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ABSTRACTS

The Union-North America Region

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ABSTRACTS FOR ORAL PRESENTATION

Chest X-Ray Screening in Prediction and Prevention for Incident Cases Among TB-Exposed Children

Dr. Qi Tan, Harvard Medical School, Boston, MA, USA

Post-Tuberculosis Depression Risk and the Role of Hospital Length of Stay: A Population-Based Cohort Study of People Immigrating to British Columbia, Canada, 1985-2015

Dr. Christopher Andrew Basham, University of British Columbia, Vancouver, BC, Canada

Tuberculosis Treatment Adherence in the Era of COVID-19

Dr. Maunank Shah, Johns Hopkins University, Baltimore, MD, USA

Developing Data Governance Agreements with Indigenous Communities in Canada Towards Equitable Tuberculosis Programming, Research, and Reconciliation

Mr. Robin Love, University of Alberta, Edmonton, AB, Canada

Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Ms. Kamila Romanowski, BC Centre for Disease Control, Vancouver, BC, Canada

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Dr. Leonardo Martinez, Boston University, Boston, MA, USA

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A1. POST-TUBERCULOSIS DEPRESSION RISK AND THE ROLE OF HOSPITAL LENGTH OF STAY: A POPULATION-BASED COHORT STUDY OF PEOPLE IMMIGRATING TO BRITISH COLUMBIA, CANADA, 1985-2015

Basham CA[1,2], Karim ME[1,3], Cook VJ[2,4], Patrick DM[1,2], Johnston JC[1,2,4]. [1] School of Population and Public Health, University of British Columbia; [2] British Columbia Centre for Disease Control; [3] Centre for Health Evaluative and Outcome Sciences, University of British Columbia; [4] Department of Medicine, University of British Columbia, Vancouver, Canada

BACKGROUND: We aimed to (1) analyze the risk and burden of depression among people diagnosed with tuberculosis (TB) compared to non-TB controls; and (2) assess the potential mediating role of hospitalization in generating post-TB depression risk.

METHODS: A retrospective cohort study of linked healthcare claims data for people immigrating to British Columbia, Canada (1985-2015). In aim 1, we analyzed time-to-depression by TB diagnosis (Cox proportional hazards regression), as well as rates of physician visits, hospital visits, and antidepressant dispensations by TB diagnosis (Poisson regressions). In aim 2, mediation analysis decomposed the total effect of TB on risk of depression into direct and indirect effects of TB, mediated by hospital length of stay (LOS).

RESULTS: People diagnosed with TB had an adjusted hazard ratio (aHR) of 1.23 (95% CI, 1.14-1.33) for depression. This total effect was decomposed into a natural direct effect of TB of aHR=1.11 (95% CI, 1.02-1.20) and indirect effect of TB through hospital LOS of aHR=1.11 (95% CI, 1.10-1.12), indicating that TB's total effect was mediated by 50% (95% CI, 36-87%) through hospital LOS. Males had a higher aHR than females (1.53 vs 1.07) for depression risk by TB. People diagnosed with TB experienced higher physician (aRR=1.21; 95% CI, 1.19-1.24) and hospital (aRR=1.35; 95% CI, 1.02-1.79) visit rates for depression, and a higher antidepressant dispensation rate (aRR=1.29; 95% CI, 1.25-1.33).

CONCLUSION: TB increased risk of depression by 23% during long-term follow-up. Depression screening during TB treatment is warranted, and long-term follow-up is recommended. Mediation of TB's effect on depression requires further study.

A2. LUNG FUNCTION AMONGST FIRST TIME DRUG SENSITIVE TUBERCULOSIS PATIENTS IN KHAYELITSHA, SOUTH AFRICA

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BACKGROUND: Abnormal lung function in patients with multiple episodes of tuberculosis and those with multi-drug resistant tuberculosis after cure are well documented. However, the prevalence of lung function abnormality amongst patients with first time drug sensitive tuberculosis during treatment is less well known, especially in the South African context.

METHODS: A descriptive cross-sectional study was conducted amongst 314 patients with first time drug sensitive tuberculosis near completion of treatment. All patients underwent spirometry and were classified as either having normal or abnormal lung function.

RESULTS: Only 235 were able to perform acceptable and repeatable spirometry. Abnormal lung function was present in nearly a third (32%, n=76) of patients. Restrictive abnormalities were the main abnormality at 15% (n=36) while obstructive and mixed lung abnormalities made up 11% (n=25) and 6% (n=15) respectively. Univariate logistic regression analysis related to socio-economic and clinical characteristics identified female gender, primary education age older than 45 years, being HIV negative, having a primary education and being obese as associations for abnormal lung function. However, multivariate logistic regression showed only being older, specifically in the age group of 56–65 (p=0.02) and being obese (p=0.04) were significant and associated with abnormal lung function.

CONCLUSION: Even in first time drug sensitive patients with Tuberculosis, abnormal lung function is present near completion of pharmacological treatment. Screening near completion of treatment to identify those with abnormal lung function should be considered to provide a continuation of care to those in need.

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A3. INTERVENTIONS TO MITIGATE COMMON NON-COMMUNICABLE DISEASES AMONG PEOPLE WHO EXPERIENCE TUBERCULOSIS: A SCOPING REVIEW OF THE EVIDENCE

Romanowski K,[1,2] Oravec A,[1] Billingsley M,[3] Shearer K,[4] Gupte A,[5,6,7] Huaman MA,[8] Fox GJ,[9,10] Jonathan Golub,[4] Johnston JC,[1,2]. [1]Department of Medicine, University of British Columbia; [2]Provincial TB Services, BC Centre for Disease Control, Vancouver, Canada; [3]School of Public Health, Johns Hopkins University; [4]Department of Medicine, Johns Hopkins University School of Medicine; [5]Center for Tuberculosis Research, Johns Hopkins University, School of Medicine; [6]Center for Clinical Global Health Education, Johns Hopkins School of Medicine; [7]Division of Infectious Diseases, Johns Hopkins School of Medicine, Baltimore, Maryland; [9]Department of Internal Medicine, University of Cincinnati, Ohio, USA; [8]Faculty of Medicine and Health, The University of Sydney, NSW; [10]Woolcock Institute of Medical Research, Glebe, NSW, Australia

BACKGROUND: Before scaling up screening for common non-communicable diseases (NCDs) within tuberculosis (TB) programs, we must ensure that screening is tied to evidence-based interventions. Thus, the objective of this scoping review was to map the existing evidence on interventions that address common NCDs among people who experience TB.

METHODS: We systematically searched PubMed, Medline, and Embase from January 1, 2000, to April 31, 2021. We included English language studies that implemented or evaluated non-pharmacological or non-surgical interventions to mitigate respiratory disease, cardiovascular disease, alcohol and substance use disorder, and mental health disorders among people who experience TB. We excluded studies that only screened for a condition but resulted in no further intervention. We also excluded studies focusing on smoking cessation interventions as guidance on implementing smoking cessation within TB programmes has been released.

RESULTS: We identified 20 studies that met our inclusion criteria. The most common intervention identified was referral for diabetes care (6/20; 30%). Other interventions included pulmonary rehabilitation (5/20; 25%), care programs for alcohol use disorder (4/20; 20%), and psychosocial support or individual counselling (5/20; 25%). A significant knowledge gap remains on the long-term durability of the identified interventions' clinical benefit, reach, and effectiveness.

CONCLUSION: We identified limited robust evidence to support individual interventions in changing outcomes and addressing the cascade of chronic disease care. We suggest future studies use behavioural theory and implementation science frameworks to support intervention design and evaluation.

A4. PREVALENCE AND FACTORS ASSOCIATED WITH DEPRESSION IN TUBERCULOSIS PATIENTS AT DIAGNOSIS IN INDIA

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BACKGROUND: Systematic reviews reveal a high proportion of depression in tuberculosis (TB) patients at diagnosis. Fewer studies have assessed factors associated with depression in TB patients.

DESIGN/METHODS: We analyzed data from a cohort study conducted in Madhya Pradesh and Uttar Pradesh, India. Samples of TB patients diagnosed by active and passive case finding were recruited from November 2019 to January 2021. A questionnaire collected within two weeks of diagnosis evaluated demographics, probable depression (PHQ-9 score >=10), probable alcohol use disorder (AUDIT score >=8), TB stigma (validated scale scored 0 to 100), food insecurity (Household Food Insecurity Access Scale) and social support (OSLO-3 scale). We performed multivariable relative risk regression to identify factors associated with probable depression.

RESULTS: Out of 704 patients, 170 (24.2%) had probable moderate depression (PHQ-9 score 10-15) and 243 (34.5%) had probable severe depression (PHQ-9 score >=15). In the regression analysis, factors independently associated with probable depression included underweight body mass index (adjusted relative risk [aRR] 1.3, 95% confidence interval [CI] 1.1-1.5), moderate or severe food insecurity (aRR 1.4, CI 1.2-1.6), poor social support (aRR 1.5, CI 1.3-1.7), elevated stigma score of 51-75 (aRR 1.7, CI 1.3-2.1), and diagnosis by passive case finding (aRR 1.2, CI 1.1-1.4). Gender, age, housing quality, alcohol use, and tobacco use were not associated with probable depression.

CONCLUSION: Stigma, poor social support, food insecurity, and undernutrition may contribute to depression at diagnosis, while demographic factors and substance use did not. Linking patients to mental health services and addressing associated factors are crucial to enhance TB care.

A5. RESPIRATORY IMPAIRMENT AND COMPLICATIONS AFTER SUCCESSFUL TREATMENT OF PULMONARY TUBERCULOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND: For many individuals, pulmonary tuberculosis (PTB) can result in a long-term health burden, even after successful treatment. We systematically reviewed the literature to estimate the incidence of respiratory impairment and complications following PTB treatment.

METHODS: Our systematic review (PROSPERO-CRD42021276327) included a search of MEDLINE, Embase, Health Star, and Cochrane from 1960 through May 2021 to identify studies describing patient cohorts that successfully completed treatment for active PTB. Reports describing the development of post-treatment respiratory complications and/or lung function measurements were included. Study characteristics and outcome-related data were abstracted. We meta-analyzed the incidence of lung function abnormalities and complications using a random effects model.

RESULTS: A total of 53 studies with 38,679 PTB patients were included (52% cross-sectional, 48% retrospective or prospective). Of these, 81% assessed populations from low-middle income countries. In preliminary analyses, 43 studies reported data on post-PTB lung function. Overall, the pooled proportion of participants with abnormal lung function was 56%. Specifically, 23% had a restrictive pattern, 20% an obstructive pattern, and 13% a mixed-pattern. Sixteen studies reported data on incidence of post-PTB complications, including 6 reporting bronchiectasis, 4 reporting lung cancer, and 3 reporting aspergilloma. PTB patients had a significantly higher risk of developing lung cancer than non-PTB controls.

CONCLUSION: The rate of post-PTB respiratory impairment as measured by spirometry is high, even after treatment completion. Our data also suggests the risk of developing lung cancer after treatment for PTB is higher as compared to non-PTB controls. These findings reinforce the importance of PTB prevention through tuberculosis preventive therapy.

A6. BARRIERS AND FACILITATORS FOR SCREENING AND TREATING DEPRESSION IN TUBERCULOSIS SERVICES IN SOUTH ASIA: PERSPECTIVES OF SERVICE USERS AND SERVICE PROVIDERS.

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BACKGROUND: Depression is common in tuberculosis and worsens tuberculosis outcomes. Although a treatable condition, depression remains undiagnosed and under-treated in developing countries. We aimed to understand the barriers and facilitators for screening and treating depression in tuberculosis services in South Asia.

METHODS: Ten focus group discussions were conducted with stakeholders in Bangladesh [N=2], India[N=6], and Pakistan[N=2] with healthcare workers[N=36], patients attending (or who had previously attended) tuberculosis services and their carers[N=38] between January - April 2021. We used the SURE framework that was developed to address and implement health system changes, to thematically categorize and organise the facilitators and barriers for recipients of care, providers of care and at the systems level.

RESULTS: People with tuberculosis and carers reported they lacked knowledge about depression services. They were keen for depression care to be offered alongside tuberculosis care; at the same time, they expressed fears of additional financial burden and stigma that might be associated with the service. Tuberculosis healthcare workers confirmed that although depression is common among tuberculosis patients, it is often unrecognised and untreated; they believed they lacked the relevant skills and training to address this gap and were also concerned about additional potential workload. Healthcare workers observed that the presence of 'Directly Observed Therapy' facilitators in TB services could be leveraged for depression recognition.

CONCLUSION: Despite the identified barriers, stakeholders strongly felt the importance of integrating depression and tuberculosis care and were willing to work with present resources to improve recognition and management of depression in TB services.

A7. CO-DESIGNING DEPRESSION CARE PATHWAYS INTEGRATED WITH TUBERCULOSIS SERVICES IN SOUTH ASIA

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BACKGROUND: Depression is prevalent in people with tuberculosis, and adversely affects treatment adherence and completion. However, there is a widely acknowledged 'treatment gap' whereby those who need care for mental disorders, do not receive it because of a lack of expertise and capacity in health services. Our goal is to develop context-appropriate depression care pathways delivered by non-mental health specialists in tuberculosis services in South Asia.

METHODS: We conducted co-design workshops in Bangladesh[N=5], India[N=8], and Pakistan[N=4], with stakeholders, including healthcare workers[N=39], people with tuberculosis and their carers[N=13], between May - July 2021. Workshop participants used the findings from a previous focus group study on potential barriers and facilitators, and their experiences to iteratively develop context-appropriate pathways.

RESULTS: Co-design workshops successfully engaged stakeholders to develop depression care pathways that could be delivered by non-mental health specialists working in TB services, and which required minimal additional resources. Patients with tuberculosis and their carers reported feeling empowered by being involved in decision-making about their care process and requested the incorporation of depression support groups and awareness materials into their care. Healthcare workers designed screening and referrals processes (which were broadly similar in the three countries). They also identified suitable personnel to implement each phase of the pathway. Health workers delivering tuberculosis services were able to liaise and strengthen the collaboration with mental health institutions.

CONCLUSION: It was possible to design pathways for integrated depression care in tuberculosis services. Our co-design approach and involvement of stakeholders may facilitate adoption, but the feasibility requires evaluation.

B. COVID

B1. CAN SARS-COV-2 SEQUENCING IMPROVE HOSPITAL INFECTION CONTROL? – A SINGLE CENTER EXPERIENCE

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BACKGROUND: By integrating SARS-CoV-2 genomic sequencing with epidemiologic contract tracing information, molecular epidemiology is an innovative way to track and identify COVID-19 transmission and risk factors. We aimed to understand how SARS-CoV-2 genomic sequencing would impact our understanding of transmission in the hospital setting.

METHODS: We whole genome sequenced all available discarded diagnostic SARS-CoV-2 RT-PCR positive specimens from Boston Medical Center healthcare workers between 12/10/2020 and 5/31/2021. Suspected transmission groups were identified through contact tracing performed by hospital infection control and employee health services. Through genomic data, cases were added to transmission groups if strains were identical and removed from transmission groups where strains were separated by >2 single nucleotide polymorphisms or were of different lineage where partially sequenced.

RESULTS: Of 7 suspected transmission groups with N>2, an average of 47% (range 0-75%) of isolates were successfully sequenced per group, limiting our ability to provide meaningful insights. However, of the remaining 5 suspected transmission groups with more than one successfully sequenced isolate (Figure), we were able to a. add cases (group G), b. confirm existing links (group E) or partially confirm existing links (group F), and c. separate suspected transmission groups as multiple introductions of SARS-CoV-2 (groups B and H).

CONCLUSIONS: Through the use of molecular epidemiology, it is possible to both differentiate suspected transmission groups by identifying multiple community SARS-CoV-2 introductions and to identify transmission links missed when using tradition contract tracing methods alone. Sequencing has the potential to be a critical tool for infection control.

Figure: Contact tracing linked groups (N>2) with >1 successfully sequenced isolate

B2. THE IMPACT OF THE BACILLUS CALMETTE-GUÉRIN (BCG) VACCINATION ON COVID-19: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND: The BCG vaccine has been known to confer non-specific benefits beyond its target pathogen, including immunoprotective effects against other respiratory infections and cancer. Recent evidence has shown that BCG vaccination could explain lower than expected COVID-19 incidence and monality rates. The present study investigates the effect of BCG vaccination on COVID-19 incidence and mortality rates.

METHODS: A systematic review and meta-analysis were performed to identify relevant studies since the start of the COVID-19 pandemic according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The strictly standardized mean difference was calculated to measure the effect size of BCG vaccination on COVID-19 incidence and mortality rates.

RESULTS: A total of 49 articles were reviewed, and 8 eligible comparative studies were used in the meta-analysis. The results showed an overall protective effect of BCG vaccination against COVID-19 mortality and incidence rates. The strictly standardized mean difference for mortality rate was 348.76. An I' value of 91.57 was found for mortality rates with BCG vaccination and of 65.56 for mortality rates without BCG vaccination. Five studies were analyzed regarding COVID-19 incidence rates. The strictly standardized mean difference for incidence rates was 1,273,584.117. An I' value of 2.84 was found for incidence rates with BCG vaccination and of 78.23 for incidence rates without BCG vaccination.

CONCLUSIONS: Our study shows that populations with BCG vaccination programs have lower COVID-19 incidence and mortality rates and highlights the need for future studies investigating the mechanisms behind the effect of BCG vaccination on COVID-19.

B3. STUDY OF THE TUBERCULOSIS CARE SERVICES CONTINUITY IN THE CONTEXT OF THE COVID-19 PANDEMIC, SENEGAL-2021.

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BACKGROUND : The focus on COVID-19 pandemic response, to the detriment of routine services including tuberculosis (TB) patients care, major the risk of services discontinuity. Thus the Senegalese National Epidemic Management Committee's objective was to study the continuity of health care services related to TB in the COVID-19 context.

METHODS : Quantitative and qualitative, structural, cross-sectional and analytical study was carried out using combination sampling methods and data were collected on telephone. Univariate, bivariate and multivariate analysis were done using simple logistic regression on Excel[2010®], EPIInfo[7.2.4.0®], Stata[SE/15.1®] and R[3.6.3®] (IRaMuTeQ[©]). Ethical considerations were effectives with the National Ethics Committee for Health Research approval.

RESULTS : 219 TB patients were interviewed, predominantly male (70.18%) with 10.94% pregnant or recently-given-birth women. The average number of children under 5 years in households was 1.56 ±1.58 and 70.83% of sputum AFBs tests came back negative and extrapulmonary TB was detected in 0.47% (15% positive ; 33.33% lymph node and osteoarticular localisations ; 16.66% multifocal). TB-HIV co-infection was sought in 85.92% (4.52% positive) with 5.5% TB services dyscontinuity in a pandemic context and statistically significant associations with the consultation cost (US$0.89-4.47) (p=0.007: ORadj=0.0479 [0.0052-0.4365]) and the search for TB-HIV co-infection (p=0.000: ORadj=4.28e+07 [2965906-6.16e+08]). Finally, the qualitative analysis showed the socio-economic barrier of COVID-19 on TB services continuity and the benefit of awareness and demystification.

CONCLUSION : COVID-19 pandemic reduced the supply-demand related to TB services and is an opportunity to prepare other health crises by developing services continuity plans.

B4. IMPACT OF MEDICAL SCHOOLS' RESPONSE TO THE COVID-19 PANDEMIC ON STUDENT SATISFACTION: A NATIONWIDE SURVEY OF US MEDICAL STUDENTS

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BACKGROUND: Over the last year, medical schools have faced various challenges in preparing their clinical students for the frontlines of a pandemic, but the effects of the pandemic on medical students on their rotations remain unclear. This study investigated medical students' satisfaction with their institutions during the COVID-19 pandemic with the intention of guiding educators in future public health crises.

METHODS: In this cross-sectional study surveying students in clinical rotations, the primary outcome was overall satisfaction regarding medical schools' responses to the pandemic, and the five secondary outcomes were demographics, school communication, exposure to COVID-19, availability of personal protective equipment, and access to COVID-19 testing.

RESULTS: The survey was distributed to 10 medical schools, of which 430 students responded for a response rate of 13.0%. While most students were satisfied (61.9%, n=266) with their schools' response, more than one in five (21.9%, n=94) were dissatisfied. Among the five secondary outcomes, communication with students was the most predictive of overall satisfaction (OR 69.058, 95% CI 17.898-266.449, $p<0.001$). Moreover, satisfied students were more likely to attend schools with smaller enrollment sizes compared to dissatisfied students (median size of 624 vs. 746, respectively, $p=0.002$). Notably, when the significant demographics were included in the overall satisfaction model, all demographic features were no longer significant.

CONCLUSION: While most medical students are satisfied with how their schools have responded to COVID-19, more than one in five students remain dissatisfied. Thus, in future crises, schools can best improve student satisfaction by prioritizing timely communication.

B5. NATIONAL TUBERCULOSIS MITIGATION PLAN AGAINST THE COVID-19 PANDEMIC IN GUYANA

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BACKGROUND: Social disruption due to the covid-19 pandemic in 2020 was devastating, where many people were forced to adopt new health seeking behaviors due to containment measures, interruption in the delivery of equitable health care services and the reallocation of resources in response to the diagnosis and management of tuberculosis.

METHODS: The NTP noted the need to widen the infection prevention and control measure, additional support to patients and staff and improve diagnostic and management approaches. These activities were critical during the COVID-19 pandemic, which eventually saw the development of a formal TB mitigation plan. This document was used to streamline further activities in curbing TB and COVID-19; and to advocate at financial institution and agencies for support and guidance.

RESULTS: TB health facilities were equipped with personal protective equipment, scale up health workers capacity in TB and COVID-19 activities through eLearning, information on safety measures mounted on clinic walls. Specially modified glass doors installed to control patient flow, additional Gene Xpert machines to support both TB and COVID-19 diagnoses. Furthermore, Video-DOT initiative to support the current DOT model to limit in-person contact, and supplying hygienic items, food hampers and hot meals to patients in need.

CONCLUSION: During the COVID-19 pandemic, TB collaborative efforts are important for the continuity of care and support for the staff, patients and their significant others.

B6. IMPACT OF TB DISEASE ON HOUSEHOLDS' SOCIO-ECONOMIC STAUS DURING COVID-19 LOCKDOWN; CASE STUDY IN HLAINGTHRAYAR TOWNSHIP, YANGON, MYANMAR.

Aung Than Oo.

BACKGROUND: TB is one of major public health problem in Myanmar. Hlaingtharyar Township is one of highest prevalence rate of TB disease. One fifth of TB patients and half of MDR TB cases mostly found in Yangon region. New sputum pulmonary TB patients case detection rate is increasing from 66.6% in 2014 and 58.8% in 2017 then to 74% in 2019. This research was conducted in Hlaingtharyar Township of Yangon. The main objective of this study to know influencing socio economic factors and economic burden among TB patients during the covid-19 and in addition, to find different social impact depend on gender.

METHODOLOGY: Using two-step probability sampling method using Taro Yamane (1967). According to the survey research finding, 81.7% of total respondents have taken major responsibility of their family before suffered from TB disease. 81% of people taking Initial Region treatment, 12% of people taking IR treatment and 6.7% of people taking MDR TB treatment are involved. Then 94.2% respondents suffered from pulmonary TB and other 5.8% got extra pulmonary TB. 59% of respondents working at government and factories and only 18% make their own business and private sector. During taking anti TB treatment, 100% of respondents have lost their previous jobs. 92% of respondents strongly agree that TB disease can cause economic burden. Although TB drugs are providing as free service, it is indicated that the direct cost is larger than indirect cost in this research. During covid-19 for taking anti TB treatment, 57% faced with financial burden and using coping mechanism.

RESULTS: Showed that living condition as well as their behavior of respondents influencing on TB disease transmission. 47% of respondents have aggregating factors for occurrence of TB disease such as DM, CKD. One-third of patients (n=90) had lived with at least one family member who suffered from TB (a clear risk factor for the transmission of TB). Nearly 31.6% of TB patients (n-38) are facing with stigma and discrimination in both genders of Hlaingtharyar Township. Beside the impact of parental illness on children's education was studied in (n_45) children of tuberculosis patients. Children of parents stricken with TB dropped out of school to earn money or care for parents.

CONCLUSION: TB patients in low- and middle-income household faced with economic burden and even they faced with catastrophic cost due to TB disease especially during covid-19. According to research finding, the following points would like to recommend, social interventions are needed to enable TB patients to access care and adhere to treatment. Availability of cash transfers and health insurance are important for as a component of the patients' socio-safety, which could potentially alleviate some of the catastrophic consequences of ill health.

B7. IMPACT OF THE COVID-19 ON THE TB PROGRAM IN HAITI

Richard M.

INTRODUCTION: Despite efforts deployed by the National Tuberculosis Program and partners, TB is still an important public health concern in Haiti; incidence and death rate are decreasing too slowly to reach the END TB targets; 14% and 24% from 2015 to 2020. Unfortunately, Covid-19 occurs while we are struggling to improve though security issues in the beginning of 2020; As all new phenomenon, almost all TB providers feared being contaminated and died, then leave facility alone and even confused TB and respiratory manifestation of Covid-19; since they scheduled special working days, they diminished access to poor TB patients that were already discriminated.

METHOD: We compared detection rate in the second quarter when covid-19 started with the previous quarter and the same one year before, and the quarter after peak July-sept 2020 to realize the situation created by covid-19 on the program

RESULTS: 44% Reduction of the detection rate comparing to the Quarter Jan-Mar 2020 and 31% to the same quarter in 2019 were observed at national level; with large variation between the departements; so that, where we had diagnosed more covid-19 cases had the greatest reduction like in West, Artibonite where they first case was detected, Centre where the Covid-19 care management started; reduction of the lost to follow-up and increase of death rate globally among TB patients.

CONCLUSION: Covid-19 has negatively impacted the program by jeopardized effort to increase TB detection rate in 2020 while increase death rate among our patients of the 2019 cohort.

B8. COVID-19 IMPACT ON US STATE AND LOCAL HEALTH DEPARTMENT TUBERCULOSIS PROGRAMS: A NATIONAL TUBERCULOSIS CONTROLLER ASSOCIATION SURVEY

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BACKGROUND: The National Tuberculosis Control Association (NTCA) conducted a survey to assess the impact of COVID-19 on TB programs at State and local health departments (LHD). State program included territory and districts whereas LHD included county, city, and regions. We report the similarities and differences state and LHD made to continue to deliver TB services.

METHOD: NTCA members from CDC Cooperative Agreement programs and LHD were surveyed January-March 2021. The National Association of County and City Health Officials sent an e-announcement to LHD.

RESULTS: A total of 46 State and 96 LDH programs responded. At the time of the survey, 50% of the LHD reported that less than a quarter of the services had returned to normal operations compared to 22% at the State level. Greater than 30% of LHD were not expecting staffing to return to normal within the following 10 months compared to 11% at the State level. Approximately 30% of both State and LHD did not know when staff would return to normal. LHD were significantly less likely to be able to work remotely. States were significantly more likely to change inclusion criteria for electronic directly observed therapy (eDOT) and issue interim TB Program operation guidance.

CONCLUSION: Challenges and opportunities were seen at both the State and LHD levels. Staffing and service delivery was particularly challenging at LHD. During a public health crisis, state and LHD need to partner on strategies, such as operationalizing interim guidance for eDOT and telemedicine, to prepare, adapt, and deliver efficient TB services.

B9. REPORTED SARS-COV-2 EXPOSURE SOURCES FOR PCR POSITIVE HEALTHCARE WORKERS AT AN ACADEMIC MEDICAL CENTER ACROSS TWO PEAKS OF THE PANDEMIC

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BACKGROUND: While healthcare workers (HCWs) are at an increased risk of SARS-CoV-2 from nosocomial transmission, they also remain at risk of community exposure. We assessed exposure sources for PCR positive HCWs in an academic medical center during two peaks of the pandemic.

DESIGN/METHODS: Information on exposure sources was collected retrospectively for 450 PCR positive HCWs. 106 HCWs tested positive between 3/13/2020 – 5/05/2020 (Time 1) during the national lockdown and 344 during 11/24/2020-4/18/2021 (Time 2). We calculated and compared the proportion of community, hospital and unknown exposures for HCW during both time periods.

RESULTS: The leading reported exposure source for Time 1 was known hospital exposures compared to unknown exposures for Time 2. Reported known hospital-exposures decreased from 55.7% (59/106) at Time 1 to 8.1% (28/344) at Time 2 ($p<0.001$). Reported known community exposures increased from 22.6% (24/106) to 32.3% (111/344, $p=0.059$). Unknown exposures increased from 27.4% (29/106) to 59.6% (205/344, $p<0.001$).

CONCLUSIONS: PCR positive HCWs reported SARS-CoV-2 exposure sources have changed as the pandemic has evolved. Known hospital exposures significantly decreased from the first to second peak of the pandemic as a proportion of all exposures. This change may be related to more intensive PPE protocols, vaccine rollout, and improved social distancing practices in the hospital and societal opening beyond the hospital. The true risk of nosocomial transmission for HCWs and how this risk evolves due to changing incidence and implementation of public health measures remains unknown.

Table 1: Reported Sars-CoV-2 Exposure Sources for Healthcare Workers

	Time 1 (N=106)	Time 2 (N=344)	p value
Known Community Exposure			0.059
Yes	24 (22.6%)	111 (32.3%)	
No	82 (77.4%)	233 (67.7%)	
Known Hospital Exposure			< 0.001
Yes	59 (55.7%)	28 (8.1%)	
No	47 (44.3%)	316 (91.9%)	
Unknown Exposure Source			< 0.001
Yes	29 (27.4%)	205 (59.6%)	
No	77 (72.6%)	139 (40.4%)	

C. PEDIATRIC

C1. INNOVATIVE PEDIATRIC ORAL FORMULATIONS FOR TUBERCULOSIS

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BACKGROUND: Medications for first-line treatment of tuberculosis (TB) have led to increasing rates of multi- and extensively drug resistant TB (MDR/XDR TB). Childhood TB represents approximately 20% of the disease burden in low-resource countries, with MDR-TB developing in 25,000 to 32,000 children annually. Currently, there are few pediatric formulations containing recommended drugs, which results in children being disproportionately affected. To meet the needs for pediatric-friendly oral anti-TB formulations, Luna is developing gummies that are palatable to children and remain stable for up to two years.

DESIGN/METHODS: Pectin-based gummies were formulated with anti-TB active pharmaceutical ingredients (APIs), including first-line drugs Pyrazinamide, Isoniazid, and Rifampicin, as well as second-line drugs Moxifloxacin, Clofazimine, Bedaquiline, and others. Initial drug-excipient compatibility was evaluated, and gummies were developed for optimal taste-masking and texture to improve palatability. Accelerated degradation studies were performed to predict two-year ambient storage. Drug loading and stability were evaluated with high performance liquid chromatography (HPLC)/mass spectrometry (MS).

RESULTS: A fixed-dose combination pediatric gummy containing first-line anti-TB drugs Pyrazinamide and Rifampicin demonstrated suitable taste and texture for pediatric patients. Accelerated degradation testing suggested stability of these APIs for up to two years. Work is ongoing to demonstrate a second-line anti-TB drug pediatric formulation.

CONCLUSION: First-line anti-TB drugs have been incorporated within palatable pectin gummy formulations with demonstrated shelf stability for up to 2 years. Future work will include pre-clinical evaluation of down-selected pediatric gummies containing second-line anti-TB drugs.

C2. THE CARE CASCADE FOR LATENT TUBERCULOSIS INFECTION IN CHILDREN AT A FEDERALLY QUALIFIED HEALTH CENTER IN NORTHERN CALIFORNIA

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BACKGROUND: It is critical to screen, diagnose and treat children with latent tuberculosis infection (LTBI), as they are at risk of severe tuberculosis (TB) disease and reservoir for future TB transmission. We analyzed six years of well-child visits to characterize the pediatric LTBI care cascade.

DESIGN/METHODS: We extracted electronic medical record (EMR) data for well-child visits in children 1-18 years old between 2014 and 2020 at a pediatric federally qualified health center in Oakland, California. Per American Academy of Pediatrics (AAP) guidelines, children should be annually screened for TB risk factors at well-child visits, and this clinic uses an EMR note template to prompt providers to complete this screen. Of those with risk factors, we determined the proportion of children with subsequent LTBI testing, chest radiography and treatment initiation.

RESULTS: We assessed 14,794 encounters with 48% of children under 5 years old. Screening was completed in 99% (14,575/14,794) of visits. However, of 715 children with risk factors, only 162 (23%) had documented testing ordered (83% with an interferon-gamma release assay). If a test was ordered, 89% (144/162) of patients completed testing and 3.5% (5/144) were positive. Of the five, 2 were previously treated, and the remaining had negative chest radiographs and were started on 4 months of daily rifampin.

CONCLUSION: While EMR note templates promoted high rates of TB risk factor screening in children, there was a gap in ordering a diagnostic test. Further work is needed to explore provider and patient barriers to testing to inform interventions to improve LTBI care for children.

C3. MULTICENTER ANALYSIS OF ATTRITION FROM THE PEDIATRIC TB INFECTION CARE CASCADE IN BOSTON

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BACKGROUND: TB care cascades describe diagnosis and treatment of TB infection. Identifying health systems factors associated with cascade completion can guide interventions to improve care for children with TB infection risk.

METHODS: We conducted a retrospective electronic health records-based cohort study of children tested for TB infection within two Boston health systems from 2017-2019, using tuberculin skin tests (TSTs) and interferon gamma release assays (IGRAs). We assessed proportion completing the care cascade and used generalized estimating equations to identify predictors of cascade completion.

RESULTS: We identified 12,867 tests among 11,264 patients. 262 tests (2%) were positive, 11,537 (90%) were negative, 297 (2%) were invalid/indeterminate, and 771 (6%) were not read (15% of all 5,274 TSTs). Among all tests, 12,024 (93%) were followed by cascade completion. Among patients with positive tests, 175 (67%) were diagnosed with TB infection and 5 (2%) were diagnosed with TB disease, 67 (26%) had false positive results, and 15 (6%) did not complete diagnostic steps. Overall, 186 (71%) patients with a positive test completed cascade diagnostic and treatment steps. Independent predictors of cascade completion included use of IGRA (ref: TST) (aOR 37, 95% CI 24-57), age ≥12 years (ref: age <5 years) (aOR 1.5, 95%CI 1.2-1.8), and public (ref: private) insurance (aOR 1.3, 95%CI 1.0-1.5).

CONCLUSION: Among children with a high proportion of negative TB infection tests, completion of the TB infection care cascade was high. IGRA testing, adolescence, and public insurance were independent predictors of cascade completion.

C4. MANAGEMENT OF CHILDREN WITH PRIMARY IMMUNODEFICIENCIES AND DISSEMINATED BCG PRE-AND POST HEMATOPOIETIC STEM CELL TRANSPLANT

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BACKGROUND: Children with primary immunodeficiencies (PID) who receive the Bacille Calmette-Guérin (BCG) vaccine are at risk for disseminated BCG disease. Many of these children require hematopoietic stem cell transplantation (HSCT) for treatment of their PID. There are limited data on optimal management of these patients, with variability in practice in the pre-and post-transplant period.

METHODS: We describe the clinical characteristics and management of three children with PID complicated by disseminated BCG who underwent HSCT and were treated at Boston Children's Hospital between 2015-2018.

RESULTS: All children were males 0-2 years old who received BCG vaccine at birth. None were tested for PID prior to receipt of the BCG vaccine. Patients were diagnosed with primary combined immune deficiency (n=1), interferon alpha and gamma receptor defects (n=1), and severe combined immunodeficiency due to RAG2 deficiency (n=1). All patients developed disseminated BCG prior to transplant. Two patients received matched related donor transplants, and one received a haploidentical HSCT for treatment of their PID. Treatment regimens and durations varied for disseminated BCG pre-and post- HSCT (Table 1). Patients experienced a variety of complications including drug interactions and IRIS. Two patients survived through completion of BCG treatment following transplant.

CONCLUSION: These cases highlight the variation in clinical course and management pre-and post- HSCT in children with PID and disseminated BCG. Further research is needed to determine optimal management of disseminated BCG in children with PID. Public health measures are needed to avert complications from BCG vaccination, such as improving newborn screening for PID worldwide.

Table 1: Clinical characteristics and management for 3 children with PID and disseminated BCG who underwent HSCT			
Variable	Patient 1	Patient 2	Patient 3
Patient characteristics			
Age at diagnosis (months)	24	2	13
Sex	Male	Male	Male
Country of origin	United Arab Emirates	Saudi Arabia	Saudi Arabia
Received BCG vaccine	Yes	Yes	Yes
Primary immunodeficiency	Primary combined immune deficiency (non-canonical NFK-B pathway defect)	Interferon alpha and gamma receptor defect	Severe Combined Immunodeficiency due to RAG2 deficiency
History of other infections	Chronic norovirus, multiple viral respiratory infections, hepatitis E	Streptococcus viridans bacteremia; CMV viremia; Mycobacterium. abscessus lymphadenitis; and osteomyelitis; myositis and osteomyelitis due to Serratia marcescens, Enterobacter cloacae, Candida albicans	Persistent Human metapneumovirus respiratory infection; Pneumocystis jirovecii pneumonia oral candidiasis; Coagulase-negative Staphylococcus bacteremia
BCG Infection Characteristics			
Categorization	Disseminated	Disseminated	Disseminated
Location of infection	Brain	Left axillary lymph nodes, bone marrow	Induration and swelling at BCG scar site; Diffuse lymphadenopathy; Hepato-splenomegaly
Management			
Diagnosis/ microbiology	Brain biopsy: AFB culture positive for MTB complex; CSF MTB GeneXpert: detected	Bone marrow biopsy: MTB complex PCR positive; Left axillary lymph node biopsy positive for MTB	Clinical diagnosis

ATT treatment used	Rifampin (20mg/kg/dose daily) Isoniazid (15mg/kg/dose daily) Pyrazinamide (20mg/kg/dose daily) Ethambutol (20mg/kg/dose daily)	Rifampin (20mg/kg/dose daily) Clarithromycin (15mg/kg/dose BID) Ciprofloxacin (15mg/kg/dose BID)	Rifampin (10 mg/kg/dose daily) Isoniazid (15 mg/kg/dose daily) Ethambutol (20 mg/kg/dose daily)
Duration of ATT treatment pre- transplant (months)	18	66	3
HSCT-characteristics			
Type of transplant	Matched related donor	Matched related donor	Haploidentical donor
Conditioning regimen	Busulfan Fludarabine	Busulfan Fludarabine	Reduced intensity fludarabine/busulfan/ rabbit ATG conditioning
IRIS	Yes	No	No
ATT treatment used post-transplant	Rifampin (30mg/kg/dose daily) Moxifloxacin (10mg/kg/dose BID) Isoniazid (20mg/kg/dose daily)	Rifampin (20mg/kg/dose daily) Clarithromycin (15mg/kg/dose BID)	Rifampin (10 mg/kg/dose daily) Isoniazid (15 mg/kg/dose daily) Ethambutol (20 mg/kg/dose daily)
Duration of ATT treatment post-transplant (months)	24	9	6
Outcomes			
Survived through BCG treatment	Yes	Yes	No (death 6 months post-transplant)

PID: primary immunodeficiency; BCG: Bacille Calmette-Guérin; HSCT: hematopoietic stem cell transplant; NF-KB: nuclear factor kappa B;
RAG2: recombination activating gene 2 protein; AFB: acid-fast bacilli; MTB: Mycobacterium tuberculosis; CSF: cerebrospinal fluid; PCR: polymerase chain reaction; ATT: anti-tuberculosis therapy; IRIS: immune reconstitution inflammatory syndrome; BID: bis en die

C5. CYTOMEGALOVIRUS ACQUISITION IN INFANCY AND THE RISK OF TUBERCULOSIS DISEASE IN CHILDHOOD: A LONGITUDINAL BIRTH COHORT IN CAPE TOWN, SOUTH AFRICA

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BACKGROUND: The risk of tuberculosis (TB) after exposure is greatest in the first few years of life, however the mechanisms responsible for this vulnerability are not understood. Acquisition of viral infections, such as cytomegalovirus, may modulate the immune system. We studied the acquisition of cytomegalovirus in infancy and subsequent development of TB throughout childhood.

DESIGN/METHODS: We enrolled pregnant women between 20–28 weeks' gestation attending antenatal care in a peri-urban South African setting in the Drakenstein Child Health Study. Nasopharyngeal swabs for cytomegalovirus detection using qPCR were done at birth, three weeks, six weeks, three months, six months, 12 months, and 24 months. Children were followed prospectively for TB using annual tuberculin skin testing, radiographic examinations with GeneXpert, culture, and smear testing. We compared TB incidence in children with and without cytomegalovirus using Cox regression and hazard ratios (HRs) with 95% confidence intervals (CIs).

RESULTS: Among 963 children tested for cytomegalovirus (N_{tests}=7,186; median 6 tests/child), 42% had cytomegalovirus by one year. Children who breastfed were at greatest risk (44% versus 14%, P<0.0001). Children were followed for TB for a median of 6.9 years (IQR, 6.0–7.8) and children with cytomegalovirus by one year had an increased hazard of subsequently developing TB (AHR, 3.2; 95% CI, 1.6–6.4) including microbiologically-confirmed disease (AHR, 4.4; 95% CI, 1.2–16.3). Infants with a high cytomegalovirus load were at consistently greatest TB risk.

CONCLUSION: TB prevention in children from high-burden countries may need to include strategies to deter or delay acquisition of cytomegalovirus in the first months of life.

C6. PEDIATRIC TUBERCULOSIS IN GUYANA: IDENTIFYING ITS TRENDS

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BACKGROUND: Tuberculosis (TB), an infectious disease caused by the bacillus Mycobacterium Tuberculosis, is among the leading annual causes of morbidity and mortality among children globally. With a lack of studies in the pediatric TB population in Guyana, this research aimed to identify trends and establish baselines.

DESIGN AND METHOD: There was a retrospective analysis of children under 15 years of age from the Georgetown Chest Clinic- representing over 95% of pediatric cases in Guyana. Data was collected from January 2010 - December 2019 from patient charts and TB registers using a literature-guided self-formulated data extraction tool. Data was analyzed using Microsoft Excel and SPSS software. Total number of all TB cases was captured for numerical comparison.

RESULTS: From a sample size of 92 from 101 children, the mean age was 7.4 years with a male predominance. African descent and Mixed ethnicity were most afflicted. 73.9% cases located in Region No.4. Pulmonary TB, diagnosed in 61.9% of cases was more common in the under 5 years and 10-15 years group (38.6% and 45.6% respectively). Overall treatment success rate was 73.9%; 3.3% died and 7.6% lost to follow-up. A 17.4% TB/ HIV coinfection rate was revealed. General gradual annual decline in TB disease incidence was seen. Half of the cases shared households with infectious TB individuals. Children represented 2.3% of all TB cases.

CONCLUSION: There is need for enhanced lost to follow-up case tracking and scale up child contact screening. Implementation of strategies such as awareness-raising activities in the community is necessary to reduce TB transmission.

D. QUAL/POLICY/ADVOC

D1. TUBERCULOSIS HEALTH CARE WORKERS' PERSPECTIVES ON EDUCATION AND COUNSELING FOR PATIENTS AND FAMILY MEMBERS WHO ARE FOREIGN-BORN

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BACKGROUND: Patients and family members experiencing tuberculosis (TB) require education and counseling to build capacity for future wellbeing. However, little is known about how to deliver high quality TB education and counseling, particularly in settings where linguistic and cultural dissonance between patients and health care workers (HCWs) is common. The purpose of this study was to explore TB HCWs' perspectives on barriers and facilitators for capacity-building education and counseling with patients and family members who are foreign-born, experiencing advanced pulmonary TB.

DESIGN/METHODS: This study formed one component of a qualitative case study in Calgary, Canada. Data were collected through semi-structured interviews and field notes and analyzed thematically. Twenty-four HCWs representing clerical staff, nurses, physicians, and allied health professionals employed in TB care were interviewed.

RESULTS: HCWs described how multi-level barriers, such as fear of death, complex intra-family communication, information-laden appointments, and patients' precarious employment collided resulting in overwhelmed patients and reduced connection to family members. Some HCWs were unsure how to discuss TB stigma with patients and family members. HCWs perceived that increased continuity and providing patients and family members with digestible amounts of information at earlier stages were important steps towards better practice. Some recommended phone counseling prior to initial appointments and improved patient education materials.

CONCLUSIONS: HCWs identified that patients and families could benefit from preparation for initial appointments, increased continuity of care, and improved patient education materials. HCWs should also receive skills-training to facilitate anti-stigma psychoeducational sessions. Future research could be directed at formative or summative evaluation of such interventions.

D2. STOP TB USA: RENEWAL IN 2021

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BACKGROUND: The WHO 2021 Global Tuberculosis (TB) Report described the first increase in TB deaths in more than a decade (1.5 million in 2020), along with a precipitous decline in TB notifications (1.3 million in 2020). The US also reported a 19.4% decrease in TB cases in 2020. The decrease in case notifications is likely due to redirection of staff and resources from TB programs for COVID-19 response; restoring public health infrastructure is critical to getting back on track to end TB.

INTERVENTION: In 2021, Stop TB USA reinvented its vision "a TB-free world by strengthening the ability to search for, treat, and prevent TB" and mission statement "to eliminate TB as a public health threat in the US." A goal-setting workgroup used SWOT analysis to identify key issues and activities. The five-year goal, to rebuild TB public health infrastructure, will be supported by the expanded Coordinating Board and membership working with partners such as DTBE, NTCA, Stop TB Partnership, and Global TB Caucus.

RESULTS: Operations and social media infrastructure were reestablished, the Coordinating Board expanded and diversified, the website updated, the TB Wire published monthly to inform and engage membership, 12 letters to policy makers signed to support TB funding, collaboration established with numerous domestic and global partners, a funding proposal submitted, and sessions at the upcoming The Union - NAR and ATS conferences planned.

CONCLUSIONS: Eliminating domestic TB requires public health infrastructure rebuilding. Funding increases, advocating for accessible TB resources, and multiple partnerships will help accomplish this goal.

D3. ADVOCATING FOR A BETTER TUBERCULOSIS CARE AND SERVICES IN CANADA DURING COVID-19: A COMMUNITY-LED SURVEY AND CALLS TO ACTION

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BACKGROUND: COVID-19 has disrupted tuberculosis (TB) services worldwide. Within Canada, progress towards ending TB in Inuit Nunangat by 2030 is now jeopardized. To regain lost progress towards ending TB in Canada, there is a need for up-to-date epidemiological TB data. Unfortunately, the most recent national TB data available for Canada are from 2017. We therefore lack the information needed to assess and mitigate the disruptive impacts of COVID-19 on TB programs in Canada. This lack of TB data in the face of a global health crisis prompted us to survey Canadian TB program leads, TB staff, and people affected by TB in order to produce a more comprehensive image of the current TB situation in Canada.

METHODS: Survey respondents were asked to describe their experiences of how COVID-19 impacted TB care and services using Likert scale questions and open-ended responses.

RESULTS: Survey respondents reported diagnostic delays and individuals presenting with more advanced disease, large-scale diversions of TB staff to COVID-19 work, significant disruptions to active case finding, contact tracing and LTBI management, and declines in quality of TB care during the COVID-19 pandemic.

CONCLUSION: Overall, the scale of these disruption points to an urgent need to address the backlog that this has created for the TB response. Based on the findings of this survey, we call for updated TB data, balancing the COVID-19 response with the need to maintain TB services, and leveraging COVID-19 tools to respond to TB.

D4. HOW CAN FINDINGS FROM COMMUNITY-BASED STIGMA ASSESSMENTS IN SOUTH AFRICA INFORM INTERVENTIONS TO CLOSE GAPS IN THE TB CASCADE OF CARE

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BACKGROUND: Stigma is a major barrier to TB care delivery. Understanding how and when TB stigma manifests is essential to design effective interventions. Yet there is limited data to understand the impact of stigma across three primary domains: enacted, anticipated, internal, and at different points in the TB cascade of care.

METHODS: Between January and July 2021, we conducted 70 community-based surveys of people who had experienced TB or been caregivers to a child who had experienced TB at a primary care clinic, Khayelitsha, Western Cape, South Africa. The survey included approximately 100 items (with some skip logic) with 5-point Likert scale parallel measures across stigma domains. We undertook descriptive analysis using SPSS (version 28.0).

RESULTS: Participants who had experienced at least one TB episode (n=46) expressed high levels of internal and anticipated stigma (6.5%-19.6%) that impacted their engagement in the TB care cascade, particularly in terms of initial care seeking behaviour. Participants who had cared for a child with TB (n=24) reported that high levels (8.4%-21.7%) of internal stigma (experienced by the child with TB) disproportionately impacted their engagement throughout the stages of the TB care cascade, compared to anticipated and enacted stigma (see Table).

CONCLUSION: Our findings suggest that interventions such as counselling to address internal and anticipated stigma may have a greater impact on reducing attrition within the TB care cascade, particularly at the earlier stages. This highlights the importance of using local data to inform stigma interventions, since manifestations of stigma are highly contextual.

Stage in TB Care Cascade	Study Group	Internal Stigma	Anticipated Stigma	Enacted Stigma
Delay in recognizing symptoms	PWTB	17.8	17.7	4.4
	Caregivers	20.8	4.3	8.4
Delay in going to the clinic	PWTB	19.6	15.9	4.4
	Caregivers	21.7	13.0	8.6
Treatment initiation	PWTB	11.6	8.9	4.4
	Caregivers	16.7	8.4	8.4
Seeking treatment adherence support	PWTB	10.8	15.2	6.5
	Caregivers	17.3	8.6	8.4
Completing treatment	PWTB	13.1	6.5	6.5
	Caregivers	20.9	8.6	8.4
Seeking post treatment follow-up services	PWTB	8.9	15.2	8.7
	Caregivers	8.4	16.7	8.4

Table 1. Percentage of people who had a history of TB (n=46) and caregivers (n=24) that 'Agreed' or 'Strongly Agreed' (survey response options included "Strongly agree, agree, neutral, disagree, strongly disagree") to statements regarding the influence of stigma categorized by domain on TB care seeking. PWTB = people who have experienced TB.

D5. STORY MAP AND STAKEHOLDER ANALYSIS TO IDENTIFY KNOWLEDGE, NEEDS AND BELIEFS ABOUT TUBERCULOSIS IN FOUR CITIES IN COLOMBIA

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BACKGROUND: Identify the interests, feelings, fears and needs regarding tuberculosis (TB) that the community have (adolescents, adults, community leaders, black/African descendants, and indigenous population) in four Colombian cities.

METHODS: We conducted a qualitative study of participatory action research. A stakeholder analysis and story map were conducted in four cities of Colombia: Medellín, Santiago de Cali, Florencia, and Chocó. The story map and focus group techniques were used to collect the information. All responses that were obtained were typed, and classified by city, groups, and resource (maps, interviews, explanations during focus groups). Then, theorical and emergent categories were identified. The information was also systematized in Microsoft Excel® and NVivo software.

RESULTS: There were 125 people that participated. People knew that TB is an infectious disease caused by a bacterium, that has cure and mainly affects the lungs, and that TB is transmitted by airborne, but they associated the transmission with direct contact with personal implements such as brushes, cutlery, and dishes, and by air pollution. In addition, people with prior history or current TB and their families mentioned that TB makes 'the poor poorer' referring to the catastrophic costs that they face, like transportation, medical leaves or not able to work due to isolation period.

CONCLUSION: This study shows the misinformation about TB among the community in each city. It is important to listen to the community in order to identify gaps and fears, and to co-design and co-develop with the community educational strategies to mitigate the stigma and discrimination against this disease.

D6. TUBERCULOSIS ELIMINATION THROUGH THE HEALTH EQUITY LENS

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BACKGROUND: Health equity is a critical aspect of tuberculosis (TB) control and elimination; preventing TB can improve health equity.

Importance: TB is preventable and treatable yet continues to disproportionately impact sub-populations defined by race, nativity, socioeconomic and immigration status in low incidence settings. In California, TB has been effectively eliminated in White, U.S.-born populations, while non-U.S.-born Californians continue to suffer from TB disease. In 2020, the case rate among non-U.S.-born Asians was 50-times higher than that of U.S.-born Whites.

Objective: Identify interventions across low incidence TB elimination plans to accelerate progress towards elimination and broader health equity; cross-compare and apply findings to California elimination efforts.

DESIGN/METHODS: Systematic search and review of low incidence TB elimination plans published 2011-2021 to identify interventions addressing health disparities and social determinants of health.

RESULTS: Of the nine low incidence elimination plans identified in nations, states, and regional consortia, all (100%) addressed health disparities. Three of the nine (33%) plans include both explicit health equity statements and interventions. The remaining six plans (67%) put forth equity-focused interventions only. As in the California plan, the plans include the following equity/patient-centered interventions: mitigation of care costs (8/9 plans); training on patient-centered approaches (8/9); engagement of high-risk group representatives (6/9); tailored/culturallyappropriate outreach (4/9); place-based screenings (4/9); and health equity metrics (4/9).

CONCLUSION: Across low incidence settings, TB elimination plans incorporate actions to mitigate health disparities, revealing widespread recognition that TB elimination and health equity are intertwined. California's Elimination Plan (2021-2025) aligns with global efforts with explicit health equity statements, interventions, and targets.

D7. STIGMA, RESISTANCE, AND VULNERABILITIES: LESSONS FOR TB FROM EFFORTS TO INITIATE OPIOID USE DISORDER (OUD) MEDICATION TREATMENT IN EMERGENCY DEPARTMENTS

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BACKGROUND: Opioid-related morbidity and mortality are a significant public health problem. This study examined several models of ED-based interventions for OUD, identifying key features, metrics for assessing effectiveness, barriers to and facilitators of success, and lessons for future programs. Potential insights for TB care are considered given the overlap in at-risk populations and similar patterns of stigma, vulnerabilities, and treatment complexity.
METHODS: The case study design of five ED-based, low-barrier OUD intervention programs in urban and rural US settings, represented a wide range of models and included interviews with stakeholders and staff and document review.
RESULTS: Barriers to enrollment and retention in treatment included stigma among clinicians, patients, and the broader community; sustainability beyond grant funding; distance to follow-up appointments; and lack of trained staff. Facilitators of success included special federal grants; attitudes of "meeting the patient where they're at;" awareness-raising posters and other normalization efforts; elimination of patient cost-sharing; the safety and effectiveness of buprenorphine; guaranteed follow-up appointments; and navigators to help with paperwork, health-related social needs, and travel to follow-ups.
CONCLUSION: ED-based OUD programs are an important component in promoting low-barrier OUD care and are a model for treatment of other substance use disorders. Cost-sharing elimination, nurse case management, community health workers, and incentives such as cab fare have been elucidated in the TB literature. Additional needs for the TB community suggested by these findings include specialized federal grants, normalization signals in the treatment setting, academic detailing for clinicians, development of shorter and safer drug regimens, and an increase in support staff.

D8. HOW TB TREATMENT AND PERCEPTION IN PERU EXACERBATES CAREGIVERS' BURDENS.

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BACKGROUND: In 2019, 12% of Peru's total reported tuberculosis (TB) cases occurred in adolescents aged 10-19 years. As adolescents are transitioning to adulthood, caregivers are essential to ensuring adolescents' treatment and providing emotional and material support. The burden of adolescents' TB illness on their caregivers is poorly understood.

DESIGN/METHODS: Semi-structured, individual, in-depth interviews were conducted with 30 caregivers of adolescents who completed or were lost from treatment for drug-susceptible TB in the preceding 12 months. One analyst coded the interviews inductively to identify themes relating to burdens that these caregivers endure during the adolescent's treatment.

RESULTS: Most caregivers were the mother or older sister of the adolescent for whom they cared. A majority stated that inadequate nutrition was the cause of TB. As cooking is perceived in Peruvian society as a female task, caregivers felt responsible for the adolescent's illness; moreover, they were blamed by others for the adolescent's illness. Caregivers supported the adolescent by motivating and accompanying the adolescent to the clinic for daily facility-based directly observed therapy. Caregivers frequently missed work to attend these visits, resulting in an economic burden. Finally, TB-related stigma led caregivers to lose their support network of extended family and friends.

CONCLUSION: To reduce caregivers' guilt about being responsible for the adolescent's illness, educational campaigns should clarify the role of malnutrition in TB pathogenesis. Reducing the number of clinic visits to receive TB medication would reduce the burden of motivating adolescents to go the clinic while also alleviating the economic burden of missing work.

E. RISK FACTORS/EPI

E1. SMOKED DRUG USE AND TUBERCULOSIS SYMTOMS: ANALYSIS OF A SOUTH AFRICAN PATIENT COHORT

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BACKGROUND: Symptom screening is commonly used to identify individuals for tuberculosis (TB) testing. TB symptoms overlap with smoked drug use symptoms such as cough and fever. It is unknown whether self-reported TB symptoms at diagnosis differ for people who use smoke drugs (PWUD), that those who do not use drugs, adjusting for disease severity.

METHODS: We analyzed data from 277 prospectively enrolled participants initiating TB treatment. Symptoms (cough, weight loss, fever, sweats) were captured individually and a symptom score was calculated by their sum at treatment initiation. Culture time to positivity and smear positivity were used as proxies for TB clinical severity. The association between each symptom, symptom length, and the between symptom score and clinical severity, stratified by smoked drug use, were assessed using Fisher exact tests and Kruskal Wallis tests.

RESULTS: 55.6% of the participants used at least one smoked drug (methamphetamine, mandrax, and/or cannabis). PWUD more frequently reported sweats than those who did not (Table1). Smear positivity (p=0.013) and time to positivity (p=0.046) were significantly different across symptom scores among participants without smoked drug use but not PWUD (Table 2b and 2a). PWUD reported more symptoms across all disease severities.

CONCLUSION AND RECOMMENDATIONS: PWUD reported similar symptoms at TB presentation to people who do not, except sweats which were higher in PWUD. TB disease severity only correlated with higher symptom scores in individuals who do not smoke drugs, indicating symptom reporting may not be as useful to identify disease in PWUD as people who do not use smoke drugs.

Table 1. Self-reported symptoms at treatment initiation by smoked drug use (n = 277)

Symptoms Symptoms Length, days	Statistics	Smoked Drug Use (N=123)	No smoked drug use (N=154)	p-value[1]
Cough	N (%)	147 (95.5%)	111 (90.2%)	0.099
Cough Length, days	Median (Q1, Q3)	28 (21,49)	28 (21,42)	0.772
Fever	N (%)	73 (47.4%)	61 (49.6%)	0.809
Fever Length, days	Median (Q1, Q3)	21(14,30)	21 (14,42)	0.193
Weight Loss	N (%)	130 (84.4%)	95 (77.2%)	0.163
Weight Loss Length, days	Median (Q1, Q3)	30 (21,60)	30 (21,60)	0.449
Sweat	N (%)	103 (66.9%)	65 (52.8%)	*0.019
Sweat Length, days	Median (Q1, Q3)	21(14,30)	21(14,60)	0.094

* $p < 0.05$

[1] Level of significance: 0.05.

[2] Statistical tests performed: Kruskal-Wallis Test and Fisher Exact Test.

[3] Only methamphetamine, mandrax, and/or cannabis were classified as smoked drugs in this study.

Table 2. Clinical severity and distribution of symptom scores among TRUST participants with smoked drug use and no smoked drug use

a. Participants with smoked drug use

	0-1 (N=14)	2 (N=38)	3 (N=43)	4 (N=59)	p value[1]
Baseline Sputum Smear Positivity					0.527
No	3 (21.4%)	3 (7.9%)	5 (11.6%)	9 (15.3%)	
Yes	11 (78.6%)	35 (92.1%)	38 (88.4%)	50 (84.7%)	
Time to positivity, days					0.845
Median (Q1, Q3)	6 (5, 7)	7 (5, 9)	7 (5, 10)	7 (5, 10)	
Missing	6	4	8	10	

* $p < 0.05$

[1] Level of significance: 0.05.

[2] Statistical tests performed: Kruskal-Wallis Test and Fisher Exact Test.

b. Participants with no smoked drug use

	0-1 (N=20)	2 (N=28)	3 (N=40)	4 (N=35)	p value[1]
Baseline Sputum Smear Positivity					0.013*
No	12 (60.0%)	9 (32.1%)	8 (20.0%)	8 (22.9%)	
Yes	8 (40.0%)	19 (67.9%)	32 (80.0%)	27 (77.1%)	
Time to positivity, days					0.046*
Median (Q1, Q3)	13 (9, 17)	11 (7, 15)	7 (5, 10)	9 (6, 11)	
Missing	12	6	9	5	

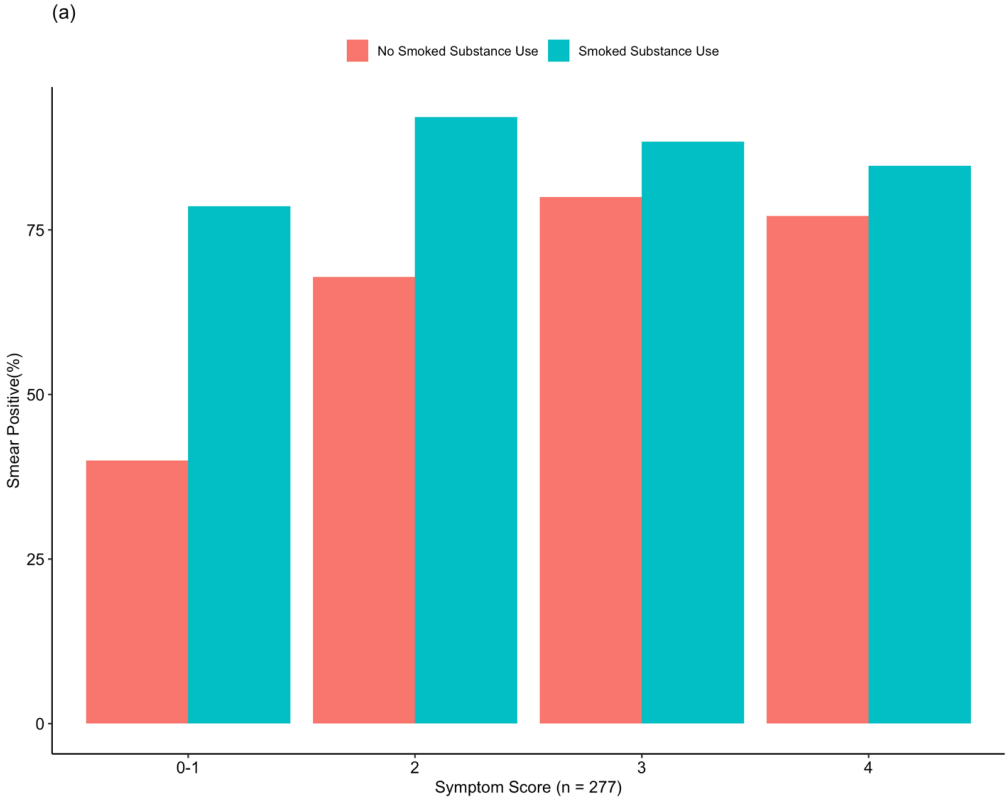
* $p < 0.05$

[1] Level of significance: 0.05.

[2] Statistical tests performed: Kruskal-Wallis Test and Fisher Exact Test.

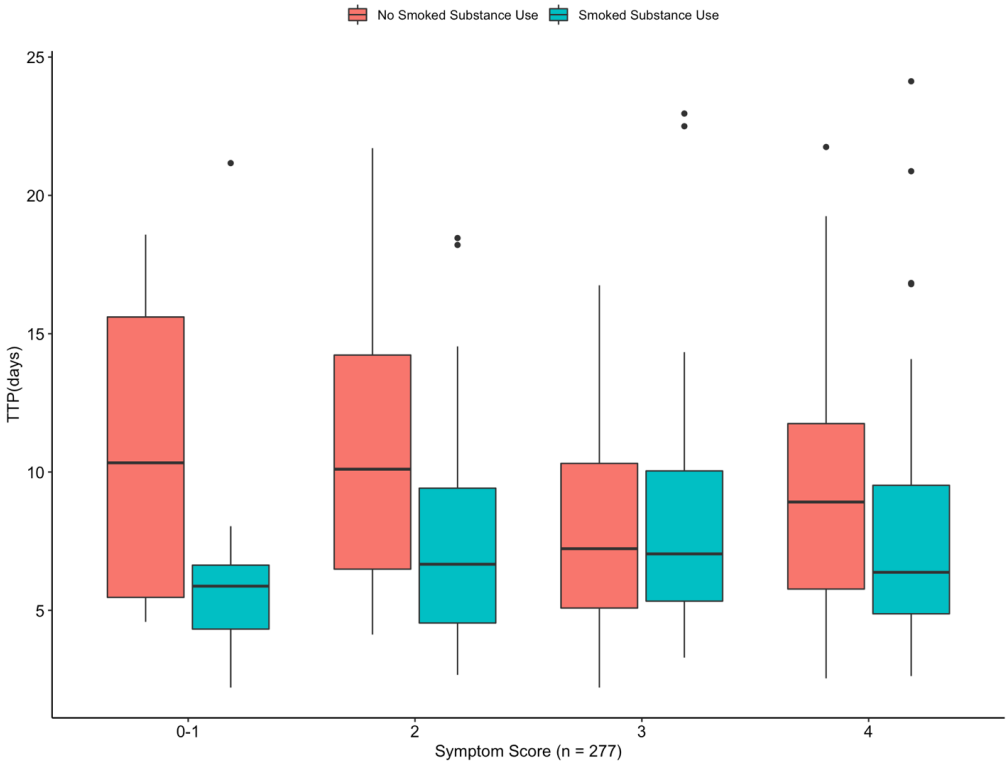
Figure 1. Smear positive rate, Time to positivity (days), and distribution of symptom score among TRUST participants (n = 277), by smoked drug use

a. Smear positive rate



[1] Only methamphetamine, mandrax, and/or cannabis were classified as smoked drugs in this study.

b. Time to positivity (days)



[1] Only methamphetamine, mandrax, and/or cannabis were classified as smoked drugs in this study.

E2. THE CHANGING PATTERN OF DISSEMINATED TUBERCULOSIS IN CANADA: A 30-YEAR CONVENTIONAL AND MOLECULAR EPIDEMIOLOGIC STUDY

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BACKGROUND: Although disseminated tuberculosis (DTB) has been considered relatively uncommon, estimated at 2-3% of all TB cases, the true extent of DTB worldwide is unknown. We sought to describe the prevalence and epidemiologic trends of DTB in Alberta, one of four high immigrant-receiving provinces in Canada.

METHODS: We used a retrospective cohort study design. All DTB patients in Alberta between January 1,1991 to December 31,2020 were included. Patients were sorted into five-year periods (1991-1995, 1996-2001, etc.) based on the date of diagnosis, then stratified based upon demographic features, infection risk factors, mycobacteriologic features, etc. Statistical analysis assessed epidemiologic trends in DTB, over time.

RESULTS: Over 30 years, 347 patients were diagnosed with DTB, representing 6.9% (range 5.3-11.0%) of all TB cases. All-cause mortality of DTB was 16.1% (range 6.5-27.3%). In the first 5 years (1991-1995), 51% of DTB patients were Canadian-born Indigenous; in the last 5 years (2016-2020), 86% were foreign-born. DNA fingerprint clustering within DTB patients was uncommon. HIV co-infection was the risk factor most commonly associated with DTB (range 15-30%). Over time, there was a trend towards increasing association with non-transplant immunosuppression (range 5.2-20.4%).

CONCLUSION: Rates of DTB in Alberta over the past 30 years were higher than previously estimated. Increasingly, the population group most affected is the foreign-born. Risk factors for DTB are similar to those for non-disseminated TB, namely HIV co-infection and other immunocompromising conditions. Further analysis should be targeted towards strategies for prevention or earlier diagnosis of this life-threatening infection.

E3. WHY DO PRESUMPTIVE TB PATIENTS IN INDIA NOT COMPLETE DIAGNOSTIC WORK-UP: A SYSTEMATIC REVIEW

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BACKGROUND: About 16% of individuals with active TB who approach government facilities in India do not get diagnosed. We conducted a systematic review to identify factors associated with non-completion of the TB diagnostic workup in India.

METHODS: We searched PubMed, Embase, and Web of Science and queried experts for studies published between January 1, 2000, and May 19, 2021, using search terms for TB, India, and loss to follow-up. Two independent reviewers identified studies of patients who: (1) did not get a chest radiography to complete workup for presumptive smear-negative TB; or (2) did not get a drug susceptibility test (DST) for workup of presumptive drug-resistant TB. We report variables with statistically significant adjusted effect estimates associated with workup non-completion.

RESULTS: Of 860 studies screened by systematic search, 19 met inclusion criteria. Factors associated with higher adjusted risk of not getting a chest X-ray included: patient unawareness that radiographs are needed for diagnosis, poor accessibility to government X-ray facilities, inability to afford private X-ray facilities, and evaluation at district (vs subdistrict) hospitals. Factors associated with a higher adjusted risk of not getting a DST included: older age, extrapulmonary disease, and being evaluated at a medical college (vs district hospitals).

CONCLUSION: Inaccessibility of radiographs—due to poverty, distance from facilities, or type of facility—contributed to non-completion of the smear-negative workup. Non-completion of the drug-resistant TB workup was driven by challenges in referring or obtaining specimens for patients who had specific DST indications or forms of TB.

E4. TUBERCULOSIS INFECTION PREVALENCE AMONG FOREIGN-BORN CANADIAN RESIDENTS IN 2016

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BACKGROUND: In Canada and the US, most TB disease occurs among foreign-born persons and reflects infection acquired before arrival. However, the prevalence of TB infection (TBI) is unknown in Canada. To better inform TB elimination strategies, we estimated TBI prevalence among foreign-born Canadian residents.

METHODS: We built on previous age-specific estimates of TBI prevalence in migrants" countries of origin. We simulated 200 annual risk of infection trajectories to generate estimates of yearly force of infection (FOI) for 217 countries, which accounted for 2.7 million (96%) of all foreign-born persons in Canada in 2016. We summed FOIs for each year of residency in the country of birth before immigration and each year of residency in Canada from 1931 to 2016. We combined these with 2016 Canadian census data to estimate TBI prevalence overall, and by age and TB incidence in country of origin.

RESULTS: Among foreign-born Canadian residents in 2016, 17% had arrived in the 5 preceding years. The overall estimated prevalence of TBI was 20% (interquartile range, IQR: 14-28%) (Table).

Prevalence increased with age, from 2% (2-3%) among persons aged <15 years to 32% (19-53%) among those ≥ 75 years. Estimated prevalence ranged from 8% (4-17%) among persons from countries where incidence was < 50 per 100,000 in 2016, to 34% (29-41%) among those from countries with incidence ≥ 200 per 100,000.

	Age in the Year 2016					
	Age <15, % (IQR)	Age 15-34, % (IQR)	Age 35-54, % (IQR)	Age 55-74, % (IQR)	Age ≥75, % (IQR)	Total, % (IQR)
TB Disease Incidence in Country of Origin per 100,000 persons (n=persons)						
0-49 (n = 3,370,095)	0.3 (0.3 – 0.4)	2 (2 – 2)	5 (3 – 8)	10 (5 – 22)	18 (7 – 40)	8 (4 – 17)
50-99 (n = 1,456,740)	1 (1 – 1)	6 (6 – 7)	20 (16 – 26)	38 (26 – 54)	58 (38 – 79)	25 (19 – 33)
100-199 (n = 579,945)	3 (2 – 3)	12 (11 – 14)	32 (22 – 46)	57 (33 – 81)	75 (45 – 94)	33 (22 – 46)
≥200 (n = 1,842,565)	4 (4 – 5)	19 (18 – 21)	38 (33 – 45)	50 (40 – 61)	61 (46 – 76)	34 (29 – 41)
Total (n = 7,249,345)	2 (2 – 3)	10 (9 – 11)	21 (17 – 26)	25 (16 – 38)	32 (19 – 53)	20 (14 – 28)

Table: Prevalence of TBI by age group and TB incidence in country of origin, Brackets indicates IQR

CONCLUSION: Approximately 1.4 million foreign-born Canadian residents have TBI. These estimates may inform future screening and treatment approach.

E5. PREDICTORS OF LOST TO FOLLOW UP AMONG TB PATIENTS IN GUYANA, CASE CONTROL STUDY

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BACKGROUND: The National Tuberculosis Programme (NTP) over the past few years has reported between 1236-1656 lost for follow up TB cases. With reducing incidence of 79 per 100,000 populations as per WHO estimates 2020, and average completion rate of 72%, lost to follow-up among TB patients remains a challenge to the NTP.

METHODS: A case control study was conducted in 7 out 10 regions with TB Basic Management Units (BMUs). A total of 25 lost to follow-up cases were randomly matched to 50 control cases (patients completing TB treatment), for the period of January to December 2020. Univariate analysis was done to check for association. A 95% confidence interval and significant alpha at 0.05 was considered. Variables included demographical data, co-morbidity, disease type, homelessness, employment status, substance abuse.

RESULTS: No variables showed significance p values, hence no further multi co linearity conducted. However, the odds ratio proved high association of lost to follow-up in patients ages 15-24; indigenous; HIV +; Extra Pulmonary TB; patients who use drugs; and unemployment. Among patients who completed treatment, a quality assessment reported that over 60S6 of patients adhere" because they wanted to get better".

CONCLUSIONS: Although this study revealed some variables that poses higher risks of a patient lost to follow- up in Guyana setting, it is important to evaluate patients' social history, pill support factors, why male preponderance; hence operational research at site levels are recommended.

E6. STUDY OF THE DETERMINANTS OF THE HIGH INCIDENCE OF TUBERCULOSIS IN THE VILLAGE OF SAVOIGNE IN THE HEALTH DISTRICT OF RICHARD-TOLL, SENEGAL

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INTRODUCTION: Savoigne is a village of 43670 inhabitants in the district of Richard-Toll, Senegal, West Africa. Access to primary health care is not sufficient. The district is currently following 178 TB patients, 7 of whom are suffering from TB resistant to 1st èreline treatment. The objective of the study was to identify the specificities of the area in order to break the chain of transmission.

METHODOLOGY: Survey form on the socio-demographic characteristics of patients, contacts, BCG vaccination status, profession, lifestyle, environment, level of knowledge about tuberculosis, clinical and paraclinical characteristics of patients, impact of Covid19 in treatment. Individual interviews, focus group were carried out.

RESULTS: There were 119 cases of TB, 7 of which were resistant TB. The population lives in great promiscuity. The main activities of the inhabitants are cattle breeding and agriculture. Most of them raise cattle which live in the concessions in close proximity to the communities. 89%% of the patients do not remember their BCG vaccination status. Patients suffering from resistant tuberculosis go every morning to the health post to take their medication in front of the nurse according to the country's strategy. Research funding would allow us to take samples from cattle in search of mycobacteria and to see if cattle are not involved in the chain of transmission.

E7. PHYSICAL INTENSITY OF OCCUPATIONS HELD AT THE TIME OF PULMONARY TUBERCULOSIS DIAGNOSIS IN A LOWER-INCOME NEIGHBOURHOOD OF KARACHI, PAKISTAN: DESCRIPTIVE ANALYSIS

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BACKGROUND: To better understand the potential impact of post-tuberculosis (TB) chronic physical impairment on the ability to work, we sought to describe occupations at the time of active TB diagnosis, in a lower-income neighborhood of Karachi, Pakistan.

DESIGN/METHODS: We did a secondary analysis of data from a study that consecutively enrolled individuals ≥ 15 years old seeking care for TB symptoms at Indus Hospital. Pulmonary TB (PTB) was diagnosed using two sputum cultures. We categorized physical intensity of occupations into High, Intermediate and Low based on Steeves (2015).

RESULTS: 2311/2370 (98%) of participants had data on occupation, 272/2370 (11%) had culture confirmed PTB. Median age was 33 years (IQR: 23-49). Amongst women with PTB, 41% (53/130) were employed, 53% (69/130) unemployed and 6% (8/130) missing data; amongst men with PTB, 81% (115/142) were employed, 16% (23/142) unemployed and 3% (4/142) missing data. The most common occupation amongst men with PTB was “Labourer” with 33% (38/115); amongst women with PTB it was “Housekeeper” with 45% (24/53). Amongst employed people with PTB, physical intensity of occupations was classified amongst women as: high, 49% (26/53); moderate, 8% (4/53); low 43% (23/53); and amongst men as: high, 57% (66/115); moderate, 21% (24/115); low 22% (25/115).

CONCLUSION: In this setting, the majority of adults with active TB were of working age. Most of those employed had high physical intensity occupations. This population is vulnerable to long term reductions in income despite PTB cure, due to the risk of chronic physical impairment post-TB.

F. SCIENCE

F1. HUMAN VITREOUS HUMOR SERVES AS A SUFFICIENT EXTRACELLULAR MATRIX FOR AN IN VITRO MODEL TO STUDY M. TUBERCULOSIS INFECTION.

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BACKGROUND: Granuloma formation is the hallmark of Mycobacterium tuberculosis infection. This blockade by leukocytes prevents dissemination and develops a niche to ensure the mycobacteria's survival. The extracellular matrix (ECM) facilitates the differentiation and activation of macrophages that compose the granuloma. Current commercially available sources of ECMs do not provide effective models to study this complex pathophysiology. Human vitreous humor (hVH) has demonstrated to work as an effective ECM for fibroblast differentiation.

DESIGN/METHODS: Here we describe the use of hVH as an ECM for an in vitro granuloma model upon Mtb infection.THP-1 human monocytes containing reporter plasmids for nuclear factor kappa-B (NFkB) and interferon (IFN) were seeded onto hVH obtained from human cadavers. Cells were then cultured under three conditions: hVH only, hVH + vitamin D, and hVH + PMA. After 3 days, macrophages were inoculated with Mtb. Formation, length, and area of granuloma were measured overtime. Supernatants were also collected to measure the activity of NFkB and IFN transcription factors.

RESULT: We observe that human monocyte-derived macrophages form granulomas in hVH as of day 7. Treatment with Vit D led to a faster granuloma formation (day 6) and of a larger area; yet formation in uninoculated and PMA-transformed cells was unremarkable. Significantly, NF-kB activation precedes IRF activation overtime in cells infected with Mtb.

CONCLUSION: Our findings support the use of hVH as a viable ECM model to study Mtb granuloma formation and provides evidence of cell activation. Inclusion of other cell types into this system may better mimic human tissue phenomena and improve our understanding of the Mtb granuloma formation process.

F2. ANTI-TUBERCULAR POTENTIAL OF SECONDARY METABOLITES OF ACTINOBACTERIA FROM A TROPICAL MANGROVE IN NORTHERN PENINSULAR MALAYSIA

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INTRODUCTION: Actinobacteria holds a prominent position in the discovery of novel antibiotics, whereas the emergence of multidrug-resistant tuberculosis (TB) strains is becoming a significant obstacle to TB control globally. Therefore, in this study, new actinobacterial secondary metabolites were isolated from tropical mangroves in the northern part of Peninsular Malaysia, an environment that has been seldom explored for actinobacterial isolation and is anticipated to represent a rare and alternative source of anti-TB compounds. Accordingly, the present study was conducted with the main objective of isolating and screening for antimycobacterial-producing actinobacteria from mangrove environments, including sediment and water samples.

METHODS: A total of 63 mangrove actinobacterial isolates were successfully isolated from the mangrove environments in Balik Pulau, Pulau Pinang and Merbok, Kedah. The isolates were identified and analyzed based on the location of the sample environment and the different sources of the samples and sites. These isolates were first screened against Methicillin-resistant Staphylococcus aureus (MRSA) and two strains of Mycobacterium tuberculosis (MTB), which served as surrogate organisms, M. smegmatis and MTB H37Ra, which are fast- and slow- growing.

RESULTS: The optimal growing conditions for the potential isolates at various salt concentrations, temperatures, and pH values were evaluated for enhanced maintenance and production of secondary metabolites. Two mangrove actinobacterial isolates with potent broad-spectrum antibacterial activity was selected for larger production using agar surface fermentation. The crude extracts of actinobacteria secondary metabolites were obtained by solvent extraction with ethyl acetate at 1:1 ratio and tested for minimum inhibitory concentration (MIC) and minimum bacterial concentration (MBC) against the fast-growing MTB surrogate organism, M. smegmatis and the slow-growing MTB surrogate organism, MTB H37Ra. Next, the crude metabolite extracts were further evaluated for their interaction with first-line anti-TB drugs against the same test organisms using checkerboard assay and time-kill assay. Identification of the most active actinobacterial ethyl acetate extracts was determined by gas chromatography-mass spectrometry (GC-MS).

CONCLUSION: In conclusion, the results of this study indicate that the tropical mangrove of northern Peninsular Malaysia are a good reservoir of antimycobacterial-producing actinobacteria that could be candidates for future anti-TB agents.

F3. EFFECT OF TITANIUM DIOXIDE IN AN IN VITRO GRANULOMA SYSTEM FOR MYCOBACTERIUM TUBERCULOSIS

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BACKGROUND. Mycobacterium tuberculosis infection is characterized by the development of granulomas. The use of in vitro models to study M.tuberculosis granulomas are important not only because they provide new insights on tuberculosis (TB) biology, but also for the evaluation of novel treatments. Such a study model of granuloma formation should mimics the structures occurring in human M.tuberculosis infection. Several studies have demonstrated an antimicrobial activity of titanium dioxide (TiO2), as well as a pro-inflammatory and granulomatous effect in the lung.
Here we investigated the effect of using a potassium-incorporated titanium dioxide (TiO2-KOH)-coated surface in an in vitro granuloma system for M.tuberculosis infection.

METHODS. We utilized human monocytic cell line (dual THP-1) cultured on a collagen matrix and incubated in the presence of 1,25-dihydroxyvitamin D3 to induce macrophage differentiation. Cells were then exposed to irradiated M.tuberculosis and UV-photoactivated discs coated with inert titanium, TiO2, and KOH-TiO2. The appearance of granuloma formation was recorded overtime.

RESULTS. We observed an increase in granuloma length and area over time upon M.tuberculosis inoculation that peaked at day 6 post-infection, and was maximal on day 7 post-infection for KOH-TiO2-treated cells. Simultaneously, activation of transcription factors NF-kB and IRF were diminished by TiO2.

CONCLUSION. Our findings show that exposure of human macrophages to TiO2 enhances granuloma formation upon M.tuberculosis infection in an in vitro granuloma system. This study demonstrates the effect of TiO2 in activation of human macrophages against an intracellular pathogen and may prompt future therapeutic strategies for TB.

F4. SPOILINEAGE VS SITVIT2 LINEAGE ASSIGNMENT IN A COLLECTION OF ISOLATES FROM A CANADIAN RECURRENT TUBERCULOSIS (TB) STUDY

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BACKGROUND: We examined results gained from lineage assignment using two spoligotype-based typing tools in a set of DNA isolates sequenced as part of a larger recurrent TB project. We are examining lineage as part of the contextual considerations around recurrent TB in Canada. We present a preliminary analysis of lineage assignment using two spoligotyping methodologies from the original sequenced isolates from two jurisdictions.

METHODS: silico spoligotyping of whole-genome sequencing (WGS) isolates from 50 sequenced recurrent TB episodes was performed using SpoTyping. Nineteen duplicates (recurrent cases) were from Alberta and six were from Saskatchewan. Spoligotype lineages were assigned using the SITVIT2 database, a collection of over 100,000 submitted clinical isolates of Mycobacterium tuberculosis (MTB), and SpolLineage, a software tool for predicting MTB lineages. Lineages considered included Indo-Oceanic (L1); Beijing (L2); East-African-Indian (L3); Euro-American (L4); West-Africa 1; West-Africa 2; and Ethiopian.

RESULTS: SITVIT2 assigned 38% of all isolates to L4, while SpolLineage assigned 52% of all isolates to L4. Fewer isolates were assigned to lineages 1, 2, and 3, while no isolates were assigned to the remaining lineages.

	SITVIT2	SpolLineage
Total L4:	19/37 = 0.51	26/48=0.54
Total L3:	6/37=0.16	10/48=0.21
Total L2:	10/37=0.27	10/48=0.21
Total L1:	2/37=0.05	2/48=0.04
Total Unknown:	13	2
Total	50	50

CONCLUSION: We compared SITVIT2 to SpolLineage for a collection of isolates to provide context as part of a recurrent TB study. We found that SpolLineage was more likely to assign a lineage than SITVIT2. Future work will examine the potential role of lineage assignment in differentiating relapse from reinfection TB.

F5. PREDICTORS OF CONTAMINATION IN SERIAL MYCOBACTERIAL SPUTUM SPECIMENS: LESSONS FROM AN OBSERVATIONAL COHORT

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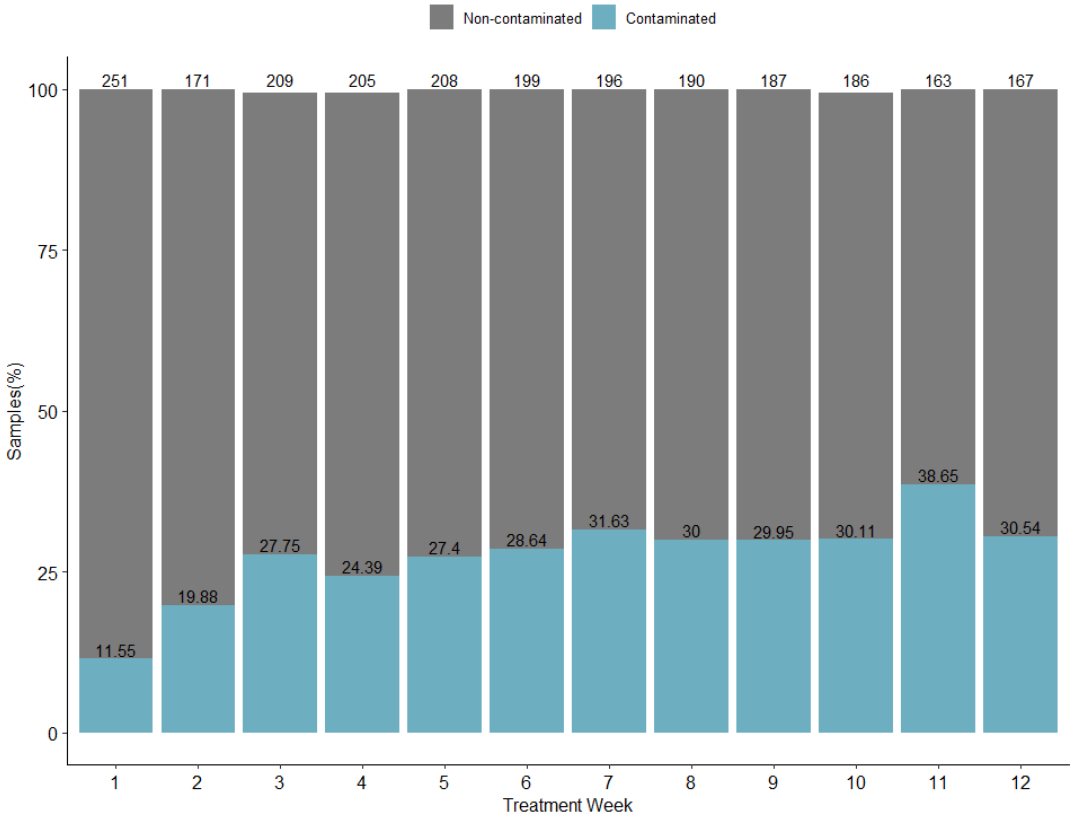
BACKGROUND: Sputum culture, the gold standard tuberculosis (TB) diagnostic, requires high quality handling and processing to avoid microbial contamination. Measurements that predict TB infectiousness, including colony forming units and time to positivity, cannot be captured with contaminated cultures. Mycobacterial culturing occurs at centralized biosafety level-3 facilities, meaning specimens often require storage and transport prior to processing. We evaluated predictors of contamination in serial specimens to improve protocols.

METHODS: We analysed 2,332 specimens from 251 participants collected weekly for 12 weeks following TB treatment initiation in a prospective longitudinal study (NIH R01AI119037). Specimen collection was classified as observed or unobserved by study staff. Samples were transported and stored at 4°C until processing. We examined associations between baseline sample contamination (blood agar or smear microscopy), demographic, clinical, and collection condition variables. We utilized logistic regression fit with Generalized Estimating Equations to analyse longitudinal associations.

RESULTS: Baseline samples stored ≥2 days between collection and processing (OR 2.48 p=0.032) were more likely to be contaminated. Unobserved expectoration was associated with contamination at baseline (OR 5.56, p<0.001) and longitudinally (OR 1.37 p=0.011). Smear grade of no AFB or scanty (OR 1.61, 2.06 p=0.027, 0.001) was more likely to be contaminated over the 12-week sampling period. Humidity and temperature on collection day were not associated with contamination (OR 1.02, 0.99, p=0.497, 0.522, respectively).

CONCLUSION: Samples are less likely to be contaminated when collection was observed by study staff and processed within two days. An inverse correlation exists between bacillary burden and contamination rates, indicating the importance of decontamination techniques.

Figure 1. Contamination rates for 12 weeks following TB treatment intiation , N=2332



Numbers above gray bars indicate total number of samples collected at each time point. Numbers above blue bars indicate percent of contaminated samples.

Table 1. Associations with baseline sputum sample contamination, N=251

	Contaminated[a] n = 29	Non-contaminated n = 222	p-value
	median (IQR) or frequency (%)		
Time to culturing >= 2 days[b]	20 (69.0%)	105 (47.3%)	0.028
Unobserved expectoration	12 (41.4%)	25 (11.3%)	< 0.001
Ambient temperature (°C)	22 (16, 25)	21 (17, 25)	0.523
Ambient humidity (%)	49 (42, 62)	53 (45, 66)	0.499
Male sex	14 (50.0%)	133 (61.0%)	0.263
Age (years)	38 (32, 49)	38 (26, 49)	0.395
HIV positive	9 (32.1%)	64 (29.5%)	0.773
Cavitary TB disease	17 (63.0%)	130 (64.7%)	0.861
Tobacco use	16 (57.1%)	152 (69.7%)	0.178
Smoked drug use[c]	12 (42.9%)	125 (57.3%)	0.146
Problem alcohol use[d]	15 (53.6%)	140 (64.2%)	0.272

[a]Presence of contaminants on blood agar plate or smear microscopy after detection of a positive MGIT culture.

[b]Time from collection to processing and BD BACTEC ™ MGIT ™ inoculation.

[c]Defined as a positive urine drug test or self-reported use of methaqualone, methamphetamine, and/or cannabis.

[d]Defined as a phosphatidylethanol (PEth) blood test > 49 ug/L and/or an Alcohol Use Disorders Identification Test (AUDIT) score > 7.

Table 2. Longitudinal associations with sputum sample contamination, N=2332			
	OR	95% CI	p-value
Unobserved expectoration	1.37	1.08, 1.74	0.011
Smear grade (ref. +++)			
No AFB[a]	1.61	1.06, 2.45	0.027
Scanty	2.06	1.32, 3.22	0.001
+	1.42	0.88, 2.29	0.157
++	1.06	0.61, 1.86	0.835
Age (years)	0.97	0.99, 1.07	0.494
Male sex	1.16	0.88, 1.53	0.308
HIV positive	0.96	0.73, 1.28	0.795

[a]Acid fast bacilli

F6. METAGENOMICS: LUNG MICROBIOME IN HIV PATIENTS - PNEUMONIA AND ITS EFFECT ON LUNG FUNCTION

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BACKGROUND: Little is known about the lung microbiome in patients with HIV and pneumonia and its effect on lung function in immunosuppressed patients.

METHODS: Prospective cohort study in patients diagnosed with community-acquired pneumonia (CAP) and / or human immunodeficiency virus in 2018 in three institutions in Medellín, Colombia. Patients who received antibiotics for more than 72 hours, severe immunosuppression from other causes, and severe lung disease were excluded. Microbiological and spirometric data were collected on admission and at six-year follow-up. Conventional microbiological and microbiome analysis was carried out and for this we amplified the 16S rRNA gene (V4 region).

RESULTS: The lung microbiome differs between the study groups, it also differs at the time of admission and during follow-up, and finally it varies between the samples of bronchoalveolar lavage and induced sputum. Regarding lung function, the HIV + CAP group had a function lower lung rate compared to the HIV group. The predicted forced vital capacity (FVC)% and predicted forced expiratory volume in 1 second (FEV1) % decreased, while the FEV1 / FVC ratio remained constant.

CONCLUSION: The lung microbiome differs between study groups, and during baseline and follow-up. There are many variables typical of the acute episode of pneumonia, and of antibiotic and antiretroviral treatment, among others, that cause its diversity to be modified. In patients with CAP, PF was affected upon admission and significantly improved in the first months after acute infection (CAP).

F7. INFERRING MYCOBACTERIUM TUBERCULOSIS LINEAGES AND ANTIMICROBIAL RESISTANCE FROM WHOLE-GENOME SEQUENCING DATA.

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BACKGROUND: Tuberculosis, caused by Mycobacterium tuberculosis (Mtb), is the leading cause of death with ten million new infections per year and 1.5 million deaths globally. The difficulty of distinguishing reinfection from novel infection is a major stumbling block in the treatment of recurrent tuberculosis. The long-term goals of the study aim to distinguish reinfection from novel infections using WGS. Here, we applied WGS to investigate the lineages and antimicrobial resistance (AMR) for 50 Mtb from Canada.

METHODS: WGS samples of 50 Mtb isolates were checked for quality using FastQC. Bioinformatics analysis was performed on cleaned WGS reads, including in-silico genotyping. Mykrobe was used for lineage-identification and AMR predictions. Single-nucleotide polymorphism (SNP) analysis will be linked with clinical data.

RESULTS: Bioinformatic analysis indicated that the genome fraction covered by the contigs was 97-98% and that the average number of genes and protein-coding sequences identified was 4,105 and 4,048, respectively. The associated lineages of the Mtb complex observed were lineage 1 (Indo-Oceanic; n=2), lineage 2.2 (Beijing; n=10), lineage 3 (East-African-Indian; n=10) and lineage 4 (Euro-American; n=28). Within lineage 4, the most prevalent genotype was s-type. AMR was observed in 2 isolates for rifampicin (rpoB_H445R and rpoB_S441L), 3 isolates for isoniazid (katG_S315T and fabG1_C-15X), and 1 isolate for streptomycin (rpsL_K43R). One isolate carried mutations for both rifampicin and isoniazid.

CONCLUSION: Multidrug resistance was observed in one isolate. Lineage 4, Euro-American, was the dominant lineage. The Mtb complex lineages will be verified by SNP analysis in future to illuminate the association between strains.

F8. HEAT PENETRATION STUDY IN ULTRAVIOLET RADIATION (UVR) AND MICROWAVE DUAL DISINFECTION SYSTEM (MWDDS) WITHIN SIMULATED BIO-MEDICAL WASTE, LOADED USING MYCOBACTERIUM TUBERCULOSIS (MTB) STRAINS.

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INTRODUCTION: Objective of Heat penetration study (HPS) is to provide documented evidence that UVR and MWDDS , manufactured equipment by Sanmit Infra Ltd, Mumbai, India ensures that live standard and wild strains of M. tuberculosis (MTB) are killed at 100 ^{0} c with 30 minutes of hold period of equipment by micro waves. Also, equipment operates properly to meet its intended function and acceptance criteria.

MATERIAL AND METHODS: Standard strain MTB H37Rv and susceptible & Multi drug resistant clinical isolates of MTB was grown on sterile Lowenstein Jensen medium (LJM) for 15 to 21 days at 37 ^{0}c. Purity of cultures was checked after the growth and were placed in UVR and MWDDS along with biological indicator as Bacillus atropheus. Decontamination program used for penetration study was 100 ^{0}c temperature and hold period of 30 minutes using thermocouple type probes having accuracy class A, range at least 0-150 ^{o} c for recording the temperature fluctuations of UVR and MWDDS . After 30 minutes unit was switched off, LJM slants were taken out, attained room temperature and added 2 ml sterile saline, were shaken. 1ml of suspension from each LJM slant (treated and untreated) was inoculated in sterile 5 ml Middle brook 7 H9 medium with OACD supplement and incubated at 37 ^{0}c for 15 days. Positive and untreated control of each MTB culture was kept in LJM slants at 2-8 ^{0}c. All the study procedures are carried out following ethical and Biosafety standard guidelines.

RESULTS: Results were documented as growth of bacteria or no growth of bacteria by checking the turbidity in the Middle brook 7 H9 medium tubes and carrying out acid fast staining. No turbidity was found in medium after 15 days of incubation showed proper decontamination by UVR and MWDDS. Biological indicator showed proper decontamination. Also, thermocouple showed variation in temperature of not more than 5^{0}C temperature while hold period of 30 minutes.

CONCLUSION: Hence UVR and MWDDS can be taken in regular use for decontamination of Bio-waste containing MTB. Microwaves along with UVR can be alternate cheap and easy to use methodology for decontamination.

G. SCREENING/TREATMENT

G1. A SYSTEMIC REVIEW OF ACTIVE CASE FINDING FOR TUBERCULOSIS IN INDIA

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BACKGROUND: Active case finding (ACF) for tuberculosis (TB) is the cornerstone case-finding strategy in India's national TB policy. We reviewed the literature assess the yield of ACF for different risk groups, implementation strategies, and screening criteria; and estimate losses to follow-up (LTFU) in screening and diagnosis.

METHODS: We searched PubMed, EMBASE, Scopus, and the Cochrane library to identify studies with ACF for TB in India from November 2010 to December 2020. We calculated 1) weighted mean number needed to screen (NNS) stratified by risk group, implementation strategy, and screening strategy; and 2) the proportion of LTFU.

RESULTS: Of 27416 abstracts screened, we included 45 studies conducted in India. There was considerable heterogeneity in risk groups screened and ACF methodology across studies. The weighted mean NNS was lower for people living with HIV (21, range 3-89, n=5) and people living with diabetes (65, range 21-undefined, n=3), rural populations (131, range 23-737, n=5), tribal populations (50, range 40-286, n=3), and household contacts of people with TB (50, range 3-undefined, n=12). ACF using facility-based screening (452, range 40-4085, n=16), and using the WHO symptom screen (135, 3-undefined, n=20) also had lower weighted mean NNS within their respective strata. Median screening LTFU was less than 15%. Median pre-diagnosis LTFU in facility-based screening was 55% (range 0-83%, n=7).

CONCLUSION: For ACF to be effective and efficient in India, its design must be based on contextual understanding. The narrow evidence base available currently is insufficient for effectively targeting ACF programming in a large and diverse country.

G2. LEVERAGING PROGRAMMATIC DATA TO EVALUATE AI-BASED CXR ANALYSIS IN A LOW-TB INCIDENCE SETTING: INTRODUCING MCI-TuXEDO

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BACKGROUND: Studies estimating the diagnostic accuracy of computer-aided detection (CAD) software for identifying possible pulmonary TB (PTB) on chest radiographs (CXR) have mostly been undertaken in high-TB burden countries, here most patients have smear positive disease. We sought to create a CXR- microbiologic database for use in evaluating CAD in a low-TB incidence setting.

METHODS: We collected Mycobacteriology lab results and CXR meta-data for all adult patients seen at the McGill University Health Centre (Montreal) from January 1, 2006 to December 31, 2016. We included patients with identifiers common across datasets, and ≥1 CXR. Based on mycobacterial culture results, we classified patients as PTB (if ≥1 positive culture), or PTB-negative (≥2 negative cultures, or no cultures performed). The earliest eligible CXR was selected into the database. We added a randomly selected set of CXR from other patients in whom mycobacterial sputum tests were never performed.

RESULTS: During the study period, 64586 microbiologic samples were tested, and 776374 CXRs were performed. The final database consists of 5832 patients – 336 PTB-positive, 5496 PTB-negative (4996 with negative cultures, 500 with no cultures performed). Median age (IQR) was 52 years (37-67), 2615 (45%) were women. Amongst the PTB-positive, 99 (30%) were smear positive. Amongst those with negative sputum cultures, 532 (11%) had results positive for non-TB mycobacteria.

CONCLUSION: The Montreal Chest Institute Tuberculosis X-ray E-chart Database (MCI-TuXEDo) will be used to assess diagnostic accuracy of CAD in a low-TB incidence setting where the majority of TB was smear negative, and NTM infection more common than PTB.

G3. IS IT ISONIAZID RESISTANCE: WHAT SHOULD WE DO IN THE ABSENCE OF DST

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BACKGROUND: Guyana acquired its first Xpert MTB/RIF in 2014 and begun testing for rifampicin resistance rifampicin, one of the most potent first lines anti TB drug among the high-risk groups. Cases identified as rifampicin resistance (RR) TB were all treated as Multi Drug Resistance Tuberculosis (MDR-TB). Rifampicin susceptible cases were treated with 2RHZE/4HR.

METHODS: A revive of cases was conducted on 14 TB cases registered during January 2019 – June 2021 from 4 of the 10 administrative regions in Guyana. Information collected was analysed in MS Excel, 2010. Principal factors that were taken into consideration was the category of patient and the time taken to sputum convert.

RESULTS: 50% of these cases were new TB cases, the second 50% were among LTFU and relapses (28.6% & 21.4% respectively). 1 case (7.1%) was HIV positive. After receiving 2 RHZE a 71.4% of these failed to sputum convert and the other 28.6% achieved sputum conversion, however, reconverted to sputum positive by the 4-5 month of treatment. GeneXpert was repeated to identify possible acquired resistance. All of which yield MTB detected, RR not Detected. Treatment was started empirically for Hr-TB with (6RHZE+Lfx). 100% sputum conversion was achieved after the first 2 months of treatment.

CONCLUSION: Evidently, based on treatment response, we can safely assume that there are undetected Hr-TB in Guyana. Access to DST is of vital importance in the management of TB, with the availability of DST, appropriate diagnosis will be made in a timely manner and hence, patient will receive quality care with tailored treatment regimen according to their resistant pattern, improving patient outcome, reducing the burden of this disease on the families as well as reduce cost of treatment for the NTBPs.

G4. A SYSTEMATIC REVIEW AND META-ANALYSIS OF TUBERCULOUS PREVENTATIVE THERAPY ADVERSE EVENTS

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BACKGROUND: Tuberculosis preventive therapy (TPT) is a key part of the WHO's end TB strategy. However, the risk of adverse events (AE) due to TPT is a major concern. We aimed to systematically review AE during TPT with different regimens currently in use.

DESIGN/METHODS: Our systemic review (PROSPERO CRD42021269551) included a search of MEDLINE, Health Star, EMBASE and Cochrane from 1952 to April 2021. We meta-analyzed the cumulative incidence of AE that met different definitions using a generalized linear mixed random effect model, overall, stratified by regimen, age, HIV infection, country income level, and AE type.

RESULTS: We included 186 publications, with 276 cohorts, and 186,519 individuals. Of the 276 cohorts, 65% were retrospective or prospective cohorts, and 35% from randomized control trials. 29 were studies in pediatric populations, with 7132 children. 251 cohorts reported any AE, 209 reported AE resulting drug discontinuation, 18 reported AE as judged by an independent panel, and 201 reported AE resulting in death. Of the treated individuals, 71% were from high income countries. The rate of any AE occurring with TPT was 9.6%. The rate of AE leading to drug discontinuation was 4%, while the rate of death due to drug-related AE was 0.3%. In the pediatric population the rate of AE was 2.7% with 0.3% leading to drug discontinuation.

CONCLUSION: We identified many studies with a large number of individuals receiving TPT which reported AE associated with treatment. AE were substantially lower in the pediatric population than in adults.

G5. TUBERCULOSIS TREATMENT ADHERENCE IN THE ERA OF COVID-19

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BACKGROUND: In-person directly observed therapy (DOT) is commonly used for tuberculosis (TB) treatment adherence monitoring in the US, with increasing usage of video-DOT (vDOT). We evaluated the impact of the COVID-19 pandemic on TB treatment adherence, and utilization and effectiveness of vDOT.

METHODS: We abstracted routinely collected data on individuals receiving therapy for TB disease in Baltimore, Maryland between April 2019 and April 2021. Our primary outcomes were to assess vDOT utilization and treatment adherence, defined as the proportion of prescribed doses (7 days per week) verified by observation (in-person versus video-DOT), comparing individuals receiving therapy in the pre- and post-COVID (April 2020) period.

RESULTS: Among 52 individuals with TB disease (median age 43, 63% male), 24 (46%) received treatment during the COVID-19 pandemic. Overall, verified adherence was similar pre- and post-COVID (68% versus 68%, respectively, p=0.96). vDOT utilization significantly increased post-COVID (18/24[75%]) compared to pre-COVID (12/28[43%], p=0.02). Overall, adherence was significantly higher when using vDOT (median 86% [IQR 70-98%]) compared to DOT (median 59% [55%-64%], p<0.01). Verified adherence using DOT was similar pre-COVID (median 58%[IQR 53-61%]) and post-COVID (median 62% [IQR 55-66%] p=0.77); alternatively, adherence decreased when using vDOT from the pre-COVID (median 98% [78-99]) to post-COVID(median 80%[IQR 60-93%] p=0.02) periods. Nonetheless, a greater proportion of doses were verified using vDOT compared to DOT in both the pre-COVID (median 98% vs 58%, p<0.01) and post-COVID period (median 80% vs 62%, p=0.01).

CONCLUSION: vDOT utilization increased post-COVID and was more effective than in-person DOT at verifying ingestion of prescribed treatment.

G6. PREDICTORS OF TREATMENT FAILURE IN DRUG-RESISTANT TUBERCULOSIS PATIENTS IN BANGLADESH: A RETROSPECTIVE COHORT STUDY FROM 2015-2019

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INTRODUCTION: Drug-resistant tuberculosis (TB) is recognized as a significant subsidizer to global antimicrobial resistance and giving a continuing threat to public health despite a remarkable change on treatment and diagnosis in recent times in Bangladesh. The goal of this study was to evaluate the treatment outcomes and predictors of individuals with drug resistance tuberculosis.

METHODS: A retrospective cohort study was conducted from 2015 to 2019 across the country. Using the statistical modeling software Stata Version-16, the multivariate logistic regression was performed among the binary variables to assess the relationship between the treatment outcomes and predictors.

RESULTS: A total 3,679 patients were selected for this study. Of these 66.40% (n=2,443) were males and 33.60% (n= 1,236) were females. Most cases were reported from 15-34 years. The overall mean age and standard deviation of the cohort was 37.52 ± 35. The successful treatment outcome was 74.99% (n=2,759). Previous treatment history showed that most of the patients 59.72% (n=2,197) had taken at least one earlier treatment and 40.28% (n=1,482) were newly registered. The odds of successful treatment outcome (UOR: .885, 95% CI: 0.693 - 1.131) was less likely among patients older than 25-34 years of age group compared to the 4-14 years of age.

CONCLUSION: Results suggest that younger age and male gender may be independent risk factors for drug-resistance TB. National tuberculosis control programs may target to improve service scope, laboratory capacity, reliable supply of drugs and quality in the health centers to increase the drug-resistance TB case detection rate.

G7. DIAGNOSTIC ACCURACY OF COMPUTER-AIDED DETECTION OF DIGITAL CHEST RADIOGRAPHS FOR TUBERCULOSIS TRIAGE AND SCREENING OF HOSPITALIZED PATIENTS IN LIMA, PERU.

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BACKGROUND: Tuberculosis (TB) transmission in healthcare facilities is common in high-incidence countries, yet the optimal approach for screening patients remains unclear. Given the interest in computer-aided detection software for TB diagnosis, we evaluated the diagnostic accuracy of qXR (Qure.ai, India).

METHODS: We prospectively enrolled two cohorts of patients admitted to a tertiary hospital in Lima, Peru: one group had cough or TB risk factors (triage) and the other group were asymptomatic (screening). We calculated the diagnostic accuracy of qXR versions 3 and 4 using culture and Xpert as primary and secondary reference standards, using receiver operating characteristic (ROC) analysis in STATA (version 16).

RESULTS: We analyzed 714 radiographs from 494 symptomatic patients and 220 asymptomatic patients (Table). qXR detected a high prevalence of lung abnormalities in the triage group: cavitation (21%), consolidation (65%), and opacities (83%). The areas under the ROC curves (AUC) for the triage group were 0.789 and 0.771 for versions 3 and 4 respectively compared to culture and 0.777 and 0.768 compared to Xpert. When we set the threshold score such that sensitivities were >90%, specificities ranged from 39.7-43%. In the screening group, only one patient had a positive Xpert result, limiting analyses of sensitivities although specificities were consistently >90%.

CONCLUSION: In this symptomatic population with a high prevalence of radiographic lung abnormalities, while sensitivity was high, the specificity for qXR did not meet WHO triage test criteria. qXR performed better in asymptomatic patients, although the diagnostic yield of screening this group in this setting was low.

Table. Diagnostic accuracy of qXR versions 3 and 4 compared to culture (primary reference standard) and Xpert (secondary reference standard).

	Symptomatic Patients			Asymptomatic Patients		
	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
CULTURE REFERENCE STANDARD						
qXR Version 3						
Overall			0.789 (0.734, 0.844)			-
qXR threshold 0.7*	90.2% (81.7-95.7%)	43% (37.7-48.4%)	0.666 (0.624, 0.708)	^	96.9% ^ (93.4-98.9%)	-
qXR Version 4						
Overall			0.771 (0.716, 0.825)			-
qXR threshold 0.8*	90.2% (81.7-95.7%)	40.6% (35.4-46.1%)	0.654 (0.613, 0.696)	^	94.8% ^ (90.7-97.5%)	-
XPERT REFERENCE STANDARD						
qXR Version 3						
Overall			0.777 (0.722, 0.831)			0.968 (-, 1.00)
qXR threshold 0.675 *	90.1% (82.1-95.4%)	39.7% (34.6-45.1%)	0.649 (0.609, 0.689)	100% ^^ (2.5-100%)	96.6% (93.1-98.6%)	0.983 (-, 1.00)
qXR Version 4						
Overall			0.768 (0.714, 0.821)			0.961 (-, 1.00)
qXR threshold 0.79*	90.1% (82.1-95.4%)	40.3% (35.1-45.6%)	0.652 (0.612, 0.692)	100% ^^ (2.5-100%)	95.6% (91.9-98.0%)	0.978 (-, 1.00)

* qXR threshold score at which sensitivity was closest to 90% (to meet WHO triage test accuracy criteria)

^ No patients had a positive culture result in the Asymptomatic Group

^^ Only 1 patient had a positive Xpert result in the Asymptomatic Group

G8. CHEST X-RAY SCREENING IN PREDICTION AND PREVENTION FOR INCIDENT CASES AMONG TB-EXPOSED CHILDREN

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BACKGROUND: Tuberculosis (TB) is the leading cause of childhood mortality worldwide. The World Health Organization (WHO) guideline emphasizes contact investigation for TB-exposed children because they have a high yield of both Mycobacterium tuberculosis infection and disease. Critical gaps have been identified in diagnostic approaches for TB in children. We evaluate chest x-ray (CXR) screening values and the risk of TB incidence in exposed children with and without preventive therapy.

INTERVENTION/RESPONSE: In a longitudinal cohort study conducted between September 2009 and August 2012 in Lima, Peru, we retrospectively enrolled household contacts with both symptom and CXR screening (age≤15). Children who were not diagnosed with TB disease at baseline were offered isoniazid preventive therapy (IPT) in accordance with local Tuberculosis Program guidelines.

RESULTS: We enrolled 4,468 child contacts. 855 TST positive not diagnosed TB disease. Among the 46 child contacts who were asymptomatic and had an abnormal CXR at enrollment, 28 (616) were diagnosed either with co- prevalent or incident TB. Symptom-negative/CXR positive children were 25- fold more likely to have co-prevalent TB (Hazard Ratio [HR]=25.06, 95BCIs, 1.02-613.76) and 27 times more likely to develop incident TB disease (adjusted hazard ratio [aHR], 26.71, 95% Cls 10.44-68.30), The efficacy of IPT in symptom-negative/CXR-positive children was 82% (aHR=0.18, 95% Cls=0.04-0.95).

CONCLUSION: Our results strongly support CXR screening can provide diagnostic and prognostic information in child contacts and further suggest that incipient or subclinical TB disease may be characterized by abnormal CXRs in close follow-up which could even be protected by prevention therapy.

G9. PLANNING FOR TB ELIMINATION USING TABBY2: A TOOL TO ESTIMATE FUTURE TB, LATENT TB INFECTION, AND COSTS ASSOCIATED WITH STATE-LEVEL LTBI TESTING AND TREATMENT

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BACKGROUND: State health agencies make decisions to deploy resources to maximize TB prevention, yet state-level analyses to inform these decisions are often not available.

METHODS: The Prevention Policy Modeling Lab created Tabby2, an interactive webtool for US states based on a published TB transmission model. As an example, we used Tabby2 to project Massachusetts TB and LTBI cases, and to estimate the effectiveness, costs, and cost effectiveness of an intervention to double LTBI testing and treatment.

RESULTS: Over 30 years of the intervention compared with base-case projections: TB incidence could be reduced from 1.99/100K to 1.74/100K (producing 476 fewer TB cases and 48 fewer TB deaths), for which the potential societal perspective benefits (undiscounted) were estimated at $31,680,000. The intervention includes 87,640 additional people tested for TB infection and 46,960 additionally treated for LTBI. The (undiscounted) healthcare service cost of this intervention is $166,502,000, compared to $150,650,000 under current practices, an increase of $15,852,000. Including discounting of future events at 3% annually, this intervention could be considered cost effective, both from the healthcare service perspective at an estimated $41,583 per TB case prevented and from the societal perspective, at an estimated $4,864 per TB case prevented, $49,346 per TB death prevented and $37,349 per quality-adjusted-life-year gained.

CONCLUSIONS: Tabby2 showed substantial benefits of scaled-up LTBI testing/treatment in Massachusetts and can be used to further TB elimination.

H. SPECIAL POPULATIONS

H1. INTRODUCTION OF SHORT COURSE TREATMENT FOR LATENT TUBERCULOSIS INFECTION AT A PRIMARY CARE FACILITY FOR REFUGEES IN WINNIPEG CANADA: A MIXED METHODS EVALUATION

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BACKGROUND: The WHO End TB strategy document Towards tuberculosis elimination: an action framework for low incidence countries—which includes Canada— identifies screening and treatment of latent tuberculosis infection (LTBI) in groups at increased risk for TB disease, including newcomers from endemic countries as a priority.

METHODS: In 2015, Winnipeg, Canada implemented an integrated patient-centered model with LTBI screening, assessment and treatment at a primary care facility for refugees, BridgeCare Clinic, originally offering nine-months of isoniazid (9INH) as treatment. This mixed methods evaluation investigates the outcomes of introducing two short-course treatment regimens: four-months of rifampin (4RMP), and three-months of isoniazid and rifapentine (3HP).

RESULTS: We found no differences in LTBI screening, prevalence, eligibility, treatment initiation or treatment completion between males and females before and after the treatment changes Our data show that most patients took the short course treatments offered. Also found was a non-significant increase in the percentage of treatment completion (90.4%) in short treatments in comparison to 9INH (82.4%). With the new treatments, BridgeCare Clinic achieved the 90% of treatment coverage, and the 90% treatment completion rate targets recommended in the End TB Strategy.

CONCLUSION: Qualitative interviews with clinic staff further affirm the higher acceptability of the short-course treatments. While these results are limited to refugees in Winnipeg, Canada, they highlight the possibility of reaching End TB targets in a primary care setting.

H2. LATENT TUBERCULOSIS IN MIGRANTS TRAVELLING THROUGH THE NORTHEAST REGIONS OF MEXICO

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BACKGROUND: Latent tuberculosis infection (LTBI) affects nearly a quarter of the global population. Public health interventions aimed at interrupting tuberculosis transmission do not routinely include systematic screening of migrant populations for LTBI in Mexico, nor other high-income countries. However, early detection and treatment of LTBI in immigrant populations from high-burden countries are recommended by the World Health Organization.

METHODS: In this cross-sectional study, blood samples were obtained from 455 migrants living in shelters in northeastern Mexico during January 2017 to October 2019. LTBI was diagnosed using the QuantiFERON‹B-TB Gold Plus test.

RESULTS: Most of the migrants evaluated in this study were from Honduras; ~86% were male; the average age was 29 ±10 years. LTBI was identified in 18.4% of those from Central America. Migrants from El Salvador and Nicaragua were more likely to have LTBI than those from Honduras or Guatemala. Overweight or obese persons and older persons had a higher prevalence of LTBI. We detected no significant differences with respect to LTBI when the results were compared based on gender, education, or marital status.

CONCLUSION: The LTBI rates amongst migrants from Central America recently screened in shelters in northeastern Mexico appears to be relatively low given recent estimates of LTBI prevalence in Mexico.

H3. TUBERCULOSIS INFECTION SCREENING STRATEGIES FOR NEW IMMIGRANTS TO CANADA: A COST-EFFECTIVENESS ANALYSIS

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BACKGROUND: Foreign-born individuals bear 70% of the tuberculosis burden in Canada, largely driven by progression of TB infection (TBI) acquired abroad. We estimated the cost-effectiveness of targeted TBI screening strategies in new Canadian immigrants.

METHODS: A Markov model simulated different strategies using tuberculin skin test screening and four months of rifampin treatment among new immigrants to Canada. We simulated ten cohorts of 250,000 immigrants capturing the age and country of origin profile of new immigrants to Canada in 2019. TB progression risks were estimated from a population-based immigrant cohort in British Columbia; prevalence of TBI were derived from models of age-specific prevalence in countries of origin. Other epidemiologic parameters and costs (2021 $CAD) for screening and treatment were from published literature. We used a 10-year time horizon, 1.5% annual discounting, and a healthcare system perspective.

RESULTS: Without screening, estimated TB incidence rates were 15.8 per 100,000 person-years and ten-year healthcare system costs were $7.9 million. Cost-effectiveness was influenced by both TB incidence in country of origin and age at arrival (Table). The most aggressive screening strategy (screen everyone) reduced ten-year TB incidence by 37%. Screening would likely be cost-prohibitive in several subgroups. Compared to no screening, screening immigrants <15 years from countries with TB incidence ≥300 cases per 100,000 persons was most cost-effective ($54,706 per case averted), but only reduced TB incidence by 1.8%.

CONCLUSION: The impact of screening immigrants for TBI is limited and in many groups cost prohibitive. Further targeting based on demographic and other risk factors is needed.

Table. Incremental cost-effectiveness ratios for TB cases averted of various targeted screening strategies when compared to no screening. Mean values from 10 Monte Carlo simulations of 250,000 immigrants each.

Age Group TB Incidence in Country of Origin	<15 years	<35 years	<55 years	<75 years	All Age Groups
All Countries	$260,884	$172,853	$204,693	$193,401	$202,190
≥50 cases per 100,000 persons	$125,596	$101,197	$129,803	$123,836	$129,680
≥100 cases per 100,000 persons	$72,500	$81,000	$100,425	$94,800	$97,421
≥200 cases per 100,000 persons	$62,464	$73,773	$86,974	$83,439	$87,012
≥300 cases per 100,000 persons	$54,706	$73,367	$86,949	$84,332	$86,812

H4. TUBERCULOSIS RISK AMONG PREGNANT WOMEN LIVING WITH HIV IN RIO DE JANEIRO, BRAZIL

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BACKGROUND: Pregnant women living with HIV(PWLWH) are at high risk for tuberculosis (TB), but little population-level data on TB incidence has been reported. We evaluated TB incidence in PWLWH vs. non-pregnant women with HIV in Rio de Janeiro, Brazil.

DESIGN/METHODS: HIV infection has been notifiable in Brazil since 2014. We included all women with newly diagnosed HIV reported in Rio de Janeiro City from 2014-2016. We obtained data on HIV notifications, CD4 counts, viral loads, opportunistic infections, TB diagnoses, ART prescriptions, and deaths from national electronic registries. We followed patients from HIV diagnosis until TB diagnosis, death, or administrative censoring at 2-years. We calculated TB and TB/death incidence rates (IR) per 100 person-years(pys) and compared IRs of pregnant and non-pregnant women with HIV.

RESULTS: From 2014-2016, 289 pregnant and 1,272 non-pregnant women received HIV diagnoses in Rio. Pregnant women were younger (median age 25 vs. 38 years, $p<0.001$), had higher baseline CD4 counts (median 490 vs. 382.5, $p<0.001$), were less likely to have prevalent TB (1% vs. 8%, $p<0.001$), and more likely to initiate ART (62% vs. 52%, $p=0.001$) than non-pregnant women. Among 1,450 women without prevalent TB, 14 (1%) developed TB and 134 (9%) died within 2-years. PWLWH had a lower incidence of TB (0.18 vs. 0.62 per 100pys, IRR 0.29 [95%CI 0.04-2.24], $p=0.21$) and TB/death (2.17 vs. 6.31 per 100pys, IRR 0.34 [95%CI 0.19-0.62], $p<0.001$) than non-pregnant women.

CONCLUSION: TB risk among PWLWH was lower than in non-pregnant women but remains high. Interventions to reduce TB in women with HIV must be scaled-up globally.

TABLE 1

	Not pregnant (n=1,272)	Pregnant (n=289)	p-value
Median age, years (IQR)	38 (30-47)	25 (21-30)	<0.001
Median baseline CD4 (IQR)	382.5 (181-603)	490 (316-671)	<0.001
Baseline CD4 count			
<350	255 (20.05%)	66 (22.84%)	<0.001
350-500	95 (7.47%)	47 (16.26%)	
>500	181 (14.23%)	94 (32.53%)	
Unknown	741 (58.25%)	82 (28.37%)	
Opportunistic infection	358 (28.14%)	11 (3.81%)	<0.001
Prevalent TB	107 (8.41%)	4 (1.38%)	<0.001
Started ART	656 (51.57%)	180 (62.28%)	0.001
Median days to ART (IQR)	40.5 (13-93)	22.5 (6.5-47)	<0.001
Incident TB	13 (1.12%)	1 (0.35%)	0.33
Died	123 (10.56%)	11 (3.86%)	<0.001

H5. ZOONOTIC TUBERCULOSIS: CHARACTERIZATION OF INFECTIONS IN ALBERTA FROM 1995-2021

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BACKGROUND: Mycobacterium bovis infections are used as a proxy measure for prevalence of zoonotic tuberculosis, however recovery of Mycobacterium orygis in humans has prompted a broader definition that includes these cases and other zoonotic species. As there is minimal data on zoonotic tuberculosis in Canada, we have analyzed cases in Alberta.

DESIGN/METHODS: We performed a retrospective cohort study of zoonotic tuberculosis cases in Alberta from January 1995 to April 2021 using multiple health information systems. Isolates are undergoing single-nucleotide polymorphism analysis for identity confirmation. Demographics, epidemiology, and treatment outcomes were compared to culture-confirmed Mycobacterium tuberculosis cases over the same period using univariate analysis.

RESULTS: Twenty M. bovis, ten M. orygis, and one M. caprae case were identified. Incidence of M. orygis was noted to be increasing (2018–0.5%, 2019–0.9%, 2020–2.4%). Significantly more M. bovis cases were found to have originated in North Africa (10% vs. 0%, $p<0.001$), Western Asia (15% vs. 0%, $p<0.001$), Latin America (10% vs. 1%, $p=0.002$), and Western Europe (10% vs. 0%, $p<0.001$). 100% of M. orygis cases were in patients originating from India or Pakistan. All cases appear to be foreign-acquired. Both M. bovis and M. orygis infections disproportionately impact females (70% vs. 46%, $p=0.007$), while M. bovis also has sizable numbers of pregnant/post-partum patients (4/20). Extra-pulmonary involvement was higher in M. bovis and M. orygis infections (76.7% vs. 37.3%, $p<0.001$).

CONCLUSION: Alberta can now develop targeted interventions to reduce the incidence of zoonotic tuberculosis infections. Secondarily, the increasing incidence of M. orygis infections should be monitored closely.

H6. ACCESS OF MIGRANT GOLD MINERS TO COMPENSATION FOR OCCUPATIONAL LUNG DISEASE: QUANTIFYING A LEGACY OF INJUSTICE

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BACKGROUND: A legacy of the South African gold mining industry, now in decline, is a large burden of silicosis and tuberculosis among former migrant miners from rural South Africa and surrounding countries, particularly Lesotho and Mozambique. This neglected population faces significant barriers in filing claims for compensation for occupational lung disease. The objective of the study was to gain insight into the extent of such barriers, particularly for former miners and cross-border migrants.

METHODS: The database of a large gold mining company and the statutory compensation authority were analysed for the period 1973-2018 by country of origin, age, and employment status at the time of claim filing. Proportions and odds ratios (ORs) for each of the compensable diseases were calculated by the above variables. Processing delays of claims were also calculated.

RESULTS: Annual company employment declined from 240,718 in 1989 to 43,024 in 2018 and the proportion of cross-border migrants within the workforce from 51.0 to 28.1%. The compensation database contained 68,612 claims. The majority of compensable claims in all diagnostic categories were from active miners. The odds of cross-border miners relative to South African miners filing a claim depended on employment status. For example, the OR for Lesotho miners filing while in active employment was 1.86 (95% CI 1.81, 1.91), falling to 0.94 (95% CI 0.91, 0.98) among former miners. The equivalent findings for Mozambiquan miners were 0.95 (95% CI 0.91, 1.00), falling to 0.44 (95% CI 0.41, 0.47). Median processing delays over the whole period were from 1.1 years from filing to adjudication, and 3.8 years from filing to payment.

CONCLUSIONS: The findings provide a quantitative view of differential access to occupational lung disease compensation, including long processing delays, among groups of migrant miners from the South African gold mines. There is a deficit of compensable claims for silicosis and silico-tuberculosis among former miners irrespective of country of origin. While cross-border miner groups appear to file more claims while active, this is reversed once they leave employment. Current large-scale efforts to provide medical examinations and compensation justice to this migrant miner population need administrative, political and public support and scrutiny of progress.

H7. THE DEVELOPMENT OF NEW TECHNIQUES FOR INVESTIGATING OCULAR TUBERCULOSIS

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BACKGROUND: Tuberculosis (T.B.) is the leading bacterial infectious disease. While it is usually, a disease associated with the respiratory tract, it may also affect the eye causing Ocular Tuberculosis (OTB). Ocular Tuberculosis, a complex disease with poor definition and understanding, can occur with or without systemic T.B. and cause significant morbidity, including blindness. This study addressed the hypothesis that cattle infected with bovine T.B. can have OTB and be used as a model to understand human OTB.

METHOD: Naïve and bTB reactor cattle were assessed. The naive study population (n = 17) was used in a kinetic trial to evaluate changes in the eye postmortem. Bovine T.B. reactors (n = 30) were selected randomly. Images of the eye (fundus) were obtained from the EpiCam V camera and montaged using Hugin-2020 software to create an informative fundus image.

RESULTS: A time-dependent reduction of the retinal vessels was observed with accurate and viable montages captured up to 2 hours postmortem. The circular fisheye montage view provided a comprehensive view of the superior tapetal fundus and optic disc. These newly developed techniques were applied to the test population. Suspicious lesions were identified in 2 eyes of the 30 animals imaged (6.6%).

CONCLUSION: This thesis described the possible presence of ocular lesions in cattle affected by bovine T.B. Further research should be carried out to identify the nature of ocular lesions, describe the pathophysiology of OTB and assess the suitability of the cow as a model for human OTB.

H8. A COMPARATIVE ANALYSIS OF TB POLICIES AND PROGRAMS IN TIBETAN REFUGEE SETTLEMENTS IN INDIA AND INDIGENOUS COMMUNITIES IN CANADA

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BACKGROUND: Tibetan refugees in India and Indigenous persons in Canada are disproportionately impacted by TB. Parallels in the historicities of the above communities may provide novel insight into the disproportionate prevalence of TB. There is limited literature on TB in these communities using a critical, social lens.

DESIGN/METHODS: First, an integrative literature review was conducted. Next, a comparative analysis of TB policies and programs was taken on using a social determinants of health and intersectionality approach.

RESULTS: For both Tibetan refugees in India and Indigenous persons in Canada, forced displacement from traditional land and consequent social and physical isolation are major contributors to the prevalence of TB. However, policies and programs rarely integrate the social and structural determinants of TB. Treatment, rather than prevention, is prioritized whereby emphasizing the dominant biomedical narrative of TB.

CONCLUSION: The results indicate that, in order for policies and programs to be effective in the respective communities, they must address structural and social determinants of TB. It is recommended that public health practitioners cultivate an in-depth understanding of the unique social determinants of TB in these communities. Insight from this project can be applied to other communities in similar circumstances, particularly for Indigenous and refugee populations globally.

H9. DEVELOPING DATA GOVERNANCE AGREEMENTS WITH INDIGENOUS COMMUNITIES IN CANADA: TOWARDS EQUITABLE TUBERCULOSIS PROGRAMMING, RESEARCH, AND RECONCILIATION

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The Indigenous right to self-determination and data sovereignty support Indigenous-led data governance which can catalyze Indigenous-led strategic planning and decision-making in public health research and programming. Respecting Indigenous data sovereignty requires time, resources, education, and planning. Here we share our experiences and lessons learned when developing and implementing data governance agreements with First Nations and Métis partnering communities. We define the process undertaken to create a decision space, defined by data governance agreements, where researchers, program (government) stakeholders, and Indigenous community partners are equally and equitably informed, to co-develop tuberculosis public health interventions. This work is part of a larger Pathways to Health Equity for Indigenous Peoples project on tuberculosis public health, wherein Indigenous communities are resituated as equitable decision makers in health.