73)	- **0.002***
Age (years)				0.968	(0.957, 0.981)	**<0.001***
HIV *No* Yes				*Referent* 2.73	- (1.11, 6.76)	- **0.029***
Diabetes *No* *Yes*				*Referent* 2.83	- (1.32, 6.06)	- **0.007***
Sex *Male* *Female*				*Referent* *0.693*	- (0.156, 1.05)	- 0.165

D6. **TUBERCULOSE CONTINUUM OF CARE FOR CHILDREN IN SURINAME**

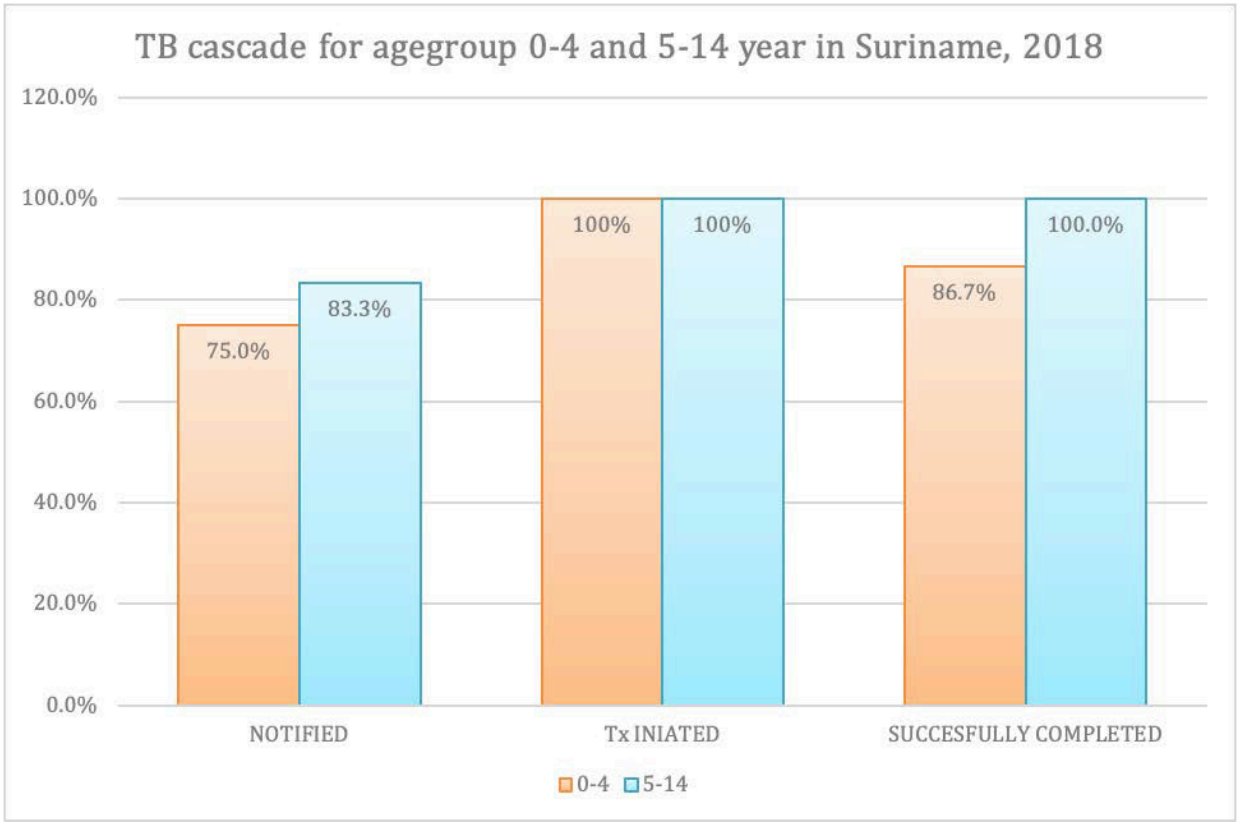
Stijnberg D[1,2,3], Commiesie E[1], Schrooten W[2]. [1]National Tuberculosis Program, Paramaribo, Suriname; [2]Hasselt University, Belgium; [3]Anton de Kom Universiteit, Suriname

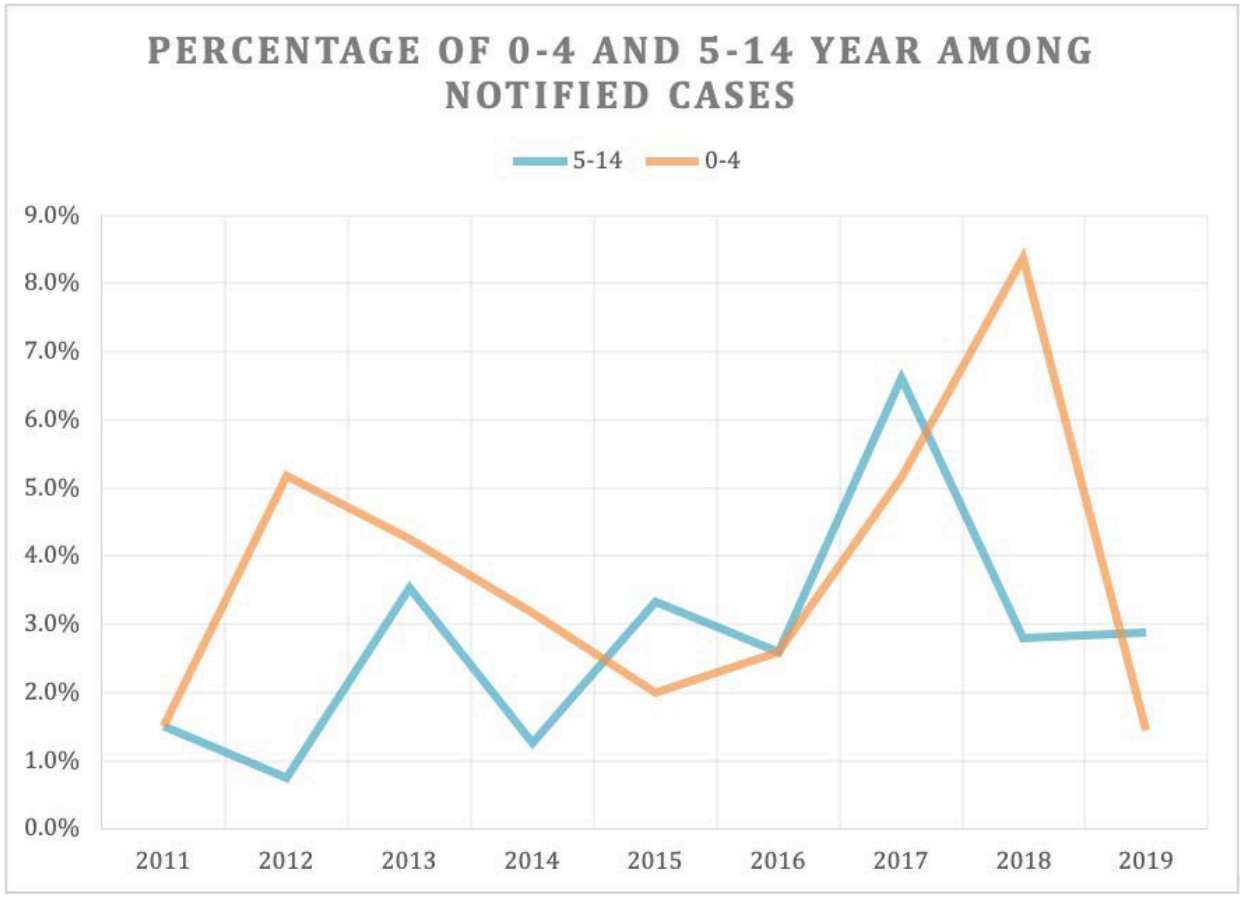
BACKGROUND
The World Health Organization (WHO) reckons that the actual burden of Tuberculosis (TB) in children is much higher than the estimated 1 million suffering from TB. It calls on all partners to put more efforts into diagnosing and treating children with TB to prevent deaths. For Suriname this is the first time that the continuum of care for children regarding TB is evaluated.

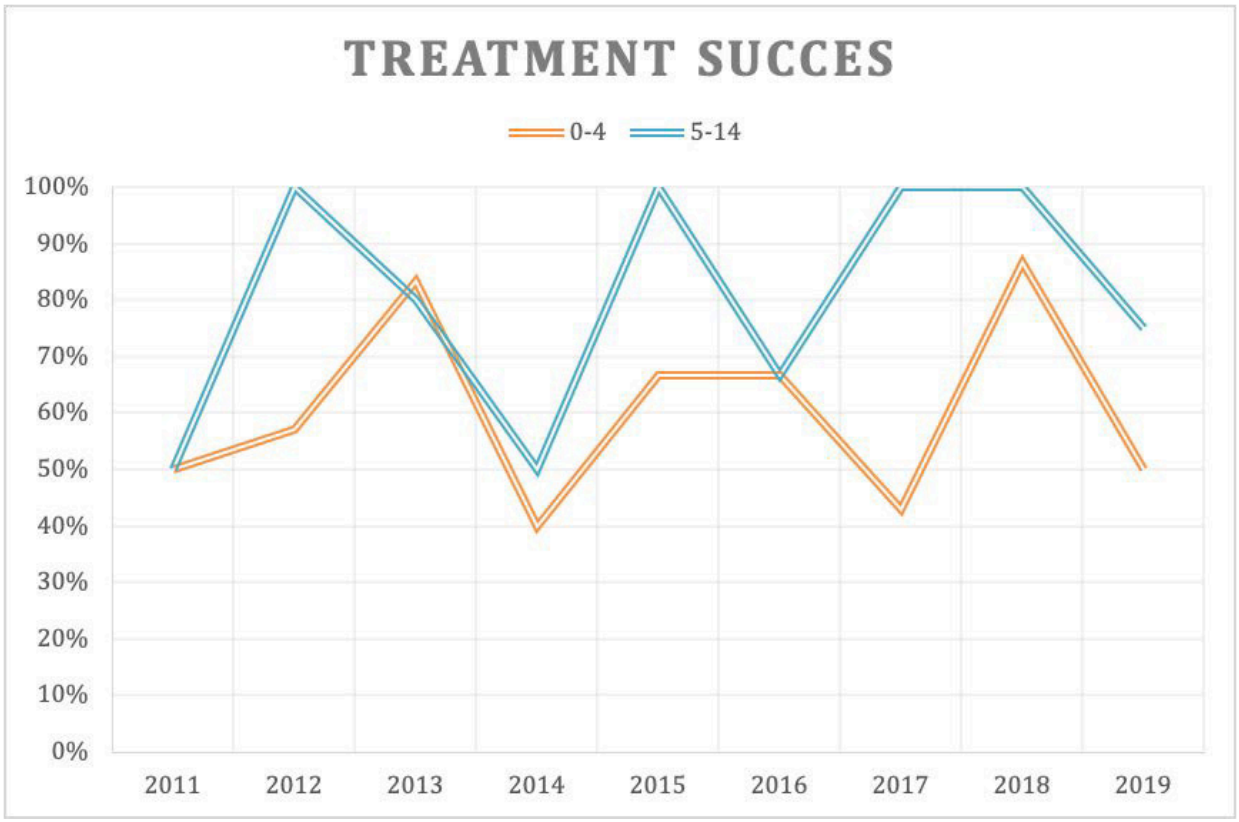
METHODS
The percentage of TB cases notified was calculated in relation to the WHO estimates. From those cases notified the percentage initiated treatment and successfully treated were calculated. This was completed for age groups 5 to 14 and under 5 years. The overall trend of the percentage of these age groups among the notified cases and their percentage successfully treated for 2011 to 2019 were also analyzed.

RESULTS
75% versus 83% of the estimated cases were notified for the age groups under 5 years and 5-14 years respectively. Treatment success rate for under 5 years was 87% in 2018 compared to 100% in the age group 5-14 years. This is the highest percentage treated successfully in the last decade for age group under 5 years. In 2018, this age group, also had their highest percentage among all notified cases in last decade (8.4%).

CONCLUSION
Children under 5 years have a lower case detection and treatment success rate. This is the overall trend from 2011 to 2019. The National TB Program needs to implement a system of closer monitoring in collaboration with the pediatricians for these children.


TB cascade for agegroup 0-4 and 5-14 year in Suriname, 2018
120.0%
100.0%
80.0%
60.0%
40.0%
20.0%
0.0%
75.0%
83.3%
100%
100%
86.7%
100.0%
NOTIFIED
Tx INIATED
SUCCESFULLY COMPLETED
0-4
5-14


PERCENTAGE OF 0-4 AND 5-14 YEAR AMONG NOTIFIED CASES
5-14
0-4
9.0%
8.0%
7.0%
6.0%
5.0%
4.0%
3.0%
2.0%
1.0%
0.0%
2011
2012
2013
2014
2015
2016
2017
2018
2019


TREATMENT SUCCES
0-4
5-14
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2011
2012
2013
2014
2015
2016
2017
2018
2019

D7. COMMUNITY MATTERS! TUBERCULOSIS (TB) PREVENTION STRATEGIES IN NORTHERN VIRGINIA

Bailey S[1], Kidanne R[2], Addo-Ayensu G[1], Fujii K[1], Poppell E[2], Dietz S[2], Ryan M[1], Chikobe J[1], Noboa W[3]. [1]Fairfax County Health Department; [2]Arlington County Public Health Division; [3]The Centers for Disease Control and Prevention

BACKGROUND
In 2019, 121/192 (63.5%) of TB cases in Virginia occurred among Northern Virginia (NOVA) residents, and over the last five years, TB rates for NOVA have been higher than state and national averages. To address prevention challenges, NOVA health districts established a taskforce and convened a Community Advisory Council (CAC) representing populations with the greatest TB burden across NOVA.

METHODS
Based on routine TB surveillance data, the taskforce compiled a list of 15 high-risk populations. The taskforce invested two years engaging with these populations to develop materials to increase TB awareness. As a result, a region-wide campaign was launched using grassroots outreach and advertising.

To assess the effectiveness and efficacy of the campaign, the taskforce developed and administered an evaluation survey to collect quantitative and qualitative information from 804 respondents.

RESULTS
359/804 (43%) of respondents recalled seeing written information about TB. Of those who saw written materials, 126 (35%) said the materials improved their understanding of TB, 170 (47%) liked the ads, and 199 (55%) thought the message was important.

Results suggest the campaign may have been effective at reaching the intended audience and engaging them in media materials. When surveyed, individuals of high TB burden communities, who recalled recently seeing TB messages, showed an increase in TB awareness and TB-related care-seeking behaviors.

CONCLUSION
Investing in community focused media campaigns can result in an increase of public health knowledge and may positively influence the public's behavior. To be effective, health departments must involve the community in efforts to improve community health and well-being.

D8. **USER EXPERIENCE OF STANDARDIZED PATIENTS WITH TUBERCULOSIS IN URBAN INDIA**

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BACKGROUND

In healthcare, quality matters as much as coverage of services. Tuberculosis (TB) remains the leading infectious-disease killer, and even when full coverage exists, mortality, missed cases and patient loss to follow-up persist. To date, no studies elucidate whether objective measures of quality correlate with whether TB patients' felt they received appropriate care.

METHODS

Using a dataset comprising 2,602 simulated patient-provider interactions across 1,203 facilities in Mumbai and Patna, we propose to assess differences between user experiences, subjective impressions of provider-patient interactions, and the quality of TB-specific care delivered by private providers.

RESULTS

To study the quality of urban-area TB care, from 2014-2017, 24 trained standardized patients (SPs) enacted four "clinical cases" depicting different stages of TB-specific progression to representatively sampled providers. SPs were subsequently asked to rank their providers from 1–10 (highest rating for satisfaction/performance). Using their ratings as the outcome, we present preliminary multiple linear regression analyses on 1148 formal and 1154 informal SP-provider interactions. Among informal providers, the estimated adjusted user ranking was 6.94 [95% CI 6.56-7.31] for clinically-correct managed cases using Indian TB care guidelines, 5.17 [95% CI 4.36-5.97] for male and 5.45 [95% CI 4.96-5.94] for female providers, and 3.31 [95% CI 2.78- 3.83] when providers appeared very knowledgeable. For formal providers, the estimated adjusted rankings were 7.34 [95% CI 6.97-7.72], 6.84 [95% CI 5.64-8.04], 6.90 [95% CI 6.12-7.69], and 3.26 [95% CI 2.38-4.14], respectively.

CONCLUSION

Additional interaction characteristics, clinical measures, and objective quality measures associated with higher versus lower user rankings will be explored.

D9. **HOW MUCH DO INDIANS PAY FOR TUBERCULOSIS TREATMENT? A COST ANALYSIS**

Sinha P[1], Carwile M[2], Bhargava A[3], Cintron C[1], Acuna-Villaorduna C[1], Liu AF[5], Kulatilaka N[6], Locks L[7], Lakshminarayan S[4], Hochberg NS[1,2].

BACKGROUND
India's National Tuberculosis Elimination Program (NTEP) covers diagnostic and therapeutic costs of tuberculosis (TB) treatment and aims to eliminate catastrophic costs, defined as treatment costs exceeding 20% of annual income, by 2020. However, persons living with TB (PLWTB) still experience high direct and indirect costs. Direct costs include payment for testing, treatment, travel, hospitalization, and food. Indirect costs consist of lost wages, loan interest, and cost of domestic helpers. We reviewed published studies to analyze the magnitude and pattern of TB-related costs from the perspective of Indian PLWTB.

METHODS
We identified relevant articles using key search terms ("tuberculosis," "India," "cost," "expenditures," "financing," "catastrophic," and "out of pocket") and calculated variance-weighted mean costs adjusted for inflation.

RESULTS
Indian patients incur substantial direct costs (mean: $46.8), but mean indirect costs ($666.6) constitute 93.4% of the net costs. Mean direct costs before diagnosis were four-fold that of costs during treatment. Private sector care can cost up to six-fold higher than public sector services. TB was associated with work absenteeism and loss of employment (up to 64% in one study). As many as one in three PLWTB in India experience catastrophic costs. Hospitalizations are associated with higher risk of catastrophic costs 26.7% in hospitalized PLWTB compared to 3.5% in ambulatory PLWTB).

CONCLUSION
Indian PLWTB continue to suffer high direct and indirect costs particularly before diagnosis. Indirect costs eclipse the direct costs in magnitude and often go unmeasured or incompletely measured in economic analyses. Ameliorating the economic devastation of TB in India requires urgent policy changes.

D10. DEPRESSION RISK TRENDS BEFORE AND AFTER TB TREATMENT: LONGITUDINAL ANALYSIS OF A SOUTH AFRICAN TB PATIENT COHORT

Weber S[1], Rooney J[1], Malatesta S[2], Carney T, Myers B, Ragan EJ[1], Bouton T[1], Horsburgh CR[1,7], Theron D[6], White LF[2], Warren RM[4,5], Jacobson KR[1]. [1]Section of Infectious Diseases, Boston Medical Center, Boston, USA; [2]Department of Biostatistics Boston University School of Public Health, Boston, MA, USA; [3]Alcohol, Tobacco and Other Drug Research Unit, South African Medical Research Council, Cape Town, South Africa; [4]Department of Science and Technology, National Research Foundation Centre of Excellence in Biomedical Tuberculosis Research, South Africa Medical Research Council for Tuberculosis Research, Cape Town, South Africa; [5]Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa; [6]Brewelskloof Hospital, Worcester, South Africa; [7]Departments of Epidemiology, Biostatistics and Global Health, Boston University School of Public Health, Boston, MA, USA

BACKGROUND

Individuals initiating TB therapy are believed at-risk for depression; the trajectory of their depressive symptoms after treatment completion is unknown. We assessed risk for depression at TB diagnosis, at end of 6-months treatment, and 6- and 12-months after treatment completion.

METHODS

We analyzed data from 192 prospective cohort participants followed from TB treatment initiation through a year post completion. Risk of depression was defined as a Center for Epidemiologic Studies Depression (CES-D) scale score ≥16. We assessed the association of depression risk at baseline with sociodemographic variables and substance use. We analyzed longitudinal associations using logistic regression models fit with Generalized Estimated Equation (GEE).

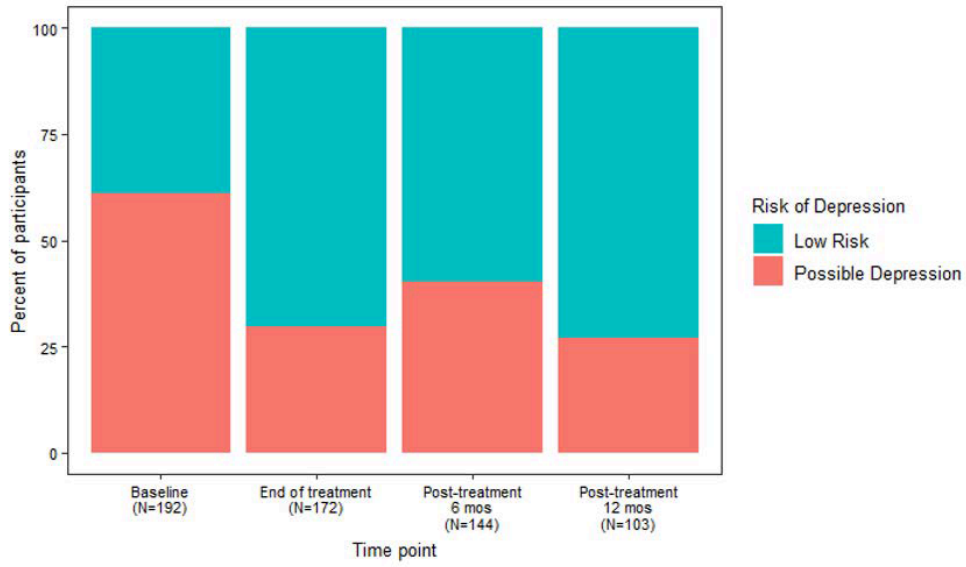
RESULTS

60.9% of participants had elevated risk of depression at treatment initiation. Depression risk was higher at baseline (OR 3.79, $p<0.01$) and 6 months following treatment completion (OR 1.57, $p=0.02$) than at treatment completion. Those with moderate- to severe-household hunger were at greater risk of depression than those without at baseline (OR 4.23, $p=0.03$) and throughout (Figure 2). Depression risk was higher for participants at risk for substance use disorder (SUD) at baseline (OR 4.82, $p<0.01$) and 6 months post-treatment (OR 4.24, $p<0.01$) compared to treatment completion, a pattern that differed from those with low risk for SUDs (Figure 3).

CONCLUSION

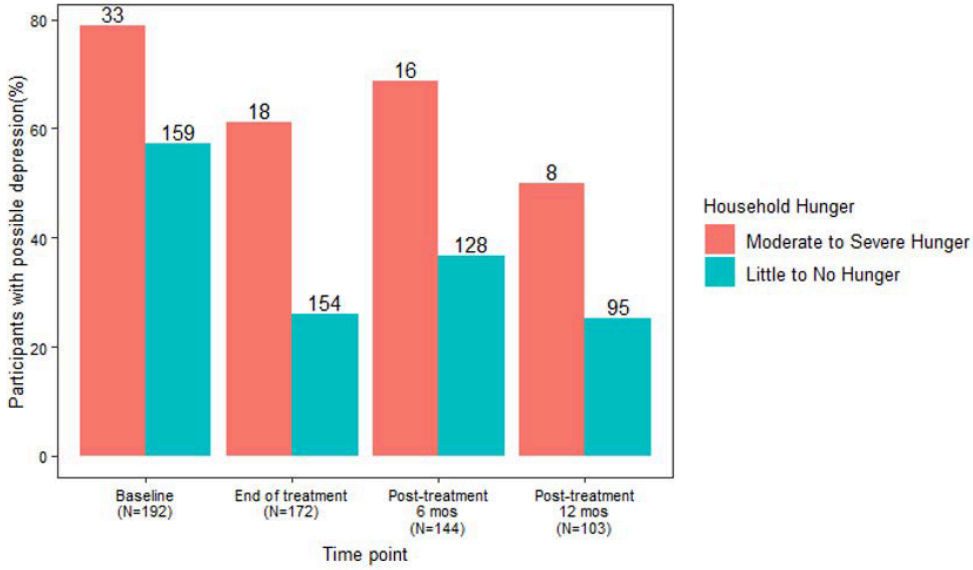
Participants who used substances had higher depression risk after treatment completion, whereas participants with household hunger had higher depression risk throughout. TB treatment offers a unique opportunity to capture depression risk and treat populations who may otherwise have limited interaction with the health care system.

Figure 1: Prevalence of Depression Over Time[1,2]



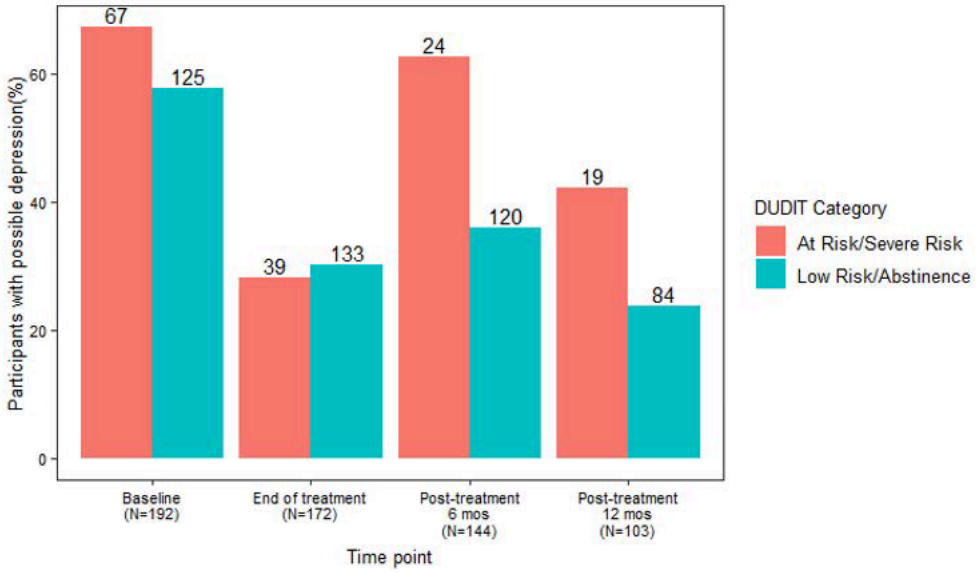
[1]The Center for Epidemiologic Studies Depression Scale (CES-D) measures depressive symptoms and generates a score used to screen individuals with possible depression.
[2]Risk of Depression: CES-D score of 16 or greater is defined as possibly depressed, and CESD score less than 16 is defined as low risk.

Figure 2: Proportion of Participants with Possible Depression Stratified by Household Hunger Status[1,2,3]



[1]N above each bar reflects the total number of participants in each subgroup at each time point.
[2]Household Hunger Scale (HHS) is a tool to measure food insecurity.
[3]Household Hunger: HHS score of 0-1 = Little to No Hunger in Household, 2-6 = Moderate to Severe Hunger in Household.

Figure 3: Proportion of Possibly Depressed Participants at Each Time Point Stratified by Substance Use Intensity[1,2,3]



[1]N above each bar reflects the total number of participants in each subgroup at each time point.
[2]Drug Use Disorders Identification Test (DUDIT) is a screening tool which provides information on an individual's drug use behaviors to identify problem drug use.
[3]DUDIT Category: DUDIT scores below 8 = low risk/abstinence; scores of 8 or greater = at risk/severe risk.

F. MDR

F1. **RIFAMPIN-RESISTANT/MULTIDRUG-RESISTANT TUBERCULOSIS IN ALBERTA, CANADA: EPIDEMIOLOGY AND TREATMENT IN A LOW-INCIDENCE SETTING**

Edwards BD[1], Edwards J[2], Cooper R[3], Kunimoto D[3], Somayaji R[1,4,5], Fisher D[1]. [1]Department of Medicine, University of Calgary, Calgary, Canada; [2]Pharmacy Services, Alberta Health Services, Calgary, Canada; [3]Department of Medicine, Division of Infectious Diseases, University of Alberta, Edmonton, Canada; [4]Department of Microbiology, Immunology, and Infectious Diseases, University of Calgary, Calgary, Canada; [5]Department of Community Health Sciences, University of Calgary, Calgary, Canada

BACKGROUND
Rifampin-resistant Tuberculosis (RR/MDR-TB) necessitates the use of medications of inferior effectiveness and increased toxicity for long durations with low success rates. We explored the epidemiology and treatment of RR/MDR-TB in a low-incidence, high-resource setting.

METHODS
We performed a retrospective cohort study of all culture-confirmed RR/MDR-TB patients in Alberta, Canada (2007-2017). Isolates demonstrating phenotypic resistance to rifampin were captured by an electronic medical record, identifying patients for inclusion. We described demographics, epidemiology, and outcomes associated with each treatment regimen. Incidence was calculated using the mid-year provincial population.

RESULTS
We identified one RR-TB and 23 MDR-TB cases (1.4% of TB cases). The mean incidence rate was 0.06/100,000 persons per year. The mean age was 38.7 years. All patients were foreign-born and median post-immigration time to diagnosis was 3 years (IQR: 0.3-7.3). Eleven patients (46%) reported prior treatment. Respiratory TB was confirmed in 71%. Twelve patients (50%) were referred by Immigration Canada for abnormal chest Xray and seven diagnosed with active MDR-TB at that assessment. The median treatment duration was 17.5 months after culture conversion (IQR: 14.8-19), with treatment success in 23/24 (96%). Adverse effects prompted medication discontinuation in 79%. Mean compliance was 95%. All patients achieved negative sputum cultures by two months with no cases of culture reversion or recurrence.

CONCLUSION
Incidence of RR/MDR-TB in Alberta remains low. Despite often short treatment with frequent adverse effects, success was high, likely as a result of effective medications, significant treatment support, and early sputum conversion. Continued exploration of shorter treatment with well-tolerated, efficacious oral agents is needed.

F2. **SURVIVAL STATUS AND PREDICTORS OF MORTALITY AMONG PATIENTS WITH MULTI-DRUG RESISTANT TUBERCULOSIS TREATED IN TREATMENT INITIATING CENTERS OF TIGRAY REGION, NORTHERN ETHIOPIA, 2018: A RETROSPECTIVE COHORT STUDY**

Embaye GK, Gebregergs GB, Gebregiorgis YS.

BACKGROUND
Multidrug-Resistant Tuberculosis (MDR TB) is an urgent global public health crisis. Ethiopia is among the 30 high MDR-TB burden countries. Understanding risk factors for MDR-TB mortality is vital to improving MDR-TB treatment outcomes. We determined survival status and predictors for MDR-TB mortality and the findings has become important to design effective interventions that might help to reduce mortality in Tigray.

METHODS
We conducted retrospective cohort study design in patients with MDR-TB enrolled for treatment in seven hospitals from February, 2013 to April, 2018. We enrolled 387 patients and data were collected consecutively by using pre-tested data abstraction format. All relevant variables were extracted from TB patients' registration log book and charts. Data were entered and analyzed by STATA version12. Cox proportional hazard regression model was built, the final result was interpreted using Adjusted Hazard Ratio (AHR) with 95% CI and statistical significance was declared at p-value <0.05.

RESULTS
During five years follow- up period 47(12.1%) patients died, making an incidence rate of 9.6 deaths per 100 Person-year in the cohort. The overall mean survival time was 1.9 years. HIV-infection [AHR=2.3, 95%CI =1.1-4.7], Presence of comorbidities [AHR =2.7, 95%CI =1.2- 6.03], Adverse drug events AHR=2.6, 95%CI=.2-5.65], and sputum culture non-converters =7.7, 95%CI =3.6-16.5] were predicted mortality.

CONCLUSION
The survival time of MDR-TB patients was low and the overall incidence rate of death was high. HIV-co-infection, comorbidities other than HIV, drug adverse effects and no sputum culture conversion at two months were factors associated with mortality. Therefore further intervention is needed to reduce deaths.

F3. **EARLY EXPERIENCE IN THE UNITED STATES USIN BEDAQUILINE, PRETOMANID, AND LINEZOLID (BPaL) TO TREAT DRUG-RESISTANT AND TREATMENT-INTOLERANT TUBERCULOSIS**

Haley C[1], Peloquin C[2], Jones B[3], Gomez M[1,4], Rowlinson MC[1,3], Ashkin D[1,4], U.S. BPaL Implementation Group. [1]Southeastern National TB Center, University of Florida, Gainesville, United States of America; [2]University of Florida, College of Pharmacy, Gainesville, United States of America; [3]Florida Department of Health, Bureau of Public Health Laboratories, Jacksonville, United States of America; [4]Florida Department of Public Health, Tuberculosis Control, Tallahassee, United States of America

BACKGROUND

The NIX-TB trial demonstrated 90% efficacy treating participants with drug-resistant (DR) or treatment-intolerant (TI) tuberculosis (TB) using bedaquiline, pretomanid, and linezolid (BPaL) for 6 months. Adverse events were common using a 1200mg linezolid initiation dose in BPaL; 85% required linezolid interruption or dose reduction. Less or no toxicity occurs with lower doses and serum linezolid trough <2mcg/mL. We describe BPaL safety and completion data among a cohort of U.S. patients initiating 600mg linezolid subsequently adjusted by therapeutic drug monitoring (TDM) and minimum inhibitory concentration (MIC) values for linezolid by culture-based antimicrobial susceptibility testing.

METHODS

Following FDA approval August 21, 2019, the Southeastern National TB Center implemented use of BPaL into clinical practice for complicated TB patients with limited treatment options. De-identified data on BPaL-treated patients was documented in an encrypted medical consultation database as part of routine care; descriptive analyses were performed.

RESULTS

Between 8/21/2019-9/28/2020, 21 patients ages 17-83 years received BPaL for DR (n=19) or TI (n=2) TB; one was HIV-infected, 8 female, and 18 non-U.S.-born. There were 17 with pulmonary TB, 2 with extrapulmonary TB and 2 with both. All initiated 600mg linezolid daily except one treated Monday/Wednesday/Friday given baseline renal disease; 10 had linezolid dose adjustment using TDM and MIC. None developed neurologic or hematologic toxicity; 11 completed and 10 remain on treatment.

CONCLUSION

For U.S. patients with TB disease, linezolid-associated toxicity and treatment completion may be optimized using lower doses adjusted by TDM and MIC. Additional data are needed to confirm BPaL efficacy with this linezolid dosing.

F4. **CLINICAL OUTCOMES AMONG PATIENTS WITH TUBERCULOSIS MENINGITIS USING AN EXPANDED MULTIDRUG REGIMEN**

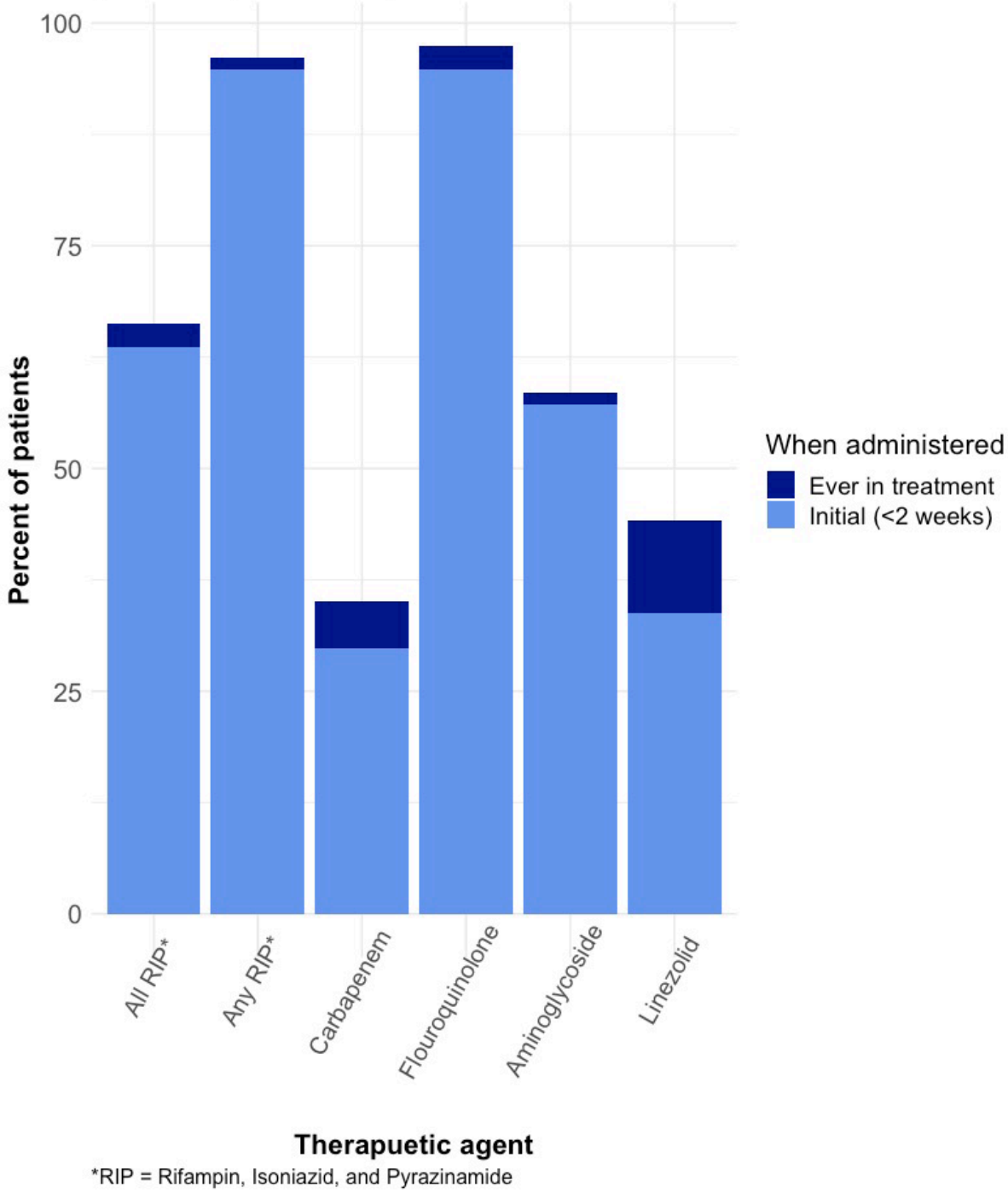
Smith A, Gujabidze M, Avaliani T, Blumberg HM, Collins J, Sabanadze S, Bakuradze T, Avaliani Z, Kempker RR, Kipiani M.

BACKGROUND
Approximately half of patients with tuberculosis meningitis (TBM) experience severe disability or death highlighting the need for novel treatment strategies. In 2015, the National Center for TB and Lung Disease (NCTLD) in Tbilisi, Georgia implemented an expanded multidrug treatment regimen including rifampin, isoniazid, pyrazinamide, levofloxacin, and injectable agent for patients with TBM. We sought to determine the clinical outcomes of patients with TBM treated with such regimens.

INTERVENTION/RESPONSE RESULTS
Among 77 patients, 11.7% (9) were HIV-positive and 6.5% (5) had confirmed MDR TBM. 30% of patients (n=23) had M. tuberculosis confirmation by molecular testing or culture. Mean CSF WBC was 212 cells/µl and with median 85% lymphocytes. Initial treatment (≤2 weeks) consisted of rifampin, isoniazid, and/or pyrazinamide in 95%, a fluoroquinolone in 95%, injectable agent in 57%, carbapenem in 35% and linezolid in 34% (Figure 1). The overall mortality rate was low at 7.8% (6/77) including one death among a patient with MDR (20%), and a higher mortality among HIV-infected persons (33%). In regard to neurological outcomes, 18%(14/76) of patients reported a Modified Rankin Score (MRS) of 0 (“I have no problems”) at start of treatment, improving to 83% (55/66) and 95%(37/39) of patients reporting MRS=0 at 6 and 12 months after treatment initiation, respectively.

CONCLUSION
Expanded multidrug treatment regimens that included a fluoroquinolone and injectable agent resulted in a lower mortality and more favorable neurological outcomes than historical controls including among patients with MDR TBM suggesting empiric expanded multidrug therapy may be beneficial for TBM.

Figure 1: Major drug types administered to TBM patients, initially (within 14 days of admission) and ever in course of treatment



*RIP = Rifampin, Isoniazid, and Pyrazinamide

F5. **SIX-MONTH ADHERENCE TO MDR-TB TREATMENT AT SIX MDR-TB TREATMENT SITES IN INDIA AND BRAZIL**

Sy KTL[1,2], Gaikwad S[3], Gajjar I[4], Palanivel C[5], Ilamathi P[6], Rolla V[7], Mello FCQ[8], Sterling T[9], Horsburgh CR[1,2,10].
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BACKGROUND
Adherence to treatment is believed to be a strong predictor of TB treatment success. However, it is often poorly documented in multidrug-resistant tuberculosis (MDR-TB) treatment.

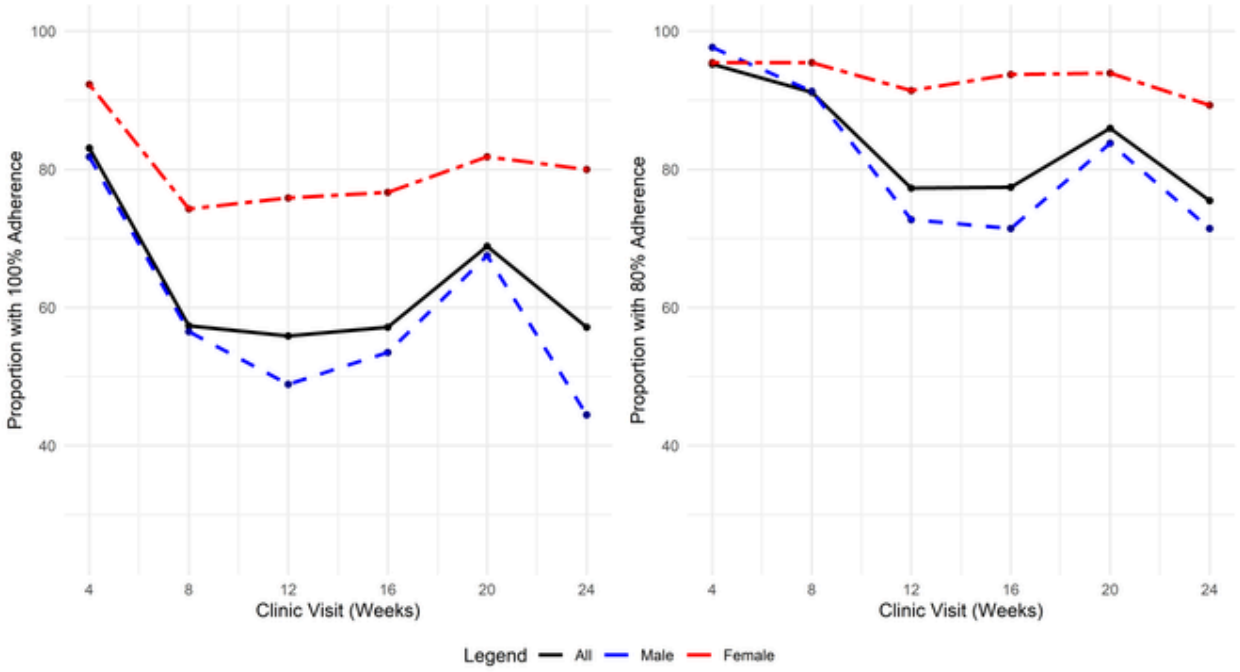
METHODS
Monthly data were collected in a prospective cohort study at four MDR-TB treatment sites in India and two sites in Brazil. Two measures of treatment adherence were collected: (1) visual analogue scale (VAS)- a self-reported percentage of medication that was taken correctly (2) days adherent - self-reported days with no missed doses in the past 30 days. Using days adherent, we created two additional variables; 100% adherence and 80% adherence, defined as 0 or <6 missed doses in the last 30-day period.

RESULTS
Among 133 enrolled participants, 77 (58%) had been enrolled 6 months or more with follow-up visits, and 73 (55%) reported adherence data. Of these 73 patients, 89% (n=67) completed follow-up, while 3 died and 3 withdrew consent. Adherence measures of patients who completed were not significantly different (VAS p=0.694, days adherent p=0.520) from those who dropped out.

Of the 73 patients, 33% were female, median age was 37.0 (IQR:24.0-50.0), and 3% were HIV+. The median VAS on all clinic visits was 89% (IQR:82-91), and the median days adherent per month was 28.50 days (IQR:25.60-29.83). 24.7% and 53.2% of patients reported 100% and 80% adherence on all clinic visits, and the proportion of patients adherent decreased over time (100% adherence p= 0.066; 80% adherence p=0.003) (Figure 1).

CONCLUSION
These results suggest that self-reported treatment adherence was high although decreased over time in this MDR-TB cohort.

Figure 1. Percentage of MDR-TB patients (n=73) with 100% and 80% treatment adherence at each study visit



H. DIAGNOSIS

H1. **ULTRASOUND FOR THE DIAGNOSIS OR SCREENING OF PULMONARY TUBERCULOSIS: A SYSTEMATIC REVIEW**

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BACKGROUND

The advent of cheap, portable ultrasound devices has led to increasing interest in the use of ultrasound for the diagnosis or screening of pulmonary TB (PTB). We undertook a systematic review of the diagnostic accuracy of ultrasound for PTB.

METHODS

Five databases were searched for articles published between January 2010 and June 2020. Two independent reviewers screened abstracts and full texts for inclusion. Risk of bias was assessed using QUADAS-2. Data on sensitivity and specificity of individual lung ultrasound (LUS) signs were collected, with variable reference standards including PCR and sputum smear microscopy.

RESULTS

6 of 5879 reviewed articles were included: 5 in adults and 1 in children, with a total sample size of 564. Studies had high risk of bias in many domains. In adults, LUS signs of subpleural nodule and lung consolidation had sensitivities ranging from 72.5% to 100.0% and 46.7% to 80.4%, with specificities of 66.7% and 35.3% in the only study reporting specificity data. Sensitivity of pleural effusion, cavitation and military pattern were below 30% in all studies. In children, only pleural gap had both sensitivity and specificity above 50%. Interrupted pleural line had sensitivity of 78.4% and specificity of 26.7%, while three signs had low sensitivity but high specificity.

CONCLUSION

LUS is a potentially useful diagnostic or screening tool for PTB in both adults and children but the evidence base is limited and has methodological flaws. New studies which minimise potential sources of bias are required to further assess the sensitivity, specificity and reproducibility of ultrasound for PTB.

H2. YIELD OF REPEAT TUBERCULIN SKIN TESTING FOR PEOPLE LIVING WITH HIV IN RIO DE JANEIRO, BRAZIL

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BACKGROUND

Brazilian guidelines recommend annual tuberculin skin tests (TST) for people living with HIV (PLWH) with CD4>350, with tuberculosis preventive therapy (TPT) provided upon test conversion. We aimed to determine the yield of repeat TST for PLWH in Brazil.

METHODS

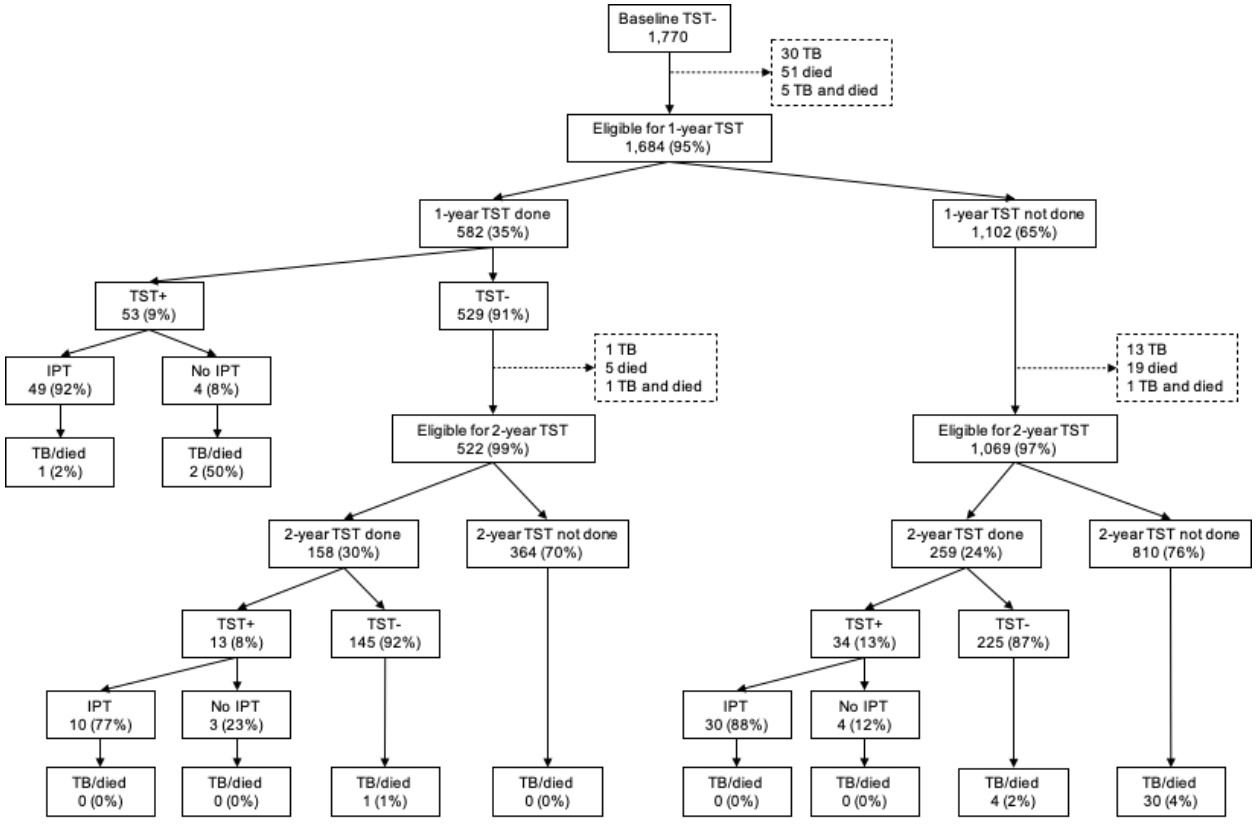
We analyzed data from the THRio study, a cluster-randomized trial that evaluated an intervention to increase TST and TPT for PLWH in Rio from 2005-2010. We calculated the number of TST conversions after 1 and/or 2 years among patients eligible for follow-up TSTs; the proportion of converters initiating TPT; and incidence of TB/death.

RESULTS

Among 1,770 PLWH with a negative baseline TST, 679 (38%) were female and median age was 36 years (IQR 29-43). Eighty-six (5%) developed TB or died within 1 year. Among 1,684 eligible for a 1-year TST, 582 (35%) were tested and 53 (9%) were positive. Forty-nine (92%) converters started TPT. Of 529 patients with a negative 1-year TST, 7 (1%) developed TB or died over the following year. Of 522 patients eligible for a 2-year TST, 158 (30%) were tested and 13 (8%) were positive. Ten (77%) converters started TPT. Of 1,102 patients who did not receive a 1-year TST, 33 (3%) developed TB or died. Of the 1,069 patients eligible for a 2-year TST, 259 (24%) were tested and 34 (13%) were positive. Thirty (88%) converters started TPT.

CONCLUSION

In this cohort of PLWH in Brazil, TST conversion was high among those re-tested, but only 48% received a follow-up TST within 2 years.


Baseline TST-
1,770
30 TB
51 died
5 TB and died
Eligible for 1-year TST
1,684 (95%)
1-year TST done
582 (35%)
1-year TST not done
1,102 (65%)
TST+
53 (9%)
TST-
529 (91%)
1 TB
5 died
1 TB and died
13 TB
19 died
1 TB and died
IPT
49 (92%)
No IPT
4 (8%)
TB/died
1 (2%)
TB/died
2 (50%)
Eligible for 2-year TST
522 (99%)
Eligible for 2-year TST
1,069 (97%)
2-year TST done
158 (30%)
2-year TST not done
364 (70%)
2-year TST done
259 (24%)
2-year TST not done
810 (76%)
TST+
13 (8%)
TST-
145 (92%)
TST+
34 (13%)
TST-
225 (87%)
IPT
10 (77%)
No IPT
3 (23%)
IPT
30 (88%)
No IPT
4 (12%)
TB/died
0 (0%)
TB/died
0 (0%)
TB/died
1 (1%)
TB/died
0 (0%)
TB/died
0 (0%)
TB/died
0 (0%)
TB/died
4 (2%)
TB/died
30 (4%)

H3. **EVALUATION OF Xpert MTB/RIF ASSAY FOR THE DIAGNOSIS OF PULMONARY TUBERCULOSIS INCHILDREN FROM STOOL SPECIMEN IN ETHIOPIA**

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BACKGROUND

Diagnosis of tuberculosis (TB) in children often relies on clinical diagnosis because they are usually unable to produce sputum specimens. Gastric lavage can be applied to obtain for microbiological diagnosis. However, these methods are complex, invasive, and not feasible in resource poor settings. In this study, we evaluated the performance of Xpert MTB/RIF for the diagnosis of pulmonary TB in children from the stool specimen.

METHODS

Gastric lavage was collected from children (<15 years old) suspected of TB and processed for Xpert MTB/RIF and culture. In addition, stool specimens were collected and tested for the presence of Mycobacterium tuberculosis by Xpert MTB/RIF assay. The diagnostic accuracy of Xpert MTB/RIF (stool versus gastric lavage) was calculated against culture and composite reference standard (CRS). The CRS made of Xpert MTB/RIF, culture and response to anti-TB treatments.

RESULTS

Of 152 children enrolled, 10(6.6%) were confirmed TB cases (culture-positive), again 10(6.6%) were probable TB (received anti-TB with good response), while 132(86.8%) were classified as “non TB” cases. Stool based Xpert MTB/RIF had a sensitivity of 100% (95%CI: 66.37-100) and specificity of 99.30% (95%CI: 96.17-99.98) compared to culture but the sensitivity was reduced 50% when compared to CRS. The Xpert MTB/RIF sensitivity from gastric lavage was 77.8% compared to culture and 40% compared to the CRS.

CONCLUSION

Stool specimens can be a promising specimen for the diagnosis of pulmonary TB by Xpert MTB/RIF for children unable to expectorate sputum specimens and can be easily implemented in the peripheral health care system.

H4. QIAreach™ QuantiFERON®-TB: A SIMPLE AND ACCURATE SOLUTION FOR DECENTRALIZED TB INFECTION SCREENING

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BACKGROUND

Interferon Gamma Release Assays (IGRAs) have known operational and performance advantages compared to the tuberculin skin test (TST) and are preferred in testing BCG vaccinated populations in North America and recommended globally by the WHO as an alternative to the TST. However, implementation of IGRA testing in low-resource settings is challenging, requiring laboratory infrastructure, and associated maintenance and support. In response for assays needed in decentralized settings, QIAGEN has developed a deployable, accurate and affordable TB infection diagnostic aid that requires minimal training. QIAreach™ QuantiFERON-TB (QIAreach QFT) is a simple, single-tube, accurate testing solution for nextday digital results. The technology uses nanoparticle fluorescence on a portable and scalable multi-test digital lateral flow platform to provide objective results within 3 to 20 minutes after sample addition to the eStick (cartridge).

METHODS

QIAreach QFT results were compared with QFT-Plus in persons with a mix of risk factors for TB infection. 111 donors were sampled over multiple days, resulting in 206 eligible individual blood samples tested by both assay detection platforms. The agreement levels of both assays are below.

RESULTS

QIAreach QFT performance versus QFT-Plus

	Frequency	Agreement	Lower 95% CI	Upper 95% CI
PPA	68/68	100%	94.7%	100%
NPA	129/135	95.6%	90.6%	98.4%
OPA*	197/206	95.6%	91.8%	98.0%

OPA: Overall percent agreement; PPA: Positive percent agreement; NPA: Negative percent agreement. *includes 3 QFT-Plus indeterminate results

CONCLUSION

QIAreach QFT shows a high level of agreement with QFT-Plus and has the potential to overcome key hurdles for TB screening in high-burden, decentralized, low-resource settings.

H5. BAYESIAN LATENT CLASS ANALYSIS VERSUS COMPOSITE REFERENCE STANDARDS FOR ASSESSING TUBERCULOSIS LYMPHADENITIS DIAGNOSTIC TEST ACCURACY

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BACKGROUND

Tuberculosis lymphadenitis (TBL) is a common form of extrapulmonary TB that is difficult to diagnose due to its non-specific clinical presentation. There is no reliable gold standard to definitively classify TBL. Despite recognition of the imperfect nature of employed reference standards, methods used to evaluate new TBL test performance, e.g. composite reference standards (CRS), fail to account for their own uncertainty. Consequently, existing estimates of TBL diagnostic test sensitivity and specificity are biased. We used Bayesian latent class analysis (LCA) to estimate Xpert MTB/RIF (Xpert) accuracy for diagnosing TBL and compared this to estimates from multiple CRSs.

METHODS

We analysed a dataset of adults presenting to a tertiary care hospital with presumptive TBL in New Delhi, India with results for bacterial culture, smear microscopy, cytopathology/ histopathology, and Xpert. A heuristic model was created to understand relationships between latent classes and tests, with a random effect to denote bacterial burden. The CRSs were defined by increasing numbers of positive component tests to estimate Xpert's accuracy. Latent class model estimation was performed using RJAGS through Rstudio.

RESULTS

Using 299 patients with suspected TBL, TBL prevalence was 60.4% (95%CrI:54.0-67.0), and Xpert sensitivity and specificity were 86.9% (95%CrI:78.7-92.4) and 98.4% (95%CrI:94.5,99.8), respectively. Xpert sensitivity varied by CRS definition: sensitivity was 79% (95%CI:72-84) with a CRS of any one positive test result and reached 100% (95%CI:92-100) with all four positive results.

CONCLUSION

Bayesian LCA produces test accuracy estimates that incorporate reference standard uncertainty and conditional dependence. Such methods should be used when evaluating new TBL diagnostic tests.

H6. **TSPOT UTILIZATION IN SOLID ORGAN TRANSPLANT RECIPIENTS: A RETROSPECTIVE COHORT STUDY**

Sandoval M, Nguyen DT, Graviss EA.

BACKGROUND
Solid organ transplant (SOT) recipients are at increased risk for tuberculosis (TB) disease. Thus, guidelines recommend screening and treatment for latent tuberculosis infection (LTBI) among potential SOT recipients prior to initiation of immunosuppressive treatment.

METHODS
A retrospective record review was conducted investigating TSPOT.TB (Oxford Immunotec, Ltd) utilization in SOT recipients. Electronic health record data was accessed, including transplant registry data, patient outcomes and laboratory results, for adults receiving a transplant from 2014-2018 at the Houston Methodist Hospital, Texas, USA.

RESULTS
Of 1505 SOT recipients, 1427 (95%) reported TSPOT. TB (TSPOT) findings. The cohort was 60% male, 56% White, 95% US citizens, and 32% diabetic and included: heart, kidney, liver, and lung recipients. The median age at transplant was 56.7 years (IQR 45.6, 64.5). In total, 104 (7%) patients had a positive TSPOT result, of which 47 (45%) patients were treated with isoniazid or rifampin. Median follow-up time from transplant was 924 days (IQR 551, 1383). An acute rejection episode was recorded in 127 (8%) patients, 66 (4%) reported graft failure, and 182 (12%) expired during the study period. TSPOT positivity was not associated with acute rejection episode in multivariable logistic analyses (aOR=0.5, pvalue=0.22), nor was it associated with graft failure in multivariable Cox proportional hazard modeling (aHR=0.83, p-value 0.77). No TB outcomes were experienced during the study period.

CONCLUSION
While TSPOT positivity was not associated with poor outcomes in a large cohort of SOT patients, screening for LTBI in SOT patients was essential for TB prevention.

H7. CHEST X-RAYS ANALYZED BY ARTIFICIAL INTELLIGENCE-BASED SOFTWARE AS TRIAGE TESTS FOR PULMONARY TUBERCULOSIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS OF DIAGNOSTIC ACCURACY FOR DETECTION OF MICROBIOLOGICALLY-CONFIRMED DISEASE

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BACKGROUND

Artificial intelligence-based software for analyzing chest X-rays (CXR) to detect pulmonary tuberculosis (PTB) are now commercially-available. We sought to assess their diagnostic accuracy in people seeking care for PTB symptoms.

METHODS

We collected individual patient data, including CXR images, from studies identified through systematic reviews. We analyzed CXR with CAD4TBv6, Lunit, and qXRv2. The reference test consisted of mycobacterial culture or Xpert MTB/Rif. Each software outputs a continuous abnormality score; for binary classification, a threshold score is chosen above which a CXR is categorized as PTB. For each software, we estimated pooled AUC via parametric meta-analysis, and identified threshold scores with pooled sensitivity of 90.0% and estimated their pooled specificity using random-effects bivariate meta-analysis. We used meta-regression to assess differences in accuracy by HIV-status, smear-status, sex, age and prior TB.

RESULTS

We included 3727/3967 individuals from 4 studies (Pakistan, South Africa, Tanzania, Zambia). Pooled AUC of the software were similar (range: 0.83 to 0.85). At sensitivity of 90.0%, pooled specificities were: CAD4TBv6, 56.9% [95%CI: 51.7-61.9]; Lunit, 54.1% [44.6-63.3]; qXRv2, 60.5% [51.7-68.6]. For all software, sensitivity was lower for smear-negative versus smear-positive PTB. For CAD4TBv6 and qXRv2, sensitivity was lower in people living with HIV (PLWH). For all software, specificity fell with increasing age, and was lower amongst men, PLWH, and individuals with prior TB.

CONCLUSION

For detecting PTB on CXR in our study populations, these software achieved high sensitivity with moderate specificity. Users should select threshold scores based on a patient's HIV-status, and the local prevalence of smear-negative disease.

Table 1|Pooled sensitivity and specificity using the threshold score that had sensitivity of 90.0% in unstratified analysis (Overall) and subgroup estimates of sex, HIV-status, smear-status, prior TB, and age. Highlighted cells indicate non-overlapping confidence intervals between subgroups.

		CAD4TB v6		Lunit		qXR v2	
Group	**Number of Studies**	**Sensitivity [95%CI]**	**Specificity [95%CI]**	**Sensitivity [95%CI]**	**Specificity [95%CI]**	**Sensitivity [95%CI]**	**Specificity [95%CI]**
Overall	4	90.4 [82.2-95.1]	56.9 [51.7-61.9]	90.3 [82.9-94.7]	54.1 [44.6-63.3]	90.0 [80.8-95.1]	60.5 [51.7-68.6]
Sex							
Women	3	89.2 [74.2-96.0]	64.6 [60.9-68.2]	86.2 [78.7-91.4]	57.4 [51.0-63.6]	87.9 [63.7-96.8]	65.4 [55.1-74.5]
Men	3	92.8 [80.6-97.6]	51.9 [42.6-61.1]	95.3 [81.7-98.9]	46.8 [34.1-59.8]	93.1 [87.3-96.4]	58.2 [45.6-69.8]
HIV status							
Uninfected	4	**94.5 [91.5-96.4]**	58.6 [53.0-64.1]	92.7 [84.9-96.6]	57.5 [53.8-61.1]	**93.9 [90.4-96.1]**	64.4 [58.5-69.9]
PLWH	3	**80.4 [62.4-91.0]**	52.0 [41.0-62.8]	86.3 [68.3-94.9]	45.2 [30.6-60.7]	**78.9 [61.7-89.7]**	51.6 [40.1-63.0]
Smear							
Positive	3	94.8 [86.1-98.2]	--	97.4 [87.0-99.5]	--	96.3 [89.7-98.7]	--
Negative	3	81.6 [56.2-93.9]	--	79.0 [65.4-88.2]	--	77.9 [48.8-92.9]	--
Prior TB							
Prior TB	3	92.2 [81.8-96.9]	**26.6 [17.2-38.7]**	90.7 [80.8-95.8]	**29.7 [22.3-38.4]**	91.9 [82.8-96.4]	**33.7 [24.4-44.4]**
No Prior TB	3	90.8 [78.9-96.3]	**66.8 [60.9-72.2]**	91.2 [84.8-95.0]	**58.0 [45.9-69.2]**	91.7 [79.1-97.0]	**69.3 [54.7-80.9]**
Age tertiles							
14 – 28 Yrs	3	93.5 [88.2-96.5]	**73.6 [61.9-82.6]**	92.1 [84.2-96.2]	**65.9 [53.0-76.9]**	96.1 [92.5-98.1]	**74.4 [61.2-84.2]**
28 – 42 Yrs	3	89.0 [75.7-95.4]	60.3 [51.5-68.5]	90.2 [82.6-94.7]	48.9 [32.7-65.3]	88.5 [72.9-95.7]	58.6 [42.4-73.2]
43 – 90 Yrs	3	91.8 [74.9-97.7]	**43.0 [39.4-46.8]**	88.0 [78.9-93.5]	**45.0 [40.1-50.0]**	90.9 [77.4-96.7]	**57.3 [54.2-60.5]**

PLWH, people living with HIV; Yrs, age in years

Table 2|Applying a meta-analysis-derived threshold with pooled overall sensitivity of 90.0%: adjusted absolute difference in sensitivity and specificity between subgroups of sex, age, past TB, HIV status, and smear-status estimated from multivariable meta-regression.

		CAD4TB v6		Lunit		qXR v2	
Group	**Number of studies**	**Difference [95%CI]**	**p-value**	**Difference [95%CI]**	**p-value**	**Difference [95%CI]**	**p-value**
Sensitivity							
Sex	3						
Women		-2.4 [-6.4, 0.7]	0.17	-1.9 [-6.7, 2.4]	0.39	N/A	N/A
Men		ref		ref		ref	
HIV Status	3						
PLWH		-13.4 [-21.1, -6.9]	<0.01	2.2 [-3.6, 6.3]	0.34	-13.4 [-21.5, -6.6]	<0.01
Uninfected		ref		ref		ref	
Smear	3						
Negative		-12.3 [-19.5, -6.1]	<0.01	-17.2 [-24.6, -10.5]	<0.01	-16.6 [-24.4, -9.9]	<0.01
Positive		ref		ref		ref	
Specificity							
Sex	3						
Men		-6.7 [-9.9, -3.6]	<0.01	-5.7 [-9.1, -2.2]	<0.01	-5.0 [-8.1, -1.9]	0.01
Women		ref		ref		ref	
HIV Status	3						
PLWH		-5.8 [-10.5, -1.2]	0.01	-6.5 [-12.9, -0.1]	0.04	-8.5 [-15.1, -2.0]	<0.01
Uninfected		ref		ref		ref	
Past TB	3						
Prior TB		-34.2 [-38.1, -30.2]	<0.01	-28.1 [-32.2, -24.0]	<0.01	-35.7 [-39.9, -31.4]	<0.01
None		ref		ref		ref	
Age tertiles	3						
14 – 23 Yrs		ref		ref		ref	
23 – 48 Yrs		-12.9 [-16.9, -8.9]	<0.01	-13.4 [-17.8, -9.0]	<0.01	-10.8 [-14.8, -6.9]	<0.01
48 – 90 Yrs		-31.7 [-35.6, -27.7]	<0.01	-24.1 [-28.3, -19.9]	<0.01	-18.0 [-21.8, -14.1]	<0.01

PLWH, people living with HIV; Yrs, age in years

Table. Percent LTBI test agreement by diabetes status

	Total (n)	Discordant Results* (%)	Both LTBI Tests + (%)	Both LTBI Tests - (%)	Total Agreement (%)	p-value
TST & QFT						
No Diabetes	409	26.1	20.8	53.1	73.9	0.45
Diabetes	62	30.6	24.2	45.2	69.4	
TST & T-SPOT						
No Diabetes	408	28.7	21.3	50.0	71.3	0.02
Diabetes	62	43.5	21.0	35.5	56.5	
QFT & T-SPOT						
No Diabetes	407	14.2	21.4	64.4	85.8	0.04
Diabetes	62	24.2	21.0	54.8	75.8	

*In addition to negative/positive result pairs, test combinations that included a T-SPOT borderline result were considered discordant.

G. SCIENCE

G1. METFORMIN EFFECT ON HUMAN MACROPHAGE INFLAMMATORY RESPONSE AND PHAGOCYTOSIS OF MYCOBACTERIUM TUBERCULOSIS

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BACKGROUND

Metformin (MTF) has a well-documented ability to control hyperglycemia, which has been shown to have effects on macrophage and lymphocyte functions that are key to controlling tuberculosis (TB) infection. We aimed to better understand the effects of MTF on the response of human macrophages to Mycobacterium tuberculosis (Mtb).

METHODS

PMA-differentiated THP-1 cells with two reporters for nuclear factor-κB (NF-κB), and interferon-regulatory factors (IRFs) were treated with 2mM of MTF for 4 hours, and then inoculated with Mtb from various lineages. Supernatants were tested with a multiplex ELISA system for 17 different analytes. Since MTF can also directly inhibit key metabolic processes of Mtb, we utilized gamma-irradiated mycobacteria. Phagocytosis was assessed by immunofluorescent assay.

RESULTS

Phagocytosis of all Mtb strains was increased in MTF-treated macrophages. A diminished NF-κB activation after Mtb stimulation was observed in MTF-treated macrophages. There was no effect on IRF activation by MTF pretreatment. Results from the multiplex ELISA showed a modulatory effect by MTF on the secretion of various inflammatory cytokines, with no effect on anti-inflammatory IL-10.

CONCLUSION

Our results indicate that MTF improves phagocytosis of Mtb by macrophages, while at the same time modulating their inflammatory response. Excessive inflammation is a phenomenon associated with active TB infection and with disruption of the granuloma architecture. MTF treatment could allow for improved activation of macrophages in the presence of TB infection. These results support the effects of MTF in key steps of TB infection control, and support its use as an additional treatment for TB.

G2. GENE EXPRESSION PROFILE OF INDIVIDUALS RECENTLY INFECTED WITH MYCOBACTERIUM TUBERCULOSIS

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BACKGROUND

People recently infected by M. tuberculosis (MTB) have a higher risk to develop active TB. We hypothesized that people with recent infection but without active TB have a unique gene expression profile that could be used as a biomarker.

METHODS

We evaluated the gene expression profile using RNA sequencing from PBMCs samples from 10 patients with pulmonary TB, 15 new tuberculin skin test convertors (negative LTBI that became positive during follow-up), and 11 people without infection after two-years of follow-up, from two Colombian prisons. The differential gene expression was assessed using the DESeq2 package in Bioconductor. Only genes with|logFC| >1.0 and an adjusted p-value <0.1 were considered to be differentially expressed. We analyzed the differences in the enrichment of KEGG pathways in each group using InterMiner (v.1.4.1).

RESULTS

The variation in the gene expression was affected by the time of incarceration. We identified group-specific differentially expressed genes between the groups: 289 in early LTBI (less than three months of incarceration at baseline), 117 in late LTBI (one or more years of incarceration at baseline), 26 in active TB, and 276 in the exposed but noninfected individuals. There were four pathways that include the largest number of downand up-regulated genes among individuals with early LTBI: cytokine signaling, signal transduction, neutrophil degranulation, and innate immune system. In individuals with late LTBI, the only enriched pathway with up-regulated genes was Emi1 phosphorylation.

CONCLUSION

recent infection with MTB is associated with an identifiable RNA pattern, related to innate immune system pathways.

G3. **IMMUNOMODULATORY EFFECT OF LEPIDIUM MEYENII IN THE INFLAMMATORY RESPONSE TO MYCOBACTERIA BY HUMAN MACROPHAGES**

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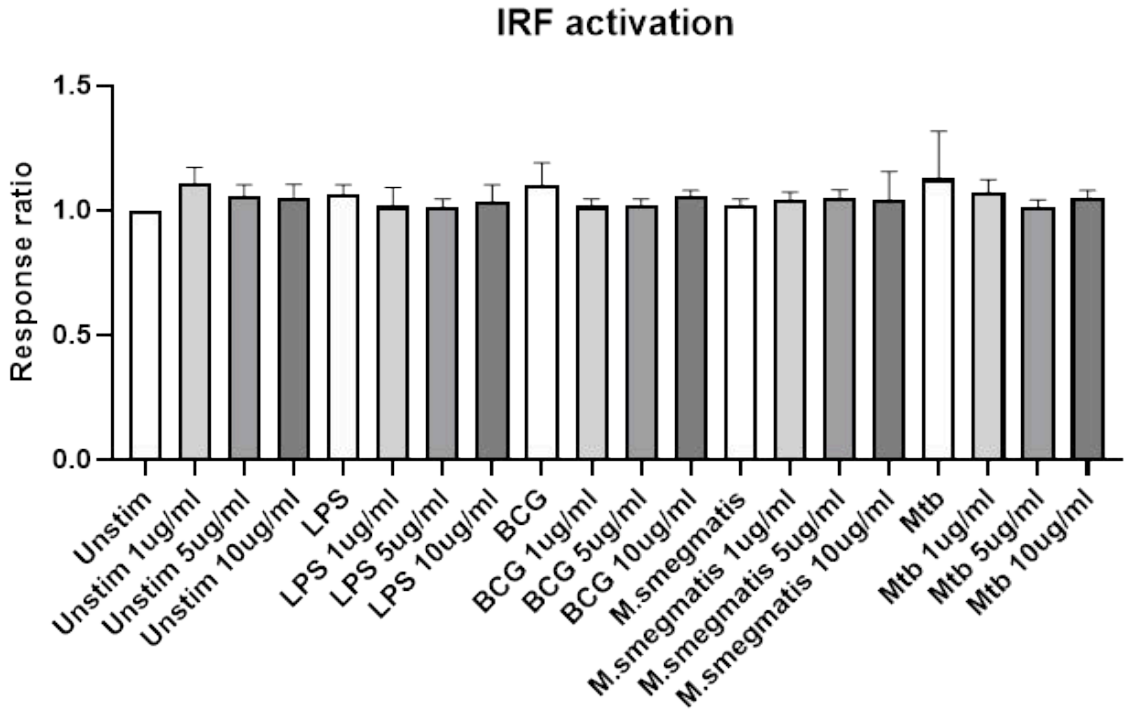
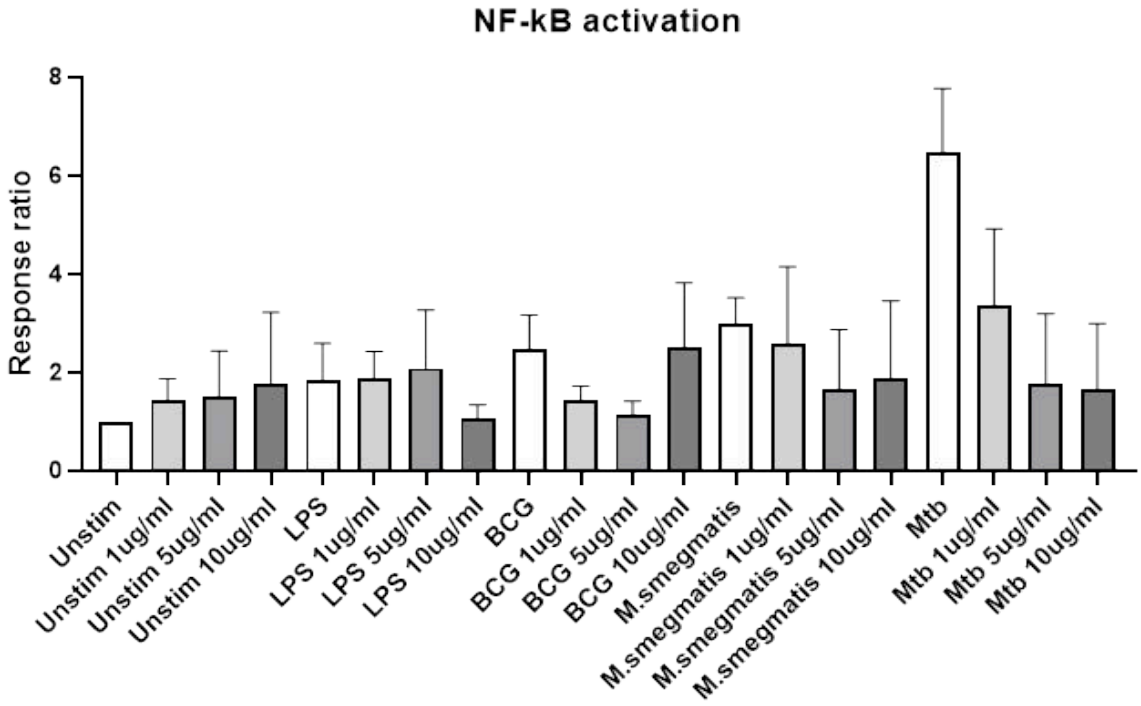
BACKGROUND
Lepidium meyenii (LM), also known as maca, is an Andean crop used medicinally for multiple purposes. Studies have shown an immunomodulatory anti-inflammatory effect in murine macrophages, able to induce M1 macrophage polarization. We aimed to assess the effect of LM on the inflammatory response of human macrophages to mycobacteria.

METHODS
Human monocytic THP-1 cells bearing two plasmid reporter systems for NF-kB and IRF activation, were differentiated into macrophages with PMA, and then treated with LM at concentrations of 1ug/ml, 5ug/ml and 10 ug/ml for 48 hours. Cells were then stimulated with LPS, Mycobacterium bovis bacillus Calmette–Guérin (BCG), Mycobacterium tuberculosis (MTB), and Mycobacterium smegmatis for 24 hours.

RESULTS
LM treatment lead to a reduction of the NF-kB activation upon inoculation with BCG, MTB, and M.smegmatis in a dose-dependent manner. No effect was observed in IRF activation.

CONCLUSION
Our results indicate that LM exerts an immunomodulatory effect on the NF-kB activation of human macrophages upon mycobacteria challenge. This is in line with previous report on the antiinflammatory effect of LM on an acute hepatitis murine model. Our findings could potentially translate into a beneficial effect in the exacerbated inflammatory response associated with active TB. LM may ultimately have the potential to be used as an adjunct therapy in TB or in BCG immunization.


IRF activation
Response ratio
1.5
1.0
0.5
0.0
Unstim
Unstim 1ug/ml
Unstim 5ug/ml
Unstim 10ug/ml
LPS
LPS 1ug/ml
LPS 5ug/ml
LPS 10ug/ml
BCG
BCG 1ug/ml
BCG 5ug/ml
BCG 10ug/ml
M.smegmatis
M.smegmatis 1ug/ml
M.smegmatis 5ug/ml
M.smegmatis 10ug/ml
Mtb
Mtb 1ug/ml
Mtb 5ug/ml
Mtb 10ug/ml


NF-kB activation
Response ratio
8
6
4
2
0
Unstim
Unstim 1ug/ml
Unstim 5ug/ml
Unstim 10ug/ml
LPS
LPS 1ug/ml
LPS 5ug/ml
LPS 10ug/ml
BCG
BCG 1ug/ml
BCG 5ug/ml
BCG 10ug/ml
M.smegmatis
M.smegmatis 1ug/ml
M.smegmatis 5ug/ml
M.smegmatis 10ug/ml
Mtb
Mtb 1ug/ml
Mtb 5ug/ml
Mtb 10ug/ml

G4. **WHOLE EXOME SEQUENCING IN PEOPLE EXPOSED BUT NON-INFECTED INDIVIDUALS, LATENT TUBERCULOSIS AND ACTIVE TUBERCULOSIS**

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BACKGROUND

There are people that no matter the duration and intensity of the exposure to Mycobacterium tuberculosis never get the infection, and once it is acquired (latent tuberculosis-LTBI), never developed the disease (tuberculosis-TB). The aim was to identify new and existing variants associated with different stages of tuberculosis.

METHODS

Cohort study. We administered a two-step tuberculin skin test (TST) at baseline and those negative were followed every 6 months for two years. The phenotype considered for the analysis were: 'Non-infected': people that never converted the TST at the end of follow-up (41 persons). 'New LTBI': those that during follow-up converted the TST (24 persons). 'Pulmonary TB': people microbiologically confirmed with pulmonary TB (29 persons). We collected sociodemographic and clinical information and took blood samples to perform whole exome sequencing.

RESULTS

A total of 329,018 variants were identified and passed quality controls. 307,953 (93.6%) were SNPs and 21,065 (6.4%) were INDELs. 40.381 SNPs were novel variants compared to dbSNP. Regarding the INDELs, 11,803 were new variants compared to dbSNP. Within 358 candidate genes, 6222 SNPs were identified, of which 1443 were synonymous, 1499 were not synonymous, and 24 variants between stopgain, stoploss, startloss and splicing. Among previously reported candidate genes, 372 were INDELs and they were divided as follow: frameshift deletion, frameshift insertion, nonframeshift deletion, nonframeshift insertion, stopgain, and unknown.

CONCLUSION

Our study found INDELs in previously identified candidate genes as well as new SNPs. Analysis is ongoing and association with SNPs with various phenotypes will be presented.

G5. GENE EXPRESSION SIGNATURES IDENTIFY BIOLOGICALLY DISTINCT ENDOTYPES IN TUBERCULOSIS

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ABSTRACT

Tuberculosis (TB) patients show incongruous immune responses that may affect the balance between effective host defense against Mycobacterium tuberculosis (Mtb) and detrimental immunopathology. We hypothesized that TB patients might express different molecular pathways that would require different host interventions. From a discovery cohort consisting of publicly available gene expression data sets including of 546 TB patients and 527 asymptomatic controls, unbiased clustering analysis identified 2 predominant and distinct TB endotypes. The two largest clusters exhibited distinct gene expression of metabolic, epigenetic and immune pathways. TB patient endotype A was characterized by increased expression of genes related inflammation, epigenetic-modifying genes, and Interferon and TNF signaling. Endotype A was associated with increased treatment failure gene expression scores. In contrast, TB patient endotype B demonstrated increased expression of genes related to glycolysis, Myc and E2F pathways. While gene expression studies were implemented on unstimulated blood, in an external cohort, mitogen stimulation demonstrates two functional TB endotypes, one with hyperinflammation (increased basal expression of cytokines and chemokines) and hyporesponsive and the other with normal responsiveness. In an external validation cohort, TB patients with gene expression signatures consistent with endotype A had increased risk of death, treatment failure and slow time to culture conversion. Library of integrated network connections (LINCs) evaluation suggests that host directed therapies beneficial for endotype A could be detrimental to endotype B. Collectively, these findings suggest that identifying distinct metabolic, epigenetic, and immune gene expression profiles within TB is an initial step towards the implementation of targeted host directed therapy.

G6. **PREVOTELLA DIFFERENTIALLY REGULATES THE INFLAMMATORY RESPONSE OF HUMAN MONOCYTES TO SARS-CoV-2 PROTEINS**

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BACKGROUND

Patients suffering severe COVID-19 show an aggressive and excessive immune response against the SARS-CoV-2 coronavirus, known as a cytokine storm. If left untreated these patients face the risk tissue damage, multi-organ failure and death. Besides treatment targeting the viral infection, other treatments aim in reducing or regulating theinflammatory process in COVID-19, to avoid the development of related complications. It has been observed that Prevotella histicola can modulate the inflammatory manifestations of autoimmune diseases like multiple sclerosis, and it is now being evaluated as a monoclonal microbial treatment in COVID-19.

METHODS

We evaluated the inflammatory response in human monocytes to various forms of SARS-CoV2 Spike glycoproteins, upon pre-inoculation with four different species from the genus Prevotella (i.e., P. histicola, P.copri, P,nigrescens, and P.oralis). Cells harbored two plasmid-reporter systems for transcription factor NF-kB, and for interferon regulatory factors (IRFs).

RESULTS

An increase in NF-kB activation was observed in response to any of the evaluated SARS-CoV-2 glycoproteins when monocytic cells had been pre-inoculated with P.histicola. An increase in the response to some of the proteins was also observed after pre-inoculation with P.copri or P.nigrescens, but to a lesser degree. Pre-inoculation with P.oralis only increased NF-kB activation in monocytes after stimulation with an stabilized trimer of an ectodomain protein of the SARS-CoV-2 spike glycoprotein. No differences were observed in IRF activation

CONCLUSION

Our findings suggest that contrary to what is expected in tissue, exposure of blood immune cells, such as monocytes, to commensal or potential pathogenic species of Prevotella may increase the inflammatory response to SARS-CoV-2 glycoproteins.

G7. **DAR-901 VACCINE FOR THE PREVENTION OF INFECTION WITH MYCOBACTERIUM TUBERCULOSIS AMONG BCG-IMMUNIZED ADOLESCENTS IN TANZANIA: A RANDOMIZED CONTROLLED, DOUBLE-BLIND PHASE 2B TRIAL**

Munseri P[1], Said J[1], Amour M[1], Magohe A[1], Matee M[1], Rees C[2], Mackenzie T[2], Tvaroha S[1], Bailey-Kellogg C[2], Maro I[4], Wieland-Alter W[1], Adams L[2], Horsburgh C.R[3], Nakamura K[4], Arbeit R[5], Pallangyo K[1], von Reyn C.F[2]. [1]Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; [2]Geisel School of Medicine at Dartmouth, Hanover, NH, USA; [3]Boston University School of Public Health, Boston, MA, USA; [4]Tokyo Medical and Dental University, Tokyo, Japan; [5]Tufts University School of Medicine, Boston, MA, USA.

BACKGROUND

SRL172 prevented disease due to Mycobacterium tuberculosis in a Phase 3 trial. DAR-901 represents a scalable manufacturing process for SRL172. We sought to determine if DAR-901 would prevent M. tuberculosis infection among BCG-primed adolescents aged 13-15 years in Tanzania.

METHODS

Adolescents with a negative T- SPOT.TBR interferon gamma release assay (IGRA) were randomized 1:1 to three intradermal injections of DAR-901 or saline placebo at 0, 2 and 4 months. Repeat IGRAs were performed at 2 months, and at 1, 2, and 3 years. The primary efficacy outcome was time to new TB infection (IGRA conversion to positive); the secondary outcome was time to persistent TB infection (IGRA conversion with repeat positive IGRA).

RESULTS

Among 936 participants screened, 667 were eligible and randomized to their first dose of vaccine or placebo (safety cohort). At 2 months, 625 participants remained IGRA-negative and were scheduled for the additional two doses (efficacy cohort). DAR-901 was safe and well-tolerated. Neither the primary nor secondary endpoints differed between the two arms ($p = 0.90$ and $p=0.20$, respectively). DAR-901 IGRA converters had median responses to ESAT-6 of 50.1 spot-forming cells (SFCs) vs. 19.6 SFCs in placebo IGRA converters ($p = 0.03$).

CONCLUSION

A three-dose series of 1 mg DAR-901 was safe and well-tolerated but did not prevent initial or persistent IGRA conversion. DAR-901 recipients with IGRA conversion demonstrated enhanced immune responses to ESAT-6. Since protection against disease may require different immunologic responses than protection against infection, a trial of DAR-901 to prevent TB disease is warranted.

G8. **BCG VACCINE POLICIES AND PRACTICES: TRACKING CHANGES IN NATIONAL POLICIES**

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BACKGROUND
Although effective at preventing severe forms of childhood tuberculosis (TB), the bacille Calmette-Guérin (BCG) vaccine effectiveness is highly variable in adults. As a result, BCG vaccine policies vary greatly and may change with countries' changing TB epidemiology. Common policies include vaccinating all neonates, only high-risk groups or no BCG vaccination. The aim of this study is to explore whether changes to national BCG vaccine policies between 2009-2019 are associated with countries' decreasing TB incidence over the same time period.

METHODS
The BCG World Atlas was updated in November 2020 with new information on past and present BCG policies. Using this database, we identified countries who changed their national policy between 2009-2019. We graphed yearly TB incidence rates (IR) from WHO for each selected country according to year of policy change. A chi-square test (X2) was used to compare the difference in TB IR for each country, before and after the policy change.

RESULTS
Out of 224 countries in the BCG Atlas, 11 changed their national policy between 2009-2019. The majority of countries changed from an all-neonates policy to only high-risk groups (8/11, 72%). The X2 test showed no significant association between this policy change and TB IR over time. However, Figure 1 shows that most of these European countries have a general decreasing trend for TB IR beginning from the year of policy change.

CONCLUSION
Several countries have moved from nationwide BCG vaccination to selected vaccination. Tracking these changes to national BCG policies and understanding the reasoning is helpful to policymakers and vaccine developers.

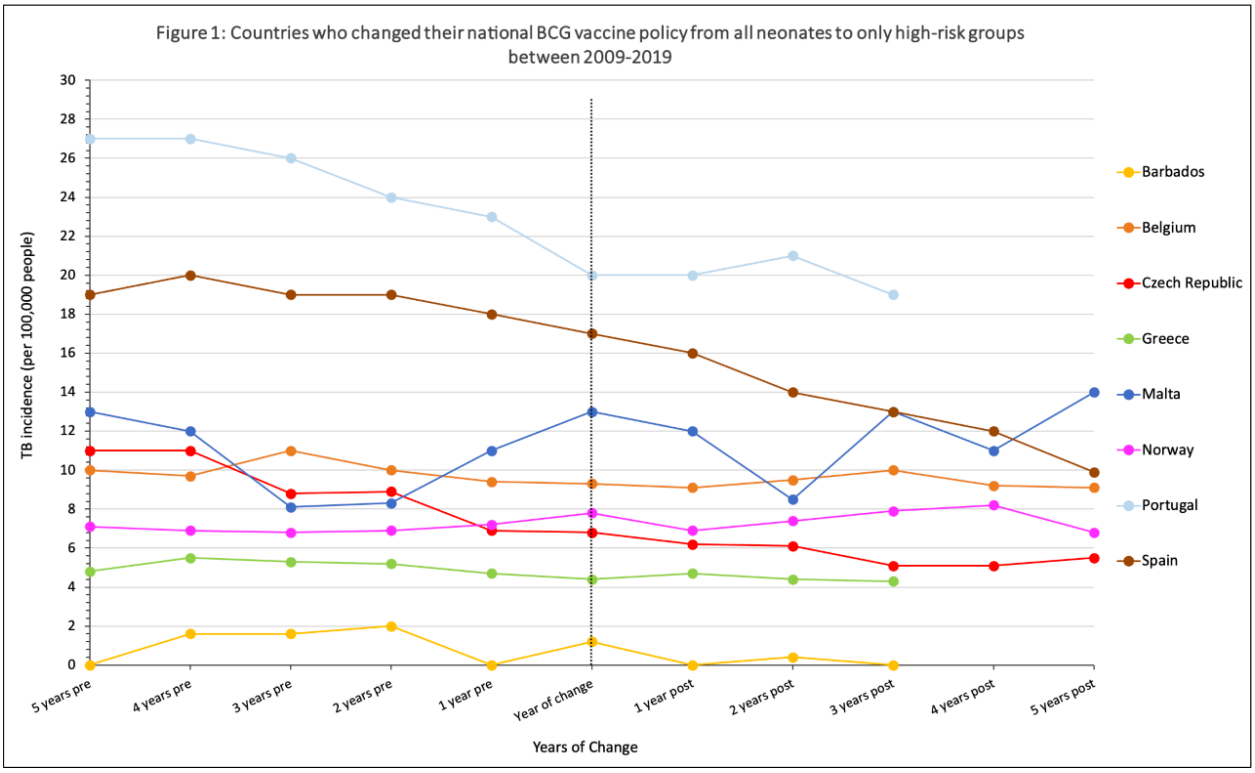
Figure 1: Countries who changed their national BCG vaccine policy from all neonates to only high-risk groups between 2009-2019
TB incidence (per 100,000 people)
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
5 years pre
4 years pre
3 years pre
2 years pre
1 year pre
Year of change
1 year post
2 years post
3 years post
4 years post
5 years post
Years of Change
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