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A. SCIENCE

A1. SPUTUM VOLATILE BIOMARKERS – A CULTURE-INDEPENDENT TOOL TO DIAGNOSE NONTUBERCULOUS MYCOBACTERIA IN PEOPLE WITH CYSTIC FIBROSIS

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BACKGROUND: Nontuberculous mycobacteria (NTM) are environmental bacteria. M. abscessus complex (MABSC) and M. avium complex (MAC) are most common pathogens causing severe lung infections in people with cystic fibrosis (pwCF). Current diagnosis of NTM is time-consuming and requires sputum culture and radiographic results confirmed by clinical presentations, which can take four to six months.

DESIGN/METHOD: Living organisms produce volatile organic compounds during metabolism. We hypothesize that volatile molecules originating from sputum can diagnose NTM lung infection and discriminate between MAC and MABSC. To test the hypothesis, 234 sputum samples were collected from pwCF with known NTM infection status enrolled in two ongoing clinical trials. The volatile molecules from sputum samples are extracted by headspace solid phase micro-extraction and desorbed into the two-dimensional gas chromatography coupled with a time-of-flight mass spectrometer for analysis. The obtained chromatograms are processed by ChromaTOF software, and the generated raw data is subject to statistical analysis by R programming.

RESULTS: The preliminary data from a subset of the samples with known culture results (MABSC n=10, MAC n=15) reveals that eight volatile molecules selected by the Boruta algorithm can distinguish between the MABSC and MAC groups (Figure 1&2). The Random Forest training model can achieve 100% AUC (Figure 3).

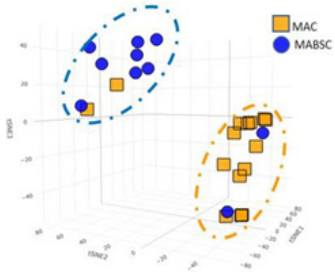

Figure 1

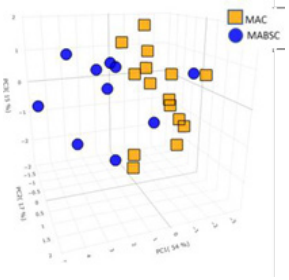

Figure 2

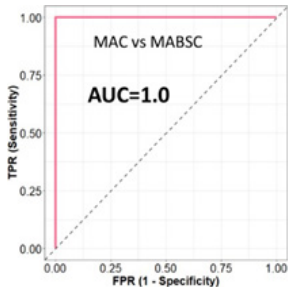

Figure 3

CONCLUSION: The preliminary results pave the way for the development of a culture-independent diagnostic tool for differentiation between MAC and MABSC in pwCF. Biomarker expansion and validation will be performed with the larger dataset of n=234 samples which will be completed by the conference.

A2. DIGITAL COUGH MONITORING PREDICTS CLINICAL OUTCOMES IN HOSPITALIZED COVID-19: A PREDICTIVE ACOUSTIC BIOMARKER STUDY

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BACKGROUND: Recent developments in the field of artificial intelligence and acoustics have made it possible to objectively monitor cough in clinical and ambulatory settings. We hypothesized that clinical prognosis tools could be derived from objectively measured COVID- 19 cough time patterns and evolution to rapidly identify patients at high risk of unfavorable clinical outcomes.

DESIGN/METHODS: Between December 2020 and June 2021, patients hospitalized with COVID-19 were enrolled at University of Florida Health Shands (n=98) and the Centre Hospitalier de l'Université de Montréal (n=25). Patients' cough was continuously monitored digitally along with clinical severity of disease until hospital discharge, intubation, or death. The natural history of cough in hospitalized COVID-19 disease was described and logistic models fitted on cough time patterns were used to predict clinical outcomes.

RESULTS: In both cohorts, higher coughing rates were associated with more favorable clinical outcomes. The transitional cough rate, or maximum cough rate per hour predicting unfavorable outcomes, was 3·40 and the AUC for cough frequency as a predictor of unfavorable outcomes was 0·761. The initial 6h (0·792) and 24h (0·719) post-enrolment observation periods showed similar predictive value.

CONCLUSION: Continuous digital cough monitoring is feasible in a hospital setting. Objectively monitored cough could be used as a prognosis biomarker to predict unfavorable clinical outcomes in COVID-19 disease. This study represents a template for the design of cough-based clinical decision tools for various other lung conditions. Such tools could be deployed on smartphones and would hence be easily deployable in low- and middle-income settings.

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A3. DETERMINATION OF MICS FOR RIFAMPIN (Rif), RIFABUTIN (Rfb) AND RIFAPENTINE (Rfp) IN MYCOBACTERIUM TUBERCULOSIS STRAINS POSSESSING VARIOUS MISSENSE MUTATIONS IN Rpoβ

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BACKGROUND: Resistance to the rifamycins RIF, RFB and RFP results from mutations in rpoB. Cross-resistance among these drugs in M. tuberculosis strains remains poorly defined. The objective of this study was to correlate rifamycin MICs with specific rpoB mutations.

METHOD: MIC testing was performed according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) method. Isolates were selected based on the presence of missense mutations in the rpoB rifampicin resistance determining region (RRDR). Seventy-seven isolates representing 22 distinct rpoB missense mutations, 18 wild-type isolates and the susceptible reference strain H37Rv were tested.

RESULTS: For H37Rv, MICs for RIF, RFB and RFP ranged from 0.125 – 0.25 μg/ml, 0.0039 – 0.0156 μg/ml, and 0.0156 – 0.0313 μg/ml, respectively. MICs for 18 isolates with wild-type rpoB ranged from 0.0313 – 0.5 μg/ml for RIF, 0.0078 – 0.125 μg/ml for RFB and 0.0078 – 0.125 μg/ml for RFP. Twenty-seven isolates, representing eight rpoB missense mutations, including those coding for Asp435Ala and Asp435Gly, had a RFB MIC of 0.5 μg/ml, similar to wild-type strains, but had high MICs for RIF (MIC ≥32 μg/ml) and RFP (MIC ≥8 μg/ml). Twenty-four isolates representing 11 different rpoB point mutations displayed similar MICs demonstrating complete cross-resistance. The remaining 8 isolates inclusive of three unique missense mutations had inconclusive RIF MIC results.

CONCLUSION: These results indicate certain rpoB mutations do not confer the same level of resistance to RIF, RFB and RFP. Eight rpoB mutations (27 isolates) evaluated had RFB MICs similar to wild-type isolates. These results may inform the treatment of patients with rifamycins.

A4. BCG MODULATES HUMAN DENTRITIC CELL RESPONSE TO SARS-COV-2 S-GLYCOPROTEIN

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BACKGROUND: As epidemiological evidence suggests a potential protective role of BCG against COVID-19, we aimed to explore if pre-exposure of human dendritic cells (DCs) to BCG could modulate their response to SARS-CoV-2 S-glycoprotein.

METHODS: Human monocytic cell line dual THP-1 (Invivogen) containing two reporter plasmids for transcription factors NF-κB and IRF was used. Cells were differentiated into DCs with commercial Mo-DC differentiation media (Milteny-Biotec), for six days, and then activated with tumor necrosis factor-α (TNF-α) for 24 hours. Half of the cells were exposed to BCG at a multiplicity-of-infection (MOI) of 10:1 for 24 hours. We then stimulated DCs with a stabilized trimer of the SARS-CoV-2 S-protein (bei resources) for 24 hours. Llipopolysaccharide (LPS) was used as control Measurement of NF-kB and IRF activation were expressed as a response ratio for each stimulus relative to the reporter activity in unstimulated cells.

RESULTS: Pre-exposure of DCs to BCG increased the activation of NF-kB and IRF upon stimulation to the S protein ($p < 0.05$). Exposure to BCG did not alter the activation of any of the two transcription factors in response to LPS.

CONCLUSION: The BCG vaccine has been shown to confer nonspecific benefits beyond its target pathogen, including immunoprotective effects against other respiratory infections and cancers. Our results show that BCG modulates the immune response of DCs to SARS CoV-2 S-glycoprotein, promoting an increase in IRF transcription factor, which may translate in higher Type I IFN levels which are known to be protective of severe COVID-19.

A5. IMPROVING WHOLE GENOME SEQUENCING-BASED RAPID ETHAMBUTOL SENSITIVITY TESTING FOR MYCOBACTERIUM TUBERCULOSIS

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BACKGROUND: Gold standard phenotypic methods for Mycobacterium tuberculosis (MTB) drug susceptibility testing (DST) have slow turnaround times, but rapid DST is possible with whole genome sequencing as implemented by the National Reference Centre for Mycobacteriology (NRCM). This requires comprehensive knowledge of molecular predictors of resistance to accurately inform treatment regimens. Rapid DST for first line drug ethambutol retains 86.7% sensitivity and 93.3% specificity (WHO) by detecting mutations in embCAB. However, there is discordance between phenotypic methods employing a 5 μg/mL critical concentration and genotypic methods detecting embB406 mutations. We aim to decipher implications of embB406 and novel mutations on ethambutol resistance.

METHODS: The NRCM MTB culture collection was screened for isolates with embB406 mutations (n=16) and pan-sensitive control isolates (n=10). Phenotypic DST for ethambutol was performed on the BACTEC MGIT 960 in duplicate by proportion method (2, 3, 4, 5 μg/mL) with H37Rv control. Whole genome sequencing was performed on Illumina Miseq for drug resistance predictions (MyKrobe), phylogenomics (SNVPhyl) and SNP analysis (Snippy).

RESULTS: Sequencing revealed two embB406 mutation subgroups (gly406asp, gly406ala) in 16 strains predicted to be resistant. However, 12 of these strains appear phenotypically sensitive at 5 ug/mL while resistant at 2-4 μg/mL. A novel frameshift mutation in regulator embR (gln258fs) was found in 9 strains with low-level resistance (2-4 μg/mL).

CONCLUSION: Mutations in embB406 are associated with low-level ethambutol resistance undetectable by current phenotypic DST. Novel mutations are predicted to exacerbate variability in resistance level. Amendment to genotypic and phenotypic DST is required to improve sensitivity and specificity of resistance predictions.

A6. DETERMINATION OF MINIMAL INHIBITORY CONCENTRATIONS (MICs) OF DRUG-RESISTANT AND SUSCEPTIBLE MYCOBACTERIUM TUBERCULOSIS ISOLATES TO THE NOVEL ANTIBIOTIC TEIXOBACTIN.

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BACKGROUND: The effective treatment of drug-resistant tuberculosis not only benefits the patient but also helps control the emergence and dissemination of these strains. The recently described Teixobactin (TXB) represents a new class of antibiotics with antimicrobial activity against gram positive bacteria. We report MICs for TXB against susceptible and drug-resistant M. tuberculosis strains.

DESIGN/METHODS: A microdilution broth assay consisting of a two-fold dilution series of TXB concentrations ranging from 0.0156 – 8.0 mg/L was used to determine MICs to TXB in the presence or absence of 0.025% Tween 80. Four susceptible, 6 multidrug-resistant (MDR), 3 pre-extensively drug-resistant (XDR) and 3 XDR clinical M. tuberculosis isolates, as well as the fully susceptible laboratory strain H37Rv, were tested.

RESULTS: MICs were impacted by the presence of Tween 80 in the culture medium. In the absence of Tween 80, MICs were > 8 mg/L for all strains tested. In medium containing Tween 80, the MIC range for strain H37Rv was 1.0 – 2.0 mg/L and among the clinical isolates the MIC ranges were ≤ 0.0156 – 0.5 mg/L, ≤ 0.0156 – 1 mg/L, and ≤ 0.0156 – 0.0625 mg/L for susceptible strains, MDR strains and pre-XDR and XDR strains respectively.

CONCLUSION: The biochemical properties of TXB requires medium containing Tween 80 for MIC testing. TXB MICs for drug-resistant strains were similar to those of susceptible strains. These in vitro results showing TXB is equally active against both drug-resistant and susceptible M. tuberculosis strains is evidence supporting TXB as a promising investigational drug for the treatment of drug-resistant tuberculosis.

A7. BREATH BIOMARKERS FOR PEDIATRIC TB USING GC×GC-ToFMS

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BACKGROUND: Pediatric tuberculosis (TB) is a global health issue with an estimation of 1.1 million children infected and 0.23 million died in 2020[1]. This issue stems from the difficulty of obtaining proper sputum specimens from the children for bacterial confirmation, resulting in about 50% cases missing[2]. To address this problem, a non-invasive, sputum free and child-friendly diagnostic method is needed. Breath shows promise because metabolic molecules of lung infection diseases will be produced by the organ as biomarkers and the portion of the molecules can be found in exhaled breath.

DESIGN/METHODS: To find TB breath biomarkers, we recruited 31 children with confirmed TB, unconfirmed TB, or unlikely TB[3]. We are also conducting a study from 57 children who have confirmed TB and are on antibiotic treatment, aiming to validate the biomarkers and track their changes during the treatment. The method of breath collection and sample analysis were described as previously reported[3]. Briefly, the child exhaled to a 1.5 L-Tedlar bag and the breath was drawn onto the thermal desorption tubes, which were then analyzed using GC×GC-ToFMS. The data was cleaned and analyzed in R with different machine learning models.

RESULTS: 1) Identified a 4-compound breathprint (4-methyloctane, decane and 2 unknown analytes) that can classify children with confirmed TB (sensitivity =80% and specificity =100%).
2) Demonstrated that this model identified patients who had unconfirmed TB and whose symptoms improved while treated for TB.

CONCLUSION: Our data shows diagnostic utility of using breath biomarker and machine learning, and requires further validation as a diagnostic tool for pediatric TB.

[1]. World Health Organization, Global tuberculosis report 2021.

[2]. Roadmap towards ending TB in children and adolescents, second edition. Geneva: World Health Organization, 2018. [3]. C. Bobak et al., Sci. Rep., 11, 2021, https://doi.org/10.1038/s41598-021-80970-w

B. SCREENING/TREATMENT

B1. COST AND COST-EFFECTIVENESS OF DIGITAL ADHERENCE TECHNOLOGIES FOR TUBERCULOSIS DISEASE AND INFECTION: A SYSTEMATIC REVIEW

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BACKGROUND: Digital adherence technologies (DATs) including video-observed therapy (VOT), and SMS-based interventions could provide a patient-centric approach for supporting TB medication adherence and improving outcomes. We synthesized evidence addressing costs and cost-effectiveness of DATs to support TB treatment.

DESIGN/METHODS: A systematic review (PROSPERO-CRD42022313531) identified relevant literature from January 2000-April 2022 in MEDLINE, Embase, CENTRAL, CINAHL, Web of Science along with preprints from medRxiv, Europe PMC and clinicaltrials.gov. Studies reporting quantitative data on the cost or cost-effectiveness of DATs for TB infection or disease treatment, with minimum 20 participants using the DAT were included. Study characteristics, cost and cost-effectiveness outcomes were extracted.

RESULTS: Of 2,390 studies identified by our systematic search, 22 met inclusion criteria. 18 provided primary cost data while the remaining 4 were modeling studies. 8 studies analyzed cost-effectiveness. Only 2 studies reported costs specific to TB infection. DATs included SMS reminders, phone-based technologies, digital pillboxes, artificial intelligence-based apps (AI), ingestible sensors and VOT. VOT was the most extensively studied (13 studies). Incremental costs per patient treated ranged from -$6200 (savings) to $1400, comparing the DAT to standard care. Cost-effectiveness findings were highly variable, ranging from no clinical effect in one study (SMS), to greater effectiveness with concurrent cost savings (VOT and AI) in others.
Few adequately reported at least 80% of the elements required by CHEERS, a standard reporting checklist for health economic evaluations.

CONCLUSION: There remains limited evidence for the cost and cost-effectiveness of DATs for TB treatment support. The scope of costs considered varies widely across studies.

B2. A COMPARISON OF THE CHEST RADIOGRAPHIC AND COMPUTED TOMOGRAPHIC FEATURES OF SUBCLINICAL PULMONARY TUBERCULOSIS

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BACKGROUND: Subclinical pulmonary tuberculosis (PTB) is a recently described intermediate state of great interest, but about which little is known. This study sought to estimate the extent to which chest radiographs (CXRs), as compared to computed tomographic (CT) scans, under-detect key radiologic features in subclinical PTBdescribe and compare the frequency of key radiologic features of subclinical PTB on chest radiograph (CXR) versus computed tomographic scan (CT), and to interpret the clinical and public health relevance of the differences.

DESIGN/METHODS: Diagnostic CXRs and CT scans of the thorax and neck in a 16-year cohort of subclinical PTB patients in Canada were re-acquired and read by two independent readers and arbitrated by a third reader. Logistic regression models were fit to determine how likely CXR features can be detected by CT scan versus CXR after adjustment for age and sex.

RESULTS: Among 296 subclinical patients, CXRs were available in 286 (96.6%) and CT scans in 94 (32.9%). CXR features in patients with and without CT scans were comparable. Lung cavitation was 4.77 times (95% CI, 1.95-11.66), endobronchial spread 19.36 times (95% CI, 8.05-46.52), and moderate/far-advanced parenchymal disease 3.23 times (95% CI, 1.66-6.30), more common on CT scan than CXR.

CONCLUSION: We conclude that the extent to which CXRs under-detect key radiologic features in subclinical PTB is substantial. This may have public health and treatment implications.

B3. INCORPORATION OF CLINICAL FACTORS TO IMPROVE THE DIAGNOSTIC ACCURACY OF ARTIFICIAL INTELLIGENCE- BASED CHEST X-RAY ANALYSIS FOR DETECTING PULMONARY TUBERCULOSIS

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BACKGROUND: Chest X-ray (CXR) analysis with computer-aided detection (CAD) produces continuous scores on a 100-point scale. Common practice involves selecting thresholds to classify CXR as compatible with tuberculosis or not; however, selecting appropriate thresholds is challenging. We hypothesized that using CAD scores in a multivariable model with clinical information would increase tuberculosis detection accuracy over CAD alone.

DESIGN/METHODS: Individual patient data was used from three studies that consecutively enrolled individuals seeking care due to symptoms of tuberculosis, and evaluated CAD using nucleic acid amplification or culture as the reference test. CXR were analyzed using two commercially-available software. Separately for each software, we used logistic regression to model tuberculosis status. Crude models included CAD scores as the predictor; adjusted models added clinical factors selected a priori (age, sex, HIV status, and prior tuberculosis). To evaluate model performance, we assessed calibration and discrimination. We internally validated models using bootstrap resampling. We compared receiver operating characteristic curves for crude and adjusted models using DeLong's p-value. We classified CXR using prediction cut-offs that achieved pre-specified sensitivities and calculated the specificity, positive predictive value, and negative predictive value.

RESULTS: 566/3308 (17%) of participants had microbiologically-confirmed pulmonary tuberculosis. Those with tuberculosis were less likely to previously had tuberculosis (13.6% vs 22.9%, p<0.001), and more likely HIV-positive (24.4% vs 12.9%, p<0.001). For both software, compared to CAD alone, predictive power improved for adjusted models (DeLong's p-value<0.001), and the specificity and positive predictive value increased for all held sensitivities.

CONCLUSION: Models incorporating clinical factors improved the predictive ability of two CAD software.

B4. THE IMPACT OF DIGITAL ADHERENCE TECHNOLOGIES ON HEALTH OUTCOMES IN TUBERCULOSIS: A SYSTEMATIC REVIEW

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BACKGROUND: Suboptimal tuberculosis (TB) treatment adherence may lead to unsuccessful treatment and relapse. Digital adherence technologies (DATs) may allow more patient-centric approaches for supporting treatment. We conducted a systematic review (PROSPERO- CRD42022313166) to evaluate the impact of DATs on health outcomes in TB.

DESIGN/METHODS: We searched MEDLINE, Embase, CENTRAL, CINAHL, Web of Science and preprints from medRxiv, Europe PMC, and clinicaltrials.gov for relevant literature from January 2000 to April 2022. We considered experimental or cohort studies reporting quantitative comparisons of clinical outcomes between a DAT and standard care —with at least 20 participants using the DAT. Risk of bias was assessed using the Cochrane risk of bias assessment tool and the Newcastle- Ottawa Scale.

RESULTS: Of 9172 records identified, 43 met inclusion criteria. Most studies (26/43) involved short message service-based interventions or video observed therapy (VOT). 8 of the 12 VOT studies included assessed its effect on treatment completion and/or success. VOT was associated with a significant increase in treatment success for persons treated for TB disease and TB infection. Randomized controlled trials of phone calls with or without SMS showed no significant effect on treatment completion. One study that combined medication sleeve-triggered phone check-ins by patients, with medication reminders and educational and motivational messages, showed a non-significant effect on treatment success.

CONCLUSION: Although evidence remains limited and highly variable, DATs may improve short- term clinical outcomes under some circumstances. Higher quality data are needed.

B5. THE ACCURACY OF DOSE REPORTS GENERATED BY DIGITAL ADHERENCE TECHNOLOGIES FOR PERSONS TREATED FOR TUBERCULOSIS DISEASE OR INFECTION: A SYSTEMATIC REVIEW

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BACKGROUND: Digital adherence technologies (DATs) including phone-based technologies and digital pillboxes, can potentially provide more patient-centric approaches for supporting TB medication adherence and improving outcomes. This study aims to investigate the accuracy of dose reporting generated by DATs to aid TB treatment support.

DESIGN/METHODS: A systematic review (PROSPERO-CRD42022313526) was conducted to identify relevant literature from January 2000 through April 2022 in MEDLINE, Embase, CENTRAL, CINAHL, Web of Science and preprints from medRxiv, Europe PMC, and clinicaltrials.gov. Studies reporting quantitative data on the accuracy (sensitivity/specificity) of DATs for TB infection or disease treatment, against a reference standard (urinalysis test, pill count, or directly observed therapy [DOT]), with at least 20 participants using the DAT were included. Accuracy outcomes were extracted.

RESULTS: Of 4,803 studies identified by our systematic search, 8 met our inclusion criteria. The accuracy of DATs was reported for phone-based technologies [3 studies], digital pillboxes [3], and ingestible sensors [2] for 1000 TB disease patients. Two studies used a digital pillbox as their reference standard, so the accuracy of the pillbox was calculated against pill count from their data. When ingestible sensors were compared to DOT for 107 patients, the probability of detecting a dose truly taken (sensitivity) was ≥95%. Across studies, the accuracy of digital pillboxes varied extremely, while sensitivity and specificity were 60-80% for phone-based technologies, specifically phone calls with medication sleeves (Figure 1).

CONCLUSION: The limited available evidence suggests variable accuracy of DATs. Future research should aim to better understand how the technology, setting, and patient characteristics impact DAT accuracy.

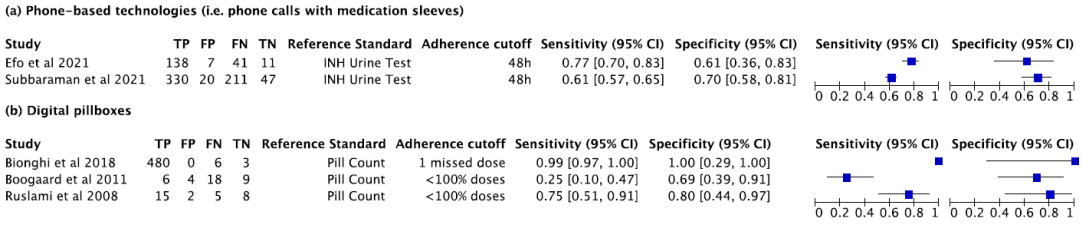

Figure 1: Forest plot of the accuracy of (a) phone-based technologies and (b) digital pillboxes in TB disease patients.

B6. TUBERCULOSIS PREVENTION IN SOUTH AFRICA: UNDERSTANDING USER EXPERIENCE AND FEASIBILITY WITH GEOLOCATION TRACKING USING A MOBILE DEVICE

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BACKGROUND: Emerging data suggest that in high-burden countries some tuberculosis (TB) transmission occurs in community settings (e.g., marketplaces), but knowledge about transmission dynamics between causal contacts is limited.1-4 GPS technologies to track persons at high-risk for TB might help identify contacts that would otherwise be missed. Our pilot study assessed acceptability and feasibility of cellphone tracking among patients with TB in East London, South Africa.

METHODS: In this mixed methods pilot study, we provided cellphones to 10 participants with the GPS tracking application, ArcGIS Field Maps, installed. De-identified tracking data were passively collected in real-time every 1-10 minutes while participants conducted day-to-day activities. Acceptability was assessed via exit interviews and feasibility was assessed by accuracy of the geodata by mapping overlays. Qualitative data were analyzed using thematic analysis.

RESULTS: We enrolled 10 Participants, ages 22-82 (50% female) during July-August 2022, two were lost to follow-up and one had the app incorrectly installed. Preliminary qualitative data analysis shows that of the 7 completed interviews, 7 (100%) participants reported they were not bothered by being tracked and their mobility remained unchanged. Three (43%) participants indicated they wanted to view their data and the three (43%) with a personal phone stated they would prefer the app installed there to avoid managing two devices. Feasibility data analysis is still ongoing.

CONCLUSION: Our findings demonstrate that geolocation tracking through a mobile application was well accepted with no activity change among a cohort of TB patients. Challenges included the difficulty managing two devices and a preference towards using personal devices.

B7. A SURVEY OF TUBERCULOSIS HOME ISOLATION PRACTICES IN THE UNITED STATES

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BACKGROUND: Persons with infectious tuberculosis (TB) may remain acid-fast bacilli (AFB) smear- and culture-positive for prolonged durations, though most are rendered noninfectious soon after initiation of appropriate treatment. Current United States (US) guidelines lack clear and consistent advice for discontinuing isolation. We surveyed state and big-city TB programs to learn about criteria used for ending home respiratory isolation (HRI) of people with suspected or confirmed TB.

METHODS: In April 2022, we sent an online survey to 68 US TB programs supported by CDC funds. The questionnaire asked about requirements for discontinuation of HRI.

RESULTS: We received 48 responses (38 states, six large cities, and four US territories; 71% of surveyed programs). Most had their own (69%, n=33) or used other (referred to CDC or other institution) (21%, n=10) HRI guidelines.

For persons with sputum AFB smear-positive, confirmed TB, most jurisdictions used three consecutive smear-negative results (75%, n=36) and/or improvement in sputum smear grade (31%, n=15) as criteria to discontinue HRI.

For smear-negative, confirmed TB, most jurisdictions (71%, n=34) required treatment with anti-TB medication for a specified number of days (range: 3-21) to discontinue HRI.

For persons with drug-resistant TB, 10% (n=5) programs required one negative culture, 38% (n=18) two negative cultures, or 8% (n=4) three negative cultures to discontinue HRI.

CONCLUSIONS: Depending on the jurisdiction, time spent in HRI could vary widely, from several weeks to months, particularly for persons with smear-positive or drug-resistant TB. The variation in responses indicates the need for better national guidelines.

B8. ACTIVE CASE FINDING IN THE SLUMS OF PORT-DE-PAIX, HAITI

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BACKGROUND: Haiti is among the top four countries in America with the highest number of estimates and detected cases; and Port-de-Paix has one of the lowest detection rate in the country; to try to reverse the tendency, the new team of the department has undertook some new interventions, like using former patients, detection in prisons and active cases finding in the main slums of the city.

METHOD: Door to door identification of respiratory symptomatic persons, collection of fresh sputum for geneXpert, treatment and contact tracing of the positive cases ; inclusion criteria were People who cough for two weeks and more, 10 years old at least, living in the city's slums; Exclusion Criteria: No cough, less than 10 years old, living outside the Slums or Port-de-Paix or refuse the test

RESULTS: 150 visits of the 168 planned were realized in the 8 identified red zones where most of the cases were diagnosed this year; 97 symptomatic were identified for whom one fresh sample was tested with geneXpert; 19 confirmed cases were detected; among them, 4 coinfected TB/HIV ; 61 RS were men and 36 were women; among19 the cases detected, 11 were men and 8 women; their mean age was : 29 years;

DISCUSSION: Though the number of cases detected for the quarter was not increased significantly as expected at departemental level, but, without this intervention most of these cases would continue to spread the disease and could delay their treatment since they did not know that they have TB

CONCLUSION: If conducted regularly and when most of the population are at home this activity could help finding the missing cases in the region

B9. LATENT TB INFECTION (LTBI) CARE CASCADE AT A COMMUNITY HEALTH CENTER IN SEATTLE, 2021-2022

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BACKGROUND: ICHS is a nonprofit community health center serving many Asian and Pacific Islander persons in Seattle; 86% of the patients are from ethnic minority groups with 76% immigrated from Asia. In 2020, the LTBI care cascade at ICHS was measured on a small scale (n=600), and barriers were identified. A significant drop off was noted in eligible high-risk patients not tested for LTBI, and the barriers included providers' limited confidence in managing patients with co-morbidities and side effects, concern about the patient's out-of-pocket cost, and lack of patient follow up.

DESIGN/METHODS: ICHS patients' demographic and clinical data was extracted from EMR for patients that were seen from October 2021 to September 2022 (n=18,260). LTBI care cascade steps were defined, and descriptive statistics used for analysis.

RESULTS: The baseline data showed 14% of eligible high-risk patients were tested for TB infection. Additionally, 61% of those tested positive for TB infection completed chest radiography, 61% of those diagnosed with LTBI after radiology review were offered treatment, 67% of those who were offered treatment started treatment, and 42% of those who started LTBI treatment completed treatment. Based on the previous study and current findings, the following four interventions will be implemented sequentially over the next 3.5 years through the TB Epidemiologic Studies Consortium (TBESC-III); (1) educational sessions and resources for medical providers, (2) funding to defray costs of testing and treatment for uninsured high-risk patients, (3) LTBI case management, and (4) electronic medical record modification to flag high risk patients for screening.

CONCLUSION: The largest drop off in the LTBI care cascade at ICHS was at the step of testing for LTBI among eligible non-U.S.–born high-risk persons.

C. DRUG RESISTANCE

C1. TREATMENT OF ISONIAZID−RESISTANT TUBERCULOSIS IN NEW YORK CITY

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BACKGROUND: Isoniazid-resistant, rifampin-susceptible tuberculosis (INH-R TB) is a common form of drug-resistant TB. In New York City (NYC), we assessed INH-R patient characteristics, TB treatment, and treatment completion.

METHODS: TB case data from 2015-2020 were obtained from NYC's TB surveillance registry. Patients without culture or with drug-resistant TB other than INH-R were excluded. We classified cases as INH-R or susceptible to all first-line drugs (DS-TB) based on drug susceptibility test results.

We compared characteristics of patients with INH-R versus DS-TB in bivariate analyses and described treatment completion among INH-R patients across ending medication regimens [rifampin/rifabutin (R), pyrazinamide (P), ethambutol (E), and/or a fluoroquinolone (FLQ)]. We compared treatment completion of INH-R with DS-TB using multivariable logistic regression.

RESULTS: We identified 1977 DS-TB and 202 INH-R cases.

INH-R and DS-TB patients were similar in age (45+ years: 61% vs 58%); and sex (males: 59% vs 63%). A higher proportion of INH-R than DS-TB patients were born in the Western Pacific (45% vs 30%, p-value=<0.001) and had pulmonary involvement (91% vs 86%, p-value=0.03). Among INH-R patients, treatment completion was higher among those who ended therapy with RPE (95%, 91/96), RE+FLQ (95%, 40/42), or RPE+FLQ (88%, 21/24), than among patients who ended on other regimens (73%, 29/40; p=0.001).

Comparing INH-R to DS-TB, treatment completion was similar (adjusted odds ratio: 1.01, 95% Cl:0.63-1.69), controlling for age, sex, birth region, and pulmonary involvement.

CONCLUSIONS: INH-R TB treatment completion was high. More evaluation is needed to understand the relationship between INH-R TB regimens and treatment completion.

C2. INITIAL EXPERIENCE WITH MODIFIED BEDAQUILINE PRETOMANID LINEZOLID (BPAL) FOR MDR TB TREATMENT IN MASSACHUSETTS. REPORT ON THREE CASES.

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BACKGROUND: In 2021, the World Health Organization (WHO) endorsed the use of a 6 month bedaquiline, pretonamid and linezolid (BPaL) all oral treatment regimen for multi drug resistant tuberculosis (MDR TB), based on studies from high incidence settings. We report here on the first three patients treated with the BPaL regimen in Massachusetts.

METHODS: We enrolled adult patients with tuberculosis (TB) who were started on modified BPaL between January 2021 and June 2022 at the Boston TB clinic in Massachusetts. Medical records were reviewed to identify clinical and radiographic characteristics of the TB cases, linezolid dosages, time to culture conversion, side effects (cytopenias and neuropathy) and treatment outcomes.

RESULTS: We identified three patients. Two had culture-proven pulmonary TB and one Xpert-positive TB lymphadenitis. Treatment indications were MDR TB for two of them and pre-XDR TB based on genotypic testing for one of them. Two received BPaL and one BPaL plus moxifloxacin (BPaLM). Linezolid was used at 600 mg daily and serum trough concentrations were below 2 ug/ml in all 3 patients. All patients received directly observed therapy. Culture conversion time was 3 and 4 weeks in the two patients with culture positive TB. No major side effects, specifically cytopenias or neuropathy, were identified. All patients showed clinical and radiographic improvement and were considered cured at the end of treatment.

CONCLUSION: The all-oral six-month BPaL and BPaLM regimens for MDR TB treatment can be safely implemented in a low incidence setting. Linezolid side effects could be minimized with therapeutic drug monitoring.

C3. RIFAMPIN MONO-RESISTANT TUBERCULOSIS IN NYC, 2010-2021

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BACKGROUND: Identification and appropriate treatment of rifampin (RIF) mono-resistant tuberculosis (RR-TB) is necessary to avoid the development of multidrug-resistant TB.

DESIGN/METHODS: Patients with RR-TB in New York City (NYC) between 2010 and 2021 were identified using NYC's TB registry. RR-TB was defined based on molecular or phenotypic drug susceptibility test (mDST/pDST) results. Most susceptibility testing was conducted at the New York State Wadsworth Laboratory, which began conducting whole genome sequencing on all TB isolates in 2016.

RESULTS: Of 7,098 TB cases reported during 2010-2021, 31 (<1%) were RR-TB. Among 27 cases with available susceptibility data, 15 (56%) were RIF-resistant by both mDST and pDST; 7 (26%) were RIF-sensitive by pDST but RIF-resistant by mDST; 4 (15%) were RIF resistant by mDST and pDST was not done; and 1 (4%) was RIF resistant by pDST and mDST was not done. Thus, 11 (7+4) RR-TB cases were identified based on mDST alone. Eight of the 27 (30%) RR-TB cases with available susceptibility data were diagnosed during 2010-2015; the other 19 (including 9 of the 11 diagnosed by mDST alone) were diagnosed during 2016-2021. Of the 31 patients with RR-TB, 18 (58%) have completed treatment, with an average treatment duration of 17 months. There was no significant change in treatment duration between 2010 and 2021.

CONCLUSIONS: mDST identified cases of RR-TB that would not have been recognized based on pDST results alone. Unfortunately, patients with RR-TB experienced long treatment duration throughout the study period. New short-course regimens will hopefully reduce treatment times for these patients.

C4. A RANDOMIZED CONTROLLED TRIAL TO IDENTIFY THE OPTIMAL DOSE OF LEVOFLOXACIN FOR THE TREATMENT OF RIFAMPICIN-RESISTANT TB

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BACKGROUND: Fluoroquinolones are important for the treatment of rifampicin-resistant tuberculosis (TB); moxifloxacin is often preferred, largely due to the absence of data on levofloxacin from clinical trials. We conducted a multi-center, double-blind, randomized, controlled trial (Opti-Q) to identify the optimal dose of levofloxacin for the treatment of rifampicin-resistant TB.

METHODS: Eligible participants with rifampicin-resistant pulmonary TB were randomized to receive levofloxacin at 11, 14, 17, or 20 mg/kg/day for 24 weeks as part of combination therapy. Primary outcomes were time to culture conversion on solid media (efficacy), the occurrence of grade 3-5 adverse events (safety), and completion of 24 weeks of levofloxacin (tolerability).

RESULTS: 111 participants from Lima, Peru and Cape Town, South Africa were enrolled; 22(20%) were HIV-positive, 75(68%) had no prior TB diagnosis, 55(50%) had a smear grade of 3+, and median (IQR) weight was 54.1(49.0,61.6) kg. All participants achieved the target levofloxacin AUC/MIC ratio of 100; AUCs were high: median 231.0, minimum 117.4μg*h/L. Median(range) MIC was 0.3(0.1,0.5). There was no difference in time to culture conversion by treatment arm (log-rank p=0.282) or by tertile of AUC/MIC (p=0.350). Culture conversion occurred later among participants with pyrazinamide-resistant TB or with higher bacillary load. Grade 3-5 adverse events were more common among participants in the highest dose group, 10(37.0%) participants, compared to 4(16.0%) in the lowest dose group (p=0.04, trend). Tolerability did not differ by treatment arm; only one death occurred.

CONCLUSIONS: Higher doses and exposures of levofloxacin did not accelerate culture conversion and were associated with more severe adverse events. Levofloxacin doses at 11-14mg/kg are efficacious and safe and are adequate to achieve target exposures.

C5. COSTS OF TREATING MULTIDRUG RESISTANT TUBERCULOSIS IN CALIFORNIA, 2022

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BACKGROUND: New, shorter regimens containing bedaquiline, pretomanid, and linezolid (BPaL) are entering clinical use for treating multidrug-resistant tuberculosis (MDR TB). Using a micro-costing approach, we estimated the direct cost of individual episodes of care for MDR TB for four different regimens and compared the cost of BPaL regimens with previously recommended, longer regimens.

METHODS: We estimated the cost of four regimens: an 18-month 5-drug regimen with an injectable agent but no bedaquiline (INJ18), a U.S. guideline-based 18-month 5-drug all oral regimen with bedaquiline (BDQ18), and two 6-month regimens: BPaL and BPaL plus moxifloxacin (BPaLM). We established a standardized set of services for each regimen, assumed no treatment side effects or treatment failure, and summed cost components in 2022 dollars. Cost components included inpatient care costs based on published literature, medication costs (340B prices) paid by California public health TB programs, outpatient laboratory, imaging and physician fees based on California Medicaid reimbursement schedule, and case management (e.g., nurse case manager or outreach worker time, adherence incentives) based on published literature.

RESULTS: Total direct cost for MDR TB care was $114,000 for BPaL/BPaLM, $146,000 for INJ18, and $156,000 for BDQ18. Hospitalization costs comprised the majority (47-66%) of direct costs for all regimens. When used, bedaquiline accounted for 60-89% of drug costs. Outpatient monitoring, including directly observed therapy, laboratory testing, and imaging, was highest for BDQ18 and INJ18 ($34,000) and lowest for BPaL/BPaLM ($11,000).

CONCLUSION: MDR TB care is costly. Despite high cost of medications, shorter BPaL/BPaLM regimens may provide cost savings.

D. DRUG RESISTANCE

D1. PREVENTION OF TUBERCULOSIS AMONG SINGLE ROOM OCCUPANCY BUILDING RESIDENTS IN SAN FRANCISCO CHINATOWN

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BACKGROUND: Tuberculosis (TB) incidence in San Francisco Chinatown is higher than San Francisco overall (38 vs 11/100,000)[1] and the United States' (US) non-US born population (12/100,000).[2] From April to May 2022, North East Medical Services (NEMS) and the San Francisco Department of Public Health (SFDPH) delivered mixed outreach methods to four high-priority single room occupancy (SRO) buildings in San Francisco Chinatown with high TB test positivity and recent TB conversion(s) based on internal NEMS TB testing data. This program evaluation examines the effect of in-person, language-concordant outreach on TB testing and treatment.

INTERVENTION/RESPONSE: Two outreach methods were utilized: (A) on-site, verbal and written education and (B) mailed educational materials, if on-site coordination was not feasible. Patients with negative TB test results ≥12 months prior or without prior TB testing were outreached to schedule a provider or Interferon-Gamma Release Assay (IGRA) lab appointment. We performed descriptive and chi-square statistical analysis to evaluate the association of outreach methods with phone follow-up and IGRA completion.

RESULTS: A greater proportion of patients were reached by phone following on-site outreach compared to mailings [69.6% (204/293) versus 57.8% (48/83), p=0.04]. Sixty-one patients completed IGRA testing, 3 tested positive, and 2 initiated treatment including 1 TB conversion. IGRA test completion was greater in patients receiving on-site outreach versus mailings [19.1% (56/293) versus 6.0% (5/83), p<0.01)].

CONCLUSION: Our findings highlight the importance of in-person TB outreach to promote TB testing and awareness. Key recommendations include utilizing language-concordant staffing and materials and varied appointment scheduling methods to increase TB testing.

D2. MORTALITY RATES AMONG PEOPLE LIVING WITH HIV AND TB IN RIO DE JANEIRO, BRAZIL

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BACKGROUND: In recent years, Brazil has expanded access to antiretroviral therapy (ART) and TB preventive therapy (TPT), which may lead to reduced TB incidence and mortality for people with HIV (PWH).

METHODS: We linked data on TB/HIV notifications and deaths from four national registries using a probabilistic strategy. We included adults (≥18 years) entering HIV care in Rio from 2010-2016, with follow-up through 2017. We assessed TB prevalence at entry into care and 2-year all-cause mortality. We compared mortality between patients with and without prevalent TB using Chi-square tests and assessed trends in TB and death by year entering care using Mann-Kendall tests for trend.

RESULTS: Among 29,936 PWH entering care, 1,019 (3.4%) had prevalent TB. Those with prevalent TB had lower baseline CD4 counts (median 175 vs. 414, $p<0.001$) and were more likely to be male (77.9% vs. 68.5%, $p<0.001$) than those without prevalent TB. A total of 2,329(7.8%) died within 2-years, including 248/1,019 (24.3%) with prevalent TB and 2,081/28,919 (7.2%) without prevalent TB. Median time to death was 59 days(IQR 28-133) for those with prevalent TB. The proportion with prevalent TB at entry into care did not change over time. Overall, 2-year mortality declined from 2011 to 2016(8.6% vs. 6.1%, $p<0.001$); among those with prevalent TB, 2-year mortality also declined from 2010 to 2016(30.5% to 13.6%, $p=0.003$).

CONCLUSIONS: Despite reductions in mortality, PWH remain at high risk of TB and death in Brazil. Continued scale-up of ART and TPT is critical to further reduce morbidity and mortality.

D3. TREATMENT COMPLETION AND CHALLENGES IN ROLLING OUT 12-DOSE WEEKLY RIFAPENTINE AND ISONIAZID FOR MYCOBACTERIUM TUBERCULOSIS INFECTION AMONG PEOPLE LIVING WITH HIV IN BRAZIL

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BACKGROUND: In 2021, the Brazilian Ministry of Health integrated 3 months weekly isoniazid-rifapentine (3HP) into the National Guidelines for Tuberculosis Control as a first line Tuberculosis Preventive Therapy (TPT) option for people living with HIV (PLHIV) and tuberculosis (TB) contacts. As part of the Unitaid-sponsored IMPAACT4TB project to implement short-course TPT, we evaluated barriers, uptake, adherence, and tolerability of 3HP for PLHIV in Brazil.

DESIGN/METHODS: We conducted a multicenter, pragmatic, and single-arm implementation project to roll out 3HP for PLHIV in two cities in Brazil. Eligible participants were identified, treated, and monitored according to national TB guidelines. De-identified patient-level data on treatment initiation, adverse events, and treatment completion was captured into a secure REDCap database.

RESULTS: Regulatory delays slowed the importation of rifapentine, delaying implementation of 3HP. From October 2021 to June 2022, 369 PLHIV were screened, 286 were TPT eligible, and 185 were enrolled. Of 101 PLHIV not enrolled, 46% did not consent and 41% were contraindicated for 3HP due to ART treatment with protease inhibitors. 183 PLHIV with treatment outcomes were included in this evaluation (75% male, median age; 40 years (IQR 30-53)). Overall, 159 (87%) completed treatment; 84 (88%) in Rio de Janeiro and 75 (86%) in Manaus (Table). Treatment discontinuation due to adverse events included: 1(0.5%) flu-like reactions, 1(0.5%) mild hepatotoxicity, 1(0.5%) systemic hypersensitivity. One participant developed active TB during TPT.

CONCLUSION: Despite bureaucratic barriers, 3HP has been successfully introduced, had high treatment completion rates and was well-tolerated. Widespread use of 3HP for TPT may accelerate TB elimination in Brazil.

Table. Demographics and Treatment Outcomes of PLHIV initiated on 3HP in Brazil.			
Demographics	Overall n=183	Rio de Janeiro n=96	Manaus n=87
Male (%)	138 (75.4)	73 (76.0)	65 (74.7)
Age, median (IQR)	40 (30-53)	41.5 (32.5-54)	36 (28-50)
BMI, median (IQR)	24.8 (22.1-28.2)	25.3 (22.8-28.6)	25.2 (21.9-27.3)
DTG-based ART (%)	143 (78.1)	76 (79.2)	67 (77.0)
Treatment Outcome			
Completed	159 (87)	84 (87.5)	75 (86)
Discontinued due to patient choice	11 (6.0)	3 (3.1)	8 (9.2)
Discontinued due to adverse event	3 (1.6)	3 (3.1)	0
Treatment changed	1 (0.5)	0	1 (1.1)
Lost to follow up	7 (3.8)	6 (6.3)	1 (1.1)
Active TB Diagnosis	1 (0.5)	0	1 (1.1)
Other	1 (0.5)	0	1 (1.1)

D4. TUBERCULOSIS DISEASE BURDEN FOR PERSONS WHO SMOKE ILLICIT DRUGS: A COMPARISON OF ACTIVE VERSUS PASSIVE CASE FINDING IN WORCESTER, SOUTH AFRICA

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BACKGROUND: People who smoke illicit drugs (PWSD) are at increased risk of tuberculosis (TB) disease and may delay seeking care when sick. Finding and linking individuals with early TB disease may improve individual outcomes and reduce transmission. We compared disease burden for PWSD newly diagnosed with TB found through active versus passive approaches.

DESIGN/METHODS: We analyzed data from 166 individuals diagnosed with TB from Worcester, South Africa. Thirty-six were recruited through respondent driven sampling for TB testing (active case finding). One-hundred-thirty were diagnosed with TB in clinic (passive case finding). All participants had microbiologically confirmed TB and self-reported or screened urine positive for methamphetamine or methaqualone. We compared demographics and disease burden using basic descriptive statistics. Disease burden was captured by culture time to positivity (TTP), Ziehl-Neelsen stain, and self-reported symptoms.

RESULTS: Median (IQR) TTP for participants found through active case finding was 13 (9, 17) days compared to 7 (5, 10) for passive case finding participants (Table 1). Participants found through active case finding were more likely to be asymptomatic (n=21, 58.3% versus n=1, 0.8%; $p<0.001$). Smear negative TB was more common among those found through active case finding (n=22, 71.0% versus n=34, 26.2%; $p<0.001$).

CONCLUSION: We found lower disease burden and more subclinical cases among PWSD with newly diagnosed TB identified through active case finding compared to individuals found in the traditional clinic setting. We report a successful model of how to find, engage, screen, and diagnose TB in PWSD with the potential to reduce additional transmission and improve individual outcomes.

Table 1. Demographics and disease burden comparison for participants newly diagnosed with TB who smoke illicit drugs from active versus passive case finding

	Active case finding (N=36)	Passive case finding (N=130)	p value1
Age, yrs	36 (30, 41)	35 (27, 48)	0.934
Male sex	30 (83.3%)	101 (77.7%)	0.463
Methamphetamine Use2	31 (86.1%)	91 (70.0%)	0.053
Methaqualone Use2	36 (100.0%)	125 (96.2%)	0.232
Cannabis Use2	21 (58.3%)	115 (88.5%)	< 0.001
Tobacco Use	33 (91.7%)	99 (76.2%)	0.041
HIV Positive	8 (22.2%)	40 (31.0%)	0.305
Imprisoned, ever	27 (75.0%)	62 (47.7%)	0.004
TTP, days3	13 (9, 17)	7 (5, 10)	< 0.001
Concentrated ZN4			<0.001
+++	2 (6.5%)	37 (28.5%)	
++	1 (3.2%)	24 (18.5%)	
+	5 (16.1%)	26 (20.0%)	
Scanty	1 (3.2%)	9 (6.9%)	
No AFB	22 (71.0%)	34 (26.2%)	
Asymptomatic5	21 (58.3%)	1 (0.8%)	< 0.001
Cough	11 (30.6%)	123 (94.6%)	< 0.001
Fever	1 (2.8%)	51 (39.2%)	< 0.001
Night Sweats	2 (5.6%)	88 (67.7%)	< 0.001
Weight Loss	8 (22.2%)	112 (86.2%)	< 0.001
Previous TB6	14 (38.9%)	53 (40.8%)	0.839

Acronyms: TB, tuberculosis; TTP, time to positivity; AFB, acid fast bacilli; ZN, Ziehl-Neelsen;

1p-value calculated using chi-square test or Kruskal-Wallis test

2Self-report or positive urine screen

3 Sputum Culture TTP for non-contaminated samples with confirmed Mycobacterium tuberculosis

4 Observed with concentrated sputum smear microscopy

5 Self-report no cough, fever, night sweats, or weight loss

6 Per study inclusion criteria, passive case finding participants cannot have had TB in the two years prior to study enrolment

D5. INNOVATIVE PEDIATRIC ORAL FORMULATIONS FOR DRUG RESISTANT TUBERCULOSIS

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BACKGROUND: Decades of first-line tuberculosis (TB) medication use have led to increasing rates of multi- and extensively drug resistant (MDR/XDR) TB. Adolescent TB represents approximately 20% of the disease burden in low-resource countries, with MDR-TB diagnosed in 25,000 to 32,000 children annually. There are few pediatric-friendly formulations containing second-line TB drugs, which results in children being disproportionately affected. To address this, Luna Labs is developing gummy formulations containing anti-TB drugs that are palatable to children and will remain stable for up to two years.

DESIGN/METHODS: Second-line anti-TB active pharmaceutical ingredient (API) candidates were selected based on the clinical needs of the TB community. Compatibility between various TB medications and expected gummy ingredients was screened, and pectin-based gummies were formulated with down-selected APIs and ingredients. Gummy taste and metrics of texture (e.g., hardness, chewiness) were assessed for pediatric palatability. High performance liquid chromatography (HPLC)/mass spectrometry (MS) methods, validated using API forced degradation studies, were used to evaluate drug loading and stability. Accelerated degradation testing was also performed and used as a predictive measure of shelf life.

RESULTS: Pediatric-friendly gummies containing second-line anti-TB medications Moxifloxacin or Clofazimine were successfully formulated. Through iterative development, the gummies were demonstrated to have suitable taste and texture. Successful API loading was measured, and extensive assessments of shelf life are ongoing.

CONCLUSION: Second-line anti-TB drugs have been incorporated within palatable, pectin-based gummy formulations. Future work will include completion of shelf-life assessments and preclinical evaluations, including demonstration of bioequivalence.

D6. LARGE PEDIATRIC TB CONTACT INVESTIGATION FOR A RURAL COMMUNITY INVOLVING COLLABORATION WITH REGIONAL MEDICAL AFFILIATIONS − CHALLENGES AND SUCCESSES

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BACKGROUND: An active TB case was identified with 75 contacts at a preschool in a rural community in TX with limited access to healthcare. 63 children were under age 5, meaning they would require window prophylaxis (WP). A TB test, chest x-ray, and full assessment were required of all contacts. Coordination between county, the local hospital, pediatricians, the preschool, and DSHS Public Health Region 8 became necessary.

INTERVENTION/RESPONSE: Challenges arose with workload, including how to arrange examinations for 75 children, educate parents, and communicate with pediatricians, operating 25 miles away. To analyze the need for services, parents were surveyed, and the results were shared with the sole county hospital to demonstrate the need for assistance with evaluations and testing. Collaborating with county hospital and judge, DSHS was able to evaluate, screen, and radiograph the exposed children with limited staff across a large distance. We also organized meetings between DSHS and providers to explain the investigation, our recommendation for starting WP, and evaluation guidelines.

RESULTS: The assistance of local health affiliations and DSHS was vital to the speed and efficiency of the investigation. This assessment resulted with 72 children testing negative and 1 testing positive. The rapid initiation of WP protected the young children from the potential for severe TB disease.

CONCLUSION: Parents expressed concerns about giving antibiotics for multiple weeks. Presentations to parents, information sharing with pediatricians, and an open, ongoing dialogue between the community helped ease fears. Questions and concerns about WP shall be integrated in an educational tool for future initiatives.

D7. INCARCERATION AND TUBERCULOSIS DISEASE HISTORY AMONG PEOPLE WHO SMOKE ILLICIT DRUGS IN WORCESTER, SOUTH AFRICA

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BACKGROUND: People who smoke illicit drugs (PWSD) are at increased risk of incarceration from drug use criminalization. Incarcerated populations experience higher tuberculosis (TB) incidence than the general population.1,2 The extent to which incarceration history is associated with TB disease among PWSD in a high TB burden setting is unclear.

DESIGN/METHODS: We analyzed data from the "Transmission of Tuberculosis Among illicit drug use linkages" study, which recruits PWSD through respondent-driven sampling in South Africa and tests for TB and HIV.3 Participants use methamphetamine and/or methaqualone, confirmed by urine drug screening. We compared sociodemographic characteristics and TB disease history by previous incarceration, defined as spending at least one night in a jail or prison.

RESULTS: Of 538 participants, 333 (61.9%) reported ever being incarcerated, 118 (35.4%) of whom reported incarceration within the last 2 years (Table 1). Participants ever incarcerated were more often older (35 vs. 30 years), male (82.3% vs. 57.1%), and more likely to report previous TB (33.6% vs. 22.9%). Of participants with previous TB, those ever incarcerated more often experienced multiple disease episodes (36.0% vs. 14.9%). At study enrollment, a higher proportion of participants ever incarcerated were Mycobacterium tuberculosis culture positive (8.9% vs. 5.1%).

CONCLUSION: In this PWSD cohort, a high proportion report previous incarceration, and those ever incarcerated are more likely to have previous and current TB disease. These findings may reflect drug use criminalization's impact on incarceration and incarceration's impact on TB disease occurrence. Increased active case finding among formerly incarcerated PWSD can improve individual outcomes and potentially avoid TB spread.

Table 1. Sociodemographic Characteristics and Tuberculosis Disease History by Previous Incarceration (N=538)

	Ever Incarcerated (N=333)	Never Incarcerated (N=205)
Sex, born male	274 (82.3)	117 (57.1)
Age, yrs (median, Q1, Q3)	35 (30, 41)	30 (24, 36)
BMI1		
Underweight	116 (35.6)	52 (25.9)
Normal weight	182 (55.8)	127 (63.2)
Overweight and Obese	28 (8.6)	22 (10.9)
Missing	7	4
HIV Status		
Positive	62 (18.6)	39 (19.0)
Negative	271 (81.4)	166 (81.0)
Incarceration, previous 2 years	118 (35.4)	0 (0.0)
Previous TB	112 (33.6)	47 (22.9)
Number of previous TB episodes (N=158)		
1	71 (64.0)	40 (85.1)
>1	40 (36.0)	7 (14.9)
TB treatment outcome, most recent episode (N=159)		
Cured	27 (24.1)	19 (40.4)
Treatment completed	75 (67.0)	22 (46.8)
Lost to follow up	10 (8.9)	5 (10.6)
Treatment failure	0 (0.0)	1 (2.1)
MTB Culture Result2 (N=498)		
MTB Positive	27 (8.9)	10 (5.1)
MTB Negative	276 (91.1)	185 (94.9)
Result Pending	30	10
Xpert Ultra Result (N=529)		
MTB detected	31 (9.5)	10 (5.0)
Trace MTB detected	3 (0.9)	3 (1.5)
MTB Not Detected	293 (89.6)	189 (93.6)
Result Pending	6	3

1Body Mass Index: Per NHLBI categories, Underweight – < 18.5, Normal Weight – 18.5-24.9, Overweight – 25-29.9 and Obese > 30

E. QUALITATIVE/ADVOCACY

E1. PATIENT AND PROVIDER PERCEPTIONS OF THE RELATIONSHIP BETWEEN ALCOHOL USE AND TB AND READINESS FOR TREATMENT: A QUALITATIVE STUDY IN SOUTH AFRICA

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BACKGROUND: Problem alcohol use is a key driver of poor TB treatment response.1 In 2020, 8.1% of new TB cases were attributable to alcohol use, globally.2, 3 We conducted a qualitative research study to understand perceptions of and changes in problem alcohol use during TB treatment, its effect on treatment, factors motivating individuals to reduce alcohol intake, and intervention readiness. This study was embedded in an ongoing prospective cohort study (R01AI19037, Jacobson).

DESIGN/METHODS: We conducted five focus group discussions with 34 individuals with current or previous drug-susceptible TB who reported current alcohol use and 8 in-depth interviews with TB providers in Worcester, South Africa (Table 1). Data were analyzed using thematic analysis.

RESULTS: Participants felt that structural drivers of problem alcohol use were widespread poverty, violence and the normalization of heavy episodic drinking. Heavy alcohol use was thought to be associated with increased TB transmission and decreased TB medication adherence. Screening for problem alcohol use and referral to specialist treatment was suggested. Participant suggestions for intervention services to reduce alcohol intake included social support by community health workers to build trust, decrease stigma and encourage adherence while barriers included affordability of services and challenges around sustained changes in alcohol use.

CONCLUSION: Effective TB treatment strategies tailored around alcohol use could improve outcomes. Participants reported a need for early identification of problem alcohol use and a readiness for non-stigmatizing intervention services. These findings lay the groundwork for the development of interventions to support alcohol reduction and improve TB treatment response.

Table 1. Demographics information for FGDs and IDIs

	IDI Participants (N=8)	FG Participants (N=34)
Age		
Mean (SD)	45.13 (8.38)	40.79 (5.87)
Gender		
Male	1 (11%)	24 (71%)
Female	7 (89%)	10 (29%)
Language		
Afrikaans	7 (89%)	34 (100%)
English	1 (11%)	0 (0%)
Profession		
TB Nurse	6 (75%)	n/a
Nurse Practitioner	1 (12.5%)	
General Nurse	1 (12.5%)	
Years in Services		
Mean (SD)	9.71 (9.61)	n/a

E2. USING COMMUNITY-BASED STIGMA ASSESSMENTS TO EXPLORE THE IMPACT OF CONTEXT ON TB STIGMA IN SOUTH AFRICA

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BACKGROUND: Major gaps remain in our ability to mitigate stigma at different stages of a person's TB care journey. Community-based participatory research offers a critical opportunity to explore the contextual aspects of stigma. As done for HIV, the use of peer research associates (PRAs) can provide additional insights into complex barriers like stigma.

METHODS: Using an adapted Stop TB Partnership stigma assessment tool, we trained two TB survivors and a community health worker as PRAs to undertake community-based surveys with people affected by TB at urban and rural clinic sites in Khayelitsha, Western Cape, and Hammanskraal, Gauteng Province, South Africa. We calculated numeric stigma scores for each domain of stigma (internal, anticipated, and enacted), which were tested for internal consistency using Cronbach's alpha, prior to generalized linear regression.

RESULTS: The overall mean internal, anticipated, and enacted stigma scores were 2.02 (SD 1.23), 2.05 (SD 1.18), and 1.82 (SD 1.07) respectively. Unadjusted linear regression analyses suggested older age, prior TB history, and extrapulmonary TB may be associated with lower stigma scores, but in adjusted analyses, only location (living in Hammanskraal compared to Khayelitsha) was associated with lower stigma scores across all three domains: internal (β coef 0.75; 95% CI: 0.47, 1.04; $p<0.001$), anticipated (β coef 0.81; 95% CI: 0.57, 1.05; $p<0.001$), and enacted (β coef 0.81; 95% CI: 0.58, 1.03; $p<0.001$).

CONCLUSIONS: Understanding the impact of context such as rural versus urban settings on stigma can help to design effective interventions. Findings will be triangulated with analyses from in-depth interviews.

Table: Factors Associated with Stigma in those who Experienced TB

	Anticipated Stigma				Enacted/External Stigma				Internal Stigma			
Variable	Crude β -coef (95% CI)	p-value	Adjusted β -coef (95% CI)	p-value	Crude β -coef (95% CI)	p-value	Adjusted β -coef (95% CI)	p-value	Crude β -coef (95% CI)	p-value	Adjusted β -coef (95% CI)	p-value
Age Categories, No (%) in years												
<30	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-
31-40	**0.45 (0.08, 0.82)**	**0.019**	-0.02 (-0.36, 0.32)	0.907	0.36 (-0.01, 0.72)	0.053	-0.17 (-0.48, 0.14)	0.290	0.36 (-0.11, 0.84)	0.133	-0.24 (-0.69, 0.22)	0.302
41-50	0.38 (-0.02, 0.77)	0.060	0.01 (-0.35, 0.35)	0.980	0.24 (-0.15, 0.62)	0.223	-0.17 (-0.49, 0.14)	0.278	0.15 (-0.36, 0.65)	0.564	-0.33 (-0.79, 0.13)	0.159
51-60	0.06 (-0.41, 0.52)	0.802	0.01 (-0.38, 0.41)	0.951	-0.11 (-0.56, 0.33)	0.614	-0.22 (-0.58, 0.14)	0.227	0.03 (-0.56, 0.62)	0.920	-0.13 (-0.66, 0.39)	0.608
>60	-0.27 (-0.94, 0.39)	0.416	-0.19 (-0.73, 0.35)	0.490	-0.25 (-0.89, 0.39)	0.445	-0.17 (-0.66, 0.32)	0.498	-0.24 (-1.08, 0.61)	0.582	-0.12 (-0.83, 0.60)	0.749
History of Previous TB, No (%)												
Yes	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-
No	**0.33 (0.08, 0.58)**	**0.012**	0.02 (-0.21, 0.25)	0.857	**0.36 (0.12, 0.60)**	**0.004**	0.08 (-0.12, 0.29)	0.424	**0.56 (0.26, 0.86)**	**<0.001**	0.27 (-0.04, 0.57)	0.083
TB Type, No (%)												
Pulmonary	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-
Extrapulmonary	-0.35 (-0.79, 0.09)	0.121	0.10 (-0.27, 0.47)	0.591	**-0.47 (-0.89, -0.05)**	**0.029**	-0.04 (-0.38, 0.30)	0.813	**-0.57 (-1.11, -0.03)**	**0.039**	-0.06 (-0.55, 0.43)	0.811
Location, No (%)												
Khayelitsha	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-	*Reference*	-
Hammanskraal	**1.47 (1.13, 1.82)**	**<0.001**	**0.82 (0.57, 1.07)**	**<0.001**	**1.39 (1.09, 1.69)**	**<0.001**	**0.81 (0.58, 1.03)**	**<0.001**	**1.50 (1.13, 1.86)**	**<0.001**	**0.84 (0.51, 1.17)**	**<0.001**

E3. A COMMUNITY HEALTH CENTER'S EXPERIENCE ON COVID-19 INFECTION AND SOCIAL DETERMINANTS AMONG ASIAN AMERICANS IN SAN FRANCISCO, CALIFORNIA

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BACKGROUND: In San Francisco (SF), California, Asians account for 34% of the population, 24% of COVID-19 cases, and 37% of COVID-19 deaths as of 9/25/22. This imbalance of COVID-19- related deaths among Asians is not reported elsewhere in the continental United States. We assessed risk factors and social determinants of patients tested for COVID-19 at North East Medical Services (NEMS) to investigate any disproportionate trends.

METHODS: We conducted a retrospective analysis of patients with SF residence who completed a COVID-19 PCR test at NEMS, a community health center (CHC) serving 47,000+ SF residents and primarily low-income Asian immigrants, between 3/1/20-12/31/21 (n=9,263). We fit logistic regression models to calculate odds ratios for COVID-19 positivity among patient demographic groups and performed two-proportion z-tests to compare patient demographic groups accessing COVID-19 PCR tests and general services.

RESULTS: In 2020, Asians ($p<0.01$) and patients with income ≤100% federal poverty level (FPL) ($p<0.01$) had lower COVID-19 testing proportions whereas Whites ($p<0.01$) and patients with income ≥200% FPL ($p<0.01$) had higher testing proportions compared to respective proportions of patients who sought general services that year. Overall, patients with Vietnamese language preference (odds ratio [OR]=1.92, $p<0.01$), Vietnam as birthplace (OR=1.54, $p<0.02$), congregate housing residence (OR=1.66, $p<0.01$), and a hypertension diagnosis (OR=1.42, $p<0.01$) showed higher odds of COVID-19 infection.

CONCLUSION: This CHC observed lower COVID-19 testing of Asians and low-income patients early in the pandemic with Vietnamese language preference showing higher likelihood for COVID-19 infection. Further research needs to be done on disaggregated Asian data to explore COVID-19 infectivity and mortality trends.

E4. Implementing Post-Tuberculosis Care in British Columbia, Canada: Understanding Healthcare Provider Perceptions Using the Theoretical Domains Framework.

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BACKGROUND: While the long-term needs of tuberculosis (TB) survivors are becoming increasingly apparent, little is known about healthcare provider (HCP) perspectives on providing post-TB care. In this study, we explored HCP perceptions of post-TB care, defined the core components of post-TB care, and identify facilitators and enablers to their successful implementation.

METHODS: First, we held virtual workshops with HCP specializing in TB care in British Columbia, Canada, to identify key components of post-TB care. Then, we surveyed HCP to explore possible factors mediating their implementation using the Theoretical Domains Framework. Lastly, we mapped the identified barriers and enablers to behaviour change techniques to inform future post-TB intervention content.

RESULTS: 11 participants attended virtual workshops, and 23 of the 51 (45.1%) HCP completed surveys. Identified core components of post-TB care included:

1. Linking people with TB to a primary care provider,
2. Referring people with TB who smoke to a smoking cessation specialist,
3. Referring people with pulmonary TB for an end-of-treatment chest x-ray and pulmonary function testing,
4. Providing an information sheet to the patient's primary care provider on post-TB health.

Environment, context, and resources scores were the lowest in the survey, possibly reflecting implementation barriers. Study findings also highlighted the need for care coordination for individuals transitioning from TB care.

CONCLUSION: HCP acknowledge that post-TB care is an integral part of comprehensive health care, but they are limited by time and resources. Care coordination services, a post-TB checklist, and information leaflets may help resolve some of the identified barriers.

E5. Assessing Patient Satisfaction with Video-Observed Therapy (VOT) for Drug-Susceptible Tuberculosis During the COVID-19 Pandemic

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BACKGROUND: Video Observed Therapy (VOT) has been proposed as an alternative to Directly Observed Therapy (DOT) for tuberculosis (TB) treatment as prior studies have demonstrated similar adherence rates. This study evaluated patient experiences with VOT after it became a standard practice in Calgary, Alberta during the COVID-19 pandemic.

METHODS: Patients ≥ 18 years with drug-susceptible TB between March and December 2020 were asked to complete a patient satisfaction survey. Twenty-two survey statements were based on previously identified themes of service quality as it pertains to VOT (examples: confidentiality, convenience) with a Likert scale of agreement (1=strongly disagree, 5=strongly agree).

RESULTS: A total of 34 participants completed the survey out of 122 eligible patients (mean age 47 years, 50% females). The majority of participants strongly agreed that VOT was easy to use and convenient (median 5, IQR 1 for both). Participants disagreed that they had connection issues during VOT (median 2, IQR 2). 38% of participants preferred a VOT schedule outside of usual clinic hours (median 3, IQR 1). Participants strongly agreed that VOT maintained their confidentiality (median 5, IQR 1). 83% of participants would recommend VOT to other patients instead of DOT (median 5, IQR 1). Adherence compared to those on DOT during the pre-pandemic period did not differ (VOT 95.5% versus DOT 94.8%, p=0.74).

CONCLUSION: Patient satisfaction rates were high with VOT. A significant proportion indicated a preference to take medications by VOT outside of usual clinic hours, highlighting asynchronous VOT as a potential intervention to further enhance patient-centered care.

E6. THE IMPACT OF PULMONARY TUBERCULOSIS ON HEALTHCARE UTILIZATION: AN INTERRUPTED TIME SERIES ANALYSIS USING LINKED ADMINISTRATIVE DATA FROM BRITISH COLUMBIA, CANADA

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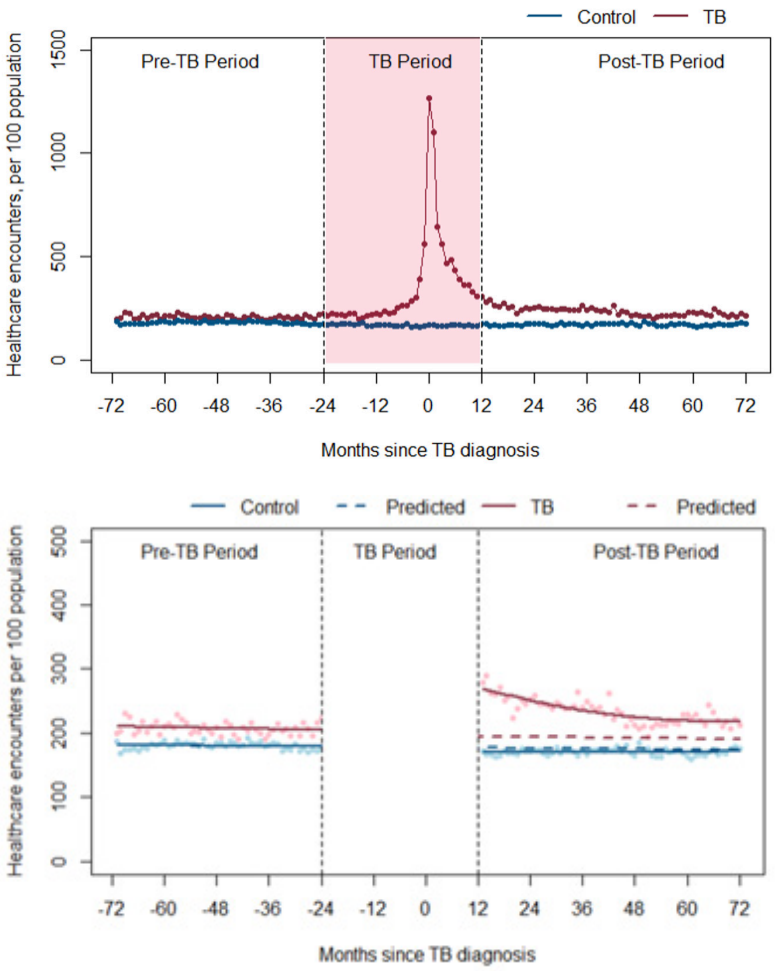
BACKGROUND: Understanding healthcare use in the years following tuberculosis (TB) treatment can help inform care for those who have survived TB. Thus, our objective for this study was to examine the impact of pulmonary TB on healthcare use in the post-TB period.

METHODS: Using linked administrative data, we identified all foreign-born individuals registered with British Columbia's Medical Service Plan who completed treatment for incident pulmonary TB between 1994 and 2019. We then imputed a TB diagnosis date for non-TB controls, and each person with TB was matched 1:4 to controls using nearest neighbour propensity score matching without replacement, based on demographic and clinical factors. Then, using an interrupted time series analysis, we investigated changes in the monthly rate of healthcare encounters for the four years before and five years after the TB period (the pre-TB and post-TB periods, respectively).

RESULTS: In total, we matched 1,491 people who completed treatment for pulmonary TB to 5,916 non-TB controls. Immediately following the TB period (i.e., 13 months after TB diagnosis date), the monthly rate of healthcare encounters per 100 population in the TB population was 72.6 (95% CI 66.2, 79.1) encounters higher than the predicted value had TB not occurred, a 36.7% (95% CI 33.5, 40.0) increase. Moreover, the monthly rate of healthcare encounters remained elevated for the duration of the post-TB period (Figure 1).

CONCLUSION: Our findings indicate that despite completing treatment, people with pulmonary TB continue to experience elevated healthcare utilization in the years following their TB diagnosis.

Figure 1. Monthly rate of unique healthcare encounters per 100 population, pre- and post-TB, in people who completed treatment for pulmonary TB and propensity score matched controls.



Note: The red rectangle in Figure 1a represents the TB period, which is the time that was not included in the model presented in Figure 1b. The start of the TB period is 24 months before the TB diagnosis date to provide a stable pre-TB estimate and account for the increase in healthcare utilization associated with TB. The end of the TB period is 12 months post TB diagnosis date to account for the duration of TB and TB treatment.

E7. CONTEXTUAL INFLUENCES ON TUBERCULOSIS EDUCATION AND COUNSELING FOR PATIENTS AND FAMILY MEMBERS WHO ARE FOREIGN-BORN IN CALGARY, CANADA

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BACKGROUND: TB education and counseling practices often fall short of meeting family needs. However, little is known about how patient and family circumstances affect learning needs, and how healthcare context affects practice. The study objective was to understand how these contexts influence TB education and counseling for patients and their family members who are born outside of Canada.

DESIGN/METHODS: Data sources for this Calgary-based, qualitative case study component included 25 institutional documents (practice guidelines and patient education materials) and 49 interviews with patients, family members, TB healthcare workers, and community and healthcare leaders. Interviews explored patient and family needs, institutional culture, and the impact of COVID-19. The education and counseling content of documents was described. Thematic, content, and framework analysis techniques were used.

RESULTS: Three dimensions of context were generated from the data: 1) adverse social determinants of health for people who are foreign-born, 2) low institutional prioritization of education and counseling, and 3) weak connections between TB healthcare providers and community partners. Practice guidelines contained little education and counseling content. Participants described how dimensions of context negatively impacted education and counseling in numerous ways, including reduced opportunities for patient-provider interaction and limited managerial time for practice improvement. Participants also noted how COVID-19 related changes increased attention to the education and counseling needs of people who are foreign-born.

CONCLUSION: TB education and counseling advocates could capitalize on pandemic-era innovations to promote solutions such as video appointments and community outreach. Practice change will require additional resources and relationships with community partners.

F. POLICY

F1. UNITING INNOVATION WITH IMPLEMENTATION: AN EVIDENCE SYNTHESIS OF IMPLEMENTATION STRATEGIES TO INCREASE THE UPTAKE AND IMPACT OF MOLECULAR WHO-RECOMMENDED RAPID TB DIAGNOSTIC TESTS

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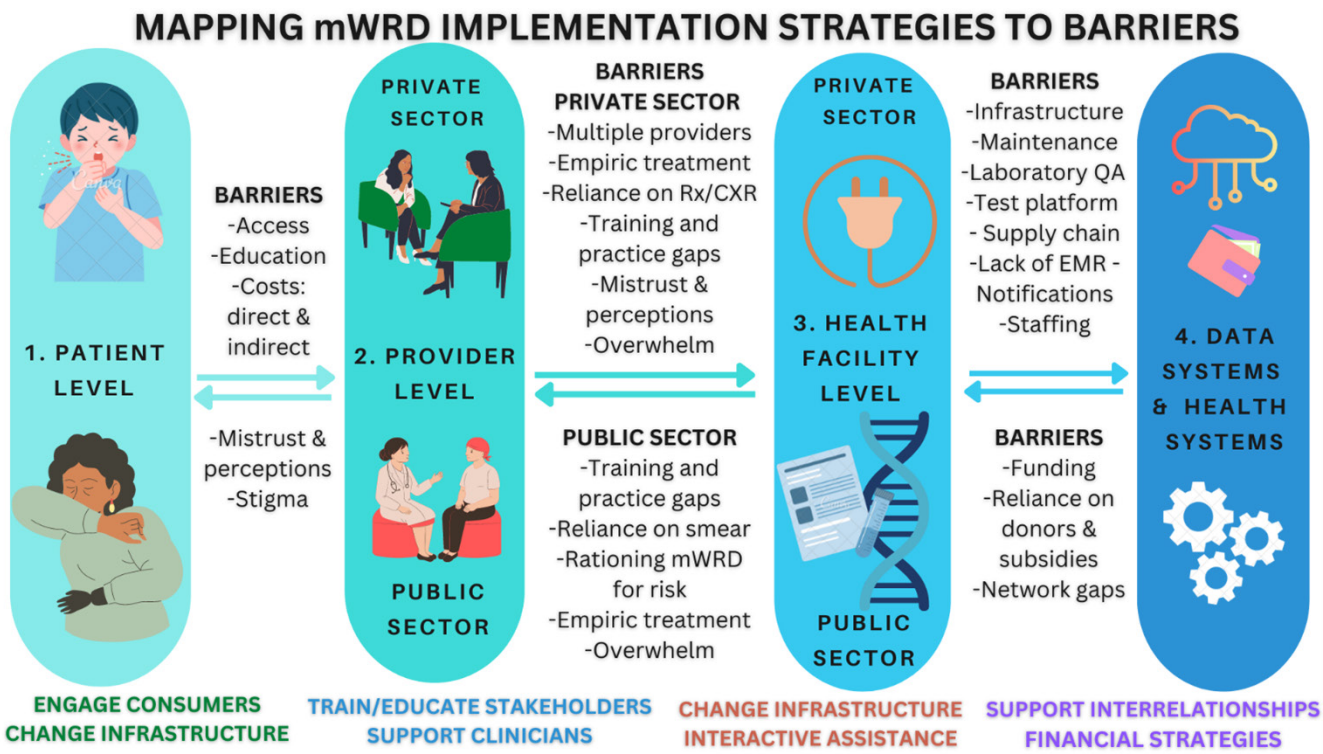
BACKGROUND: TB care cascade analyses demonstrate diagnosis remains the largest gap, which has widened due to the COVID-19 pandemic. Only one-third of patients diagnosed with TB receive a molecular WHO-recommended rapid diagnostic test (mWRD). We conducted a mixed-methods systematic review of mWRD implementation strategies to support WHO efforts to develop programmatic standards for TB diagnostics.

METHODS: Using search terms for TB, mWRDs, and implementation strategies, we searched PubMed, EMBASE, CINAHL, PsycInfo, Web of Science, and the WHO-ICTRP. Four systematic reviewers screened all abstracts, full-texts, and extracted data. We categorized included studies according to 'thickness', determined by the complexity and richness of data, analyses, and perspectives presented. We used thematic analysis to guide data analysis and derive a framework to understand how mWRD implementation strategies can address context-specific barriers and leverage enablers.\

RESULTS: After screening 3854 articles, we extracted data from 54 high-thickness studies. Studies were conducted across 18 countries, including varied public and private healthcare settings. Implementation strategies to barriers through the diagnostic cascade included: engaging patients through remote outreach programs, training and supporting clinicians using longitudinal engagement and auxiliary workers, changing infrastructure and interactive assistance using multicomponent strategies and performance feedback, improving interrelationships for health information management, and interactive assistance using diagnostic network optimization to strengthen health systems.

CONCLUSIONS: Innovative, contextually relevant implementation strategies can enable programs to realize the benefits of improved accuracy and potential expediency that using mWRDs as the initial test for TB offers. Multicomponent strategies that center equity and longitudinal iterative engagement at each health system level must be prioritized.

Figure. Mapping mWRD implementation strategies to barriers.



F2. SUPPORTING AND EMPOWERING COMMUNITIES AFFECTED BY TB TO INFORM THE TB RESPONSE

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BACKGROUND: Communities affected by TB in Canada often face barriers to accessing health services, including having limited access to social support, as a national support network for people affected by TB in Canada has been a critical missing component to the domestic TB response. Not only are people affected by TB stigmatized and isolated, but they are also consistently left out of policy decisions that directly affect them. Greater efforts must be made for people affected by TB to be supported throughout their experiences and actively involved in the TB response.

RESPONSE: A first step towards advancing meaningful engagement of communities impacted by TB is to create a network of TB-affected individuals. TBpeople Canada, a Stop TB Canada program, is a supportive community for people affected by TB committed to a common goal of providing social support, fighting stigma, and ending TB.

RESULTS: TBpeople Canada presents a space to empower TB-affected communities to be both leaders and equal partners in a people-centered response, while providing peer support and a sense of community. The network, in conjunction with TBpeople chapters globally, will help reimagine the role of communities in the fight to end TB – from victims to leaders whose voices are essential to informing the TB response.

CONCLUSIONS: TB-affected communities can offer peer support by sharing their stories and experiences, advocate based on their lived experience, and inform the overall TB response for a more rights-based, people-centered, culturally appropriate, gender transformative approach to TB care. Including their voices is not just the 'right thing to do', it is a critical step in designing and implementing local, community-led interventions that increase equitable access to TB services.

F3. UPDATES ON CDC RECOMMENDATIONS FOR TUBERCULOSIS TREATMENT

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BACKGROUND: In 2022, the Centers for Disease Control and Prevention (CDC) issued new guidance for two TB treatment regimens that are shorter in duration than traditional regimens: a 6-month (26 weeks) bedaquiline-pretomanid-linezolid (BPaL) combination regimen for treating highly drug-resistant pulmonary TB, and a 4-month (17 weeks) regimen containing rifapentine, moxifloxacin, isoniazid, and pyrazinamide for treating drug-susceptible pulmonary TB.

RESPONSE: CDC's Division of Tuberculosis Elimination staff researched evidence regarding the new regimens and drafted recommendations for the United States. Recommendations were reviewed by independent external panels and senior CDC science leaders and presented for public comment. Reviews and comments were addressed by updating CDC guidance and creating informational materials for clinicians and TB patients.

RESULTS: CDC recommends the BPaL regimen and describes considerations for patient monitoring and dose adjustment for potential drug toxicity, particularly of linezolid. CDC recommends the 4-month regimen for pulmonary TB patients with clinical characteristics consistent with study data supporting its adoption. Detailed recommendations for patients living with comorbidities are provided. Materials for clinicians include answers to frequently asked questions and resources for clinical consultation, and materials for patients include treatment guides found online at https://www.cdc.gov/tb/topic/treatment/tbdisease.htm.

CONCLUSIONS: New guidance in 2022 facilitates providers using shorter regimens for treating TB. In addition to patient medical and social history and any concomitant medications or diagnoses, access to TB diagnostics, drug susceptibility testing, and drugs affects which TB regimens may be available as treatment options and must be considered when initiating patients on a given regimen.

F4. EVALUATION OF THE THINK. TEST. TREAT TB NATIONAL LATENT TUBERCULOSIS INFECTION COMMUNICATIONS CAMPAIGN

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BACKGROUND: The Think. Test. Treat TB campaign aims to increase awareness of latent tuberculosis (TB) infection and encourage testing and treatment of Filipino and Vietnamese persons. An impact evaluation assessed engagement, perceived relevance, comprehension, and behavioral intentions relative to latent TB infection among consumers and healthcare providers exposed and not exposed to the campaign.

DESIGN/METHODS: Online surveys were conducted in Seattle, Washington from July 28, 2022, to August 22, 2022, among non-U.S.—born Filipino or Vietnamese persons 20 to 65 years old, and healthcare providers in primary care settings serving a patient population of >20% non-U.S.—born Asian persons. Frequencies and proportions were calculated.

RESULTS: A total of 173 consumers and 44 healthcare providers participated. Consumers considered the campaign relevant to them (87.3%) or their family (80.9%). Most (91.3%) felt the information was important and 69.9% trusted the information. More exposed (87.8%) than non-exposed (64%) consumers indicated they would discuss TB with their healthcare provider, and slightly more exposed (49.6%) than non-exposed (48%) with family/friends. Among healthcare providers, all thought campaign materials were relevant to their patient population, almost all (95.5%) felt the materials were relevant to healthcare providers who serve patients at risk for TB, and all agreed the information was important. Yet only 29.5% considered themselves the intended audience. More exposed (57.6%) than non-exposed (45.5%) healthcare providers indicated they would increase TB testing in their practices.

CONCLUSION: The campaign was relevant to consumers. Healthcare providers found the campaign relevant and important, but the majority did not consider themselves the intended audience.

F5. ENCOURAGING HEALTHCARE PROVIDERS TO THINK. TEST. TREAT TB

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BACKGROUND: In March 2022, the Centers for Disease Control and Prevention's (CDC) Division of Tuberculosis Elimination (DTBE) launched Think. Test. Treat TB, the first national communications campaign to raise awareness of TB prevention and encourage healthcare providers to test for and treat latent TB infection among patients at risk for TB.

INTERVENTION/RESPONSE: The campaign was designed to reach healthcare providers working in community-based clinics, including Federally Qualified Health Centers in Seattle, Washington, and Los Angeles, California. Elements of the campaign were available nationwide. Digital advertisements were placed on professional websites, newsletters, and other digital platforms for healthcare providers. Based on provider feedback, CDC developed five new patient education materials to facilitate patient-provider conversation.

RESULTS: Digital advertisements generated over 1.3 million views and 1,770 clicks to the campaign website. Overall, digital advertisements delivered a strong click-through-rate of 0.13%, exceeding industry benchmarks of 0.05%. Messages featuring an image of a healthcare provider and that emphasized healthcare providers' responsibility to protect their communities performed well. Over 2,000 patient education materials were downloaded from the campaign website, and over 35,000 printed materials were ordered from CDC.

CONCLUSION: Healthcare providers are engaged with advertisements on professional association websites, newsletters, and other digital platforms. Future efforts should develop multiple concepts for digital advertisements to further explore messages that resonate with providers and leverage larger channels for reach and efficiency, as well as smaller localized channels to lend credibility.

F6. A SURVEY OF ACCESS TO RAPID DIAGNOSTIC TESTS FOR TUBERCULOSIS DIAGNOSIS IN THE UNITED STATES

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BACKGROUND: United States (US) guidelines recommend the use of rapid diagnostic tests (RDTs) to evaluate persons with suspected pulmonary tuberculosis (TB); since 2013, Cepheid Xpert® MTB/RIF assay has been recommended. A recent evaluation of reported US TB cases from 2011-2017 noted increasing RDT use, though by 2017, 33.6% of reported cases still did not have RDT results. We surveyed state and big-city TB programs to learn about RDT access for detecting TB and their use for home respiratory isolation (HRI) decisions for persons with suspected infectious TB.

METHODS: The online survey was sent in April 2022 to 68 US TB programs supported by CDC funds.

RESULTS: Programs in 38 states, six large cities, and four US territories (71% of surveyed programs) responded. Nearly all jurisdictions (n=47/48) reported having access to RDTs; 44 (92%) reported “all” or “most” areas in their jurisdiction had access. Forty had access to the Cepheid Xpert® MTB/RIF assay, four to the GenoType MTBDRplus line probe assay, 17 to “In-house developed PCR tests”, and three to “Other” tests.

For persons with suspected infectious TB, 31 (65%) jurisdictions considered negative RDT results as part of their criteria for discontinuation of HRI, regardless of AFB smear result.

CONCLUSIONS: RDTs were available to most US TB programs. However, fewer jurisdictions reported using such tests to make HRI decisions. The reason for not using these tests need to be further explored. A limitation is that we did not survey the hospitals where many persons with TB are initially evaluated.

F7. PUBLIC HEALTH AND M. TUBERCULOSIS-COMPLEX NUCLEIC ACID AMPLIFICATION (NAA) TESTING: FINDING A BALANCE

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BACKGROUND: In June 2021 the State of Arizona Tuberculosis Program (AZ-TB) launched a 12-month NAA testing collaborative with the State Public Health Lab (AZ-Lab). AFB smear(-) clinical sputa, not normally triggering NAA reflux, would be assessed for possible NAA testing. A goal was to determine the right balance of testing based on resources and patient impact.

INTERVENTION/RESPONSE: AZ-TB evaluated whether broader NAA testing, alongside the existing reflux after AFB sputum smear(+) result, would promote earlier treatment initiation. Inclusion criteria were: 1-public health submitters without in-house NAA capabilities; 2-clinical sputum sample; 3-AFB smear(-); and 4-no prior NAA or culture(+) within the last 365-days.
AZ-TB reviewed samples daily and notified AZ-Lab which sample(s) to include.

RESULTS: During the 12-month process, 214 samples met inclusion criteria, resulting in an increase of 12.5 NAAs per month. Four samples were AFB smear(-) and NAA(+), accounting for
<2% of all NAAs. Of those four, treatment started 1-day prior to NAA result for one patient and 3, 7, and 23-days after NAA result for the remaining three patients.

CONCLUSIONS: Highlights of the testing collaborative included exploring a deeper connection with laboratory data, automating morning emails for eligible samples to review, an expansion to selected correctional partners, and reenforcing the lab/program partnership. It's unclear if universal NAA testing on sputum smear(-) samples impacts treatment initiation and public health interventions among patients already followed by public health. The NAA testing collaborative continues and will be adapted based on ongoing analysis and building upon lessons learned.

F8. CHALLENGES TO PROGRAM IMPLEMENTATION OF THE FOUR-MONTH RIFAPENTINE-MOXIFLOXACIN REGIMEN FOR THE TREATMENT FF DRUG-SUSCEPTIBLE TUBERCULOSIS IN NEW YORK CITY

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BACKGROUND: In February 2022, the U.S. Centers for Disease Control and Prevention (CDC) recommended a new four-month rifapentine and moxifloxacin-containing treatment regimen (4-HPMZ) to shorten duration of treatment for drug-susceptible pulmonary tuberculosis (TB). We designed a program to support adoption of 4-HPMZ at New York City Department of Health (DOH) TB clinics.

INTERVENTION: DOH formed a multidisciplinary workgroup to develop a 4-HPMZ program protocol. We developed job aides for staff, provided training, retrospectively reviewed medical records, and notified providers of potential 4-HPMZ candidates with daily emails. Persons meeting DOH's eligibility criteria for 4-HPMZ were screened by physicians for potential 4-HPMZ.

RESULTS: Between mid-April and mid-September 2022, 110 persons with confirmed or probable TB visited DOH TB clinics. Of these, 52 (47%) did not meet eligibility criteria: 32 had taken TB medications for over 30 days before their initial clinic visit, 12 had non-pulmonary TB, 6 had rifampin- or isoniazid-resistant TB, and 2 were pregnant. Of 58 eligible patients, 27 (47%) were screened. Of these, 8 (29%) were prescribed 4-HPMZ. To date, only one has completed 4-HPMZ, one discontinued treatment due to fluoroquinolone resistance, and six are still undergoing 4-HPMZ treatment. Reasons for not prescribing 4-HPMZ to the other 19 patients have included provider medical decision (n=13, 48%), patient refused treatment due to pill burden (n=5, 19%), and other patient refusal (n=1, 4%).

CONCLUSION: Adoption of 4-HPMZ has been limited to date. DOH is working to understand why less than half of eligible patients were screened and to identify and address barriers to prescribing 4-HPMZ.

F9. MEDICAL CONSULTATIONS FROM PANEL PHYSICIANS TO U.S. TUBERCULOSIS CENTERS OF EXCELLENCE, 2018-2020

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BACKGROUND: Applicants seeking entry into the United States are examined overseas for tuberculosis (TB) by panel physicians, international practitioners in countries guided by Centers for Disease Control and Prevention (CDC) Technical Instructions. To support this effort, the CDC-funded TB Centers of Excellence provide web-based expert consultation regarding persons with complex TB. Consult documentation is stored in a Medical Consultation Database (MCD). Analysis of consultations can reveal inquiry trends among panel physicians worldwide.

METHODS: Panel physician queries in MCD 1/1/2018--12/31/2020 were analyzed. Entries were classified with qualitative analysis, specifically a descriptive coding scheme developed through inductive analysis, allowing multiple themes per entry.

RESULTS: 156 queries were analyzed, pertaining to 94 TB cases in 25 countries. 57 (37%) consultations related to initial treatment. 54 (35%) involved modifying regimens, for reasons including adverse reactions (n=24) and drug-susceptibility results (n= 22). 58 (37%) consultations were for clarifying the technical instructions. 39 (25%) queries involved comorbidities affecting TB treatment. 17 (11%) involved management of multidrug (MDR) or extensively-drug-resistant (XDR) TB. Qualitative analysis identified other unclassified themes including management of incidental pleural effusions and clarification of immigration status.

CONCLUSIONS: Our analysis suggests areas for further education of panel physicians, including choice of MDR/XDR-TB regimens, comorbidity management, and additional clarity to aid understanding the technical instructions. Providing focused education on these topics will address knowledge gaps to allow for streamlined TB diagnosis and treatment among individuals seeking to immigrate to the United States.

G. RISK FACTORS/EPI

G1. EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF PEOPLE WITH OCULAR TUBERCULOSIS IN THE UNITED STATES, 1993–2019

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BACKGROUND: Data on ocular tuberculosis (OTB) in the United States have not been previously reported. We evaluated trends of OTB compared with other extrapulmonary TB (ETB).

DESIGN/METHODS: We estimated the proportion of ETB cases with OTB, defined as tuberculosis of the "Eye or Ear Appendages," reported to the National Tuberculosis Surveillance System during 1993–2019. We compared demographics and clinical characteristics of people with OTB and other ETB during 2010–2019. P-values were calculated by chi-square test for categorical variables and Kruskal-Wallis for continuous variables.

RESULTS: During 1993–2019, 1,766 OTB cases were reported, representing 1.6% of 107,340 ETB cases: 200 (0.5% of 36,505) during 1993–1999, 395 (1.0% of 41,094) during 2000–2009, and 1,171 (3.9% of 29,741) during 2010–2019.
Compared with other ETB, persons with OTB were older (median: 48 vs 44 years, $p<0.01$), more likely to be U.S.-born (35% vs 28%, $p<0.01$) and have diabetes (17% vs 13%, $p<0.01$), less likely to have HIV (1% vs 8%, $p<0.01$), and not significantly different by sex. OTB was less likely to be laboratory confirmed (5% vs 75%, $p<0.01$) but more likely to be tested by interferon gamma release assay (IGRA; 84% vs 56%, $p<0.01$) and IGRA positive (96% vs 80%, $p<0.01$).

CONCLUSION: Reported OTB increased during 1993–2019 despite decreasing TB, including ETB; the largest increase occurred during 2010–2019. OTB was rarely laboratory confirmed and primarily diagnosed in conjunction with IGRA results. More research is needed to understand the epidemiology of OTB to inform clinical and diagnostic practices.

G2. PERIPHERAL LYMPH NODE-ASSOCIATED PULMONARY TUBERCULOSIS: RARE HAPPENSTANCE OR COMMON CONCURRENCE?

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BACKGROUND: The prevalence of concurrent pulmonary tuberculosis (PTB) in peripheral lymph node (PLN) TB patients, its clinical and radiographic features, predictors, and public health consequences, are unknown.

METHODS: We developed a 10-year (2010-2019) population-based cohort of PLNTB patients in Canada, supplemented with systematically collected primary source data and expert reader chest radiograph interpretations. Multivariable logistic regression was applied to determine associations between sputum culture-positivity, and demographic, clinical and radiographic features. Public health risks were estimated from transmission events among contacts of patients with PLNTB.

RESULTS: There were 306 patients with PLNTB among whom 283 (92.5%) were 15-64 years of age, 159 (52.0%) female, and 293 (95.8%) foreign-born. Respiratory symptoms were present in 21.6%: an abnormal chest radiograph in 23.2%. Sputum was culture-positive in 63 (20.6%) PLNTB patients. Respiratory symptoms, abnormal lung parenchyma, and HIV-coinfection (borderline) were independent predictors of sputum culture-positivity (odds ratio [OR] 2.24 [95%CI 1.15-4.39], p< 0.018, OR 4.78 [95%CI 2.41-9.48], p< 0.0001, and OR 2.54 [95%CI 0.99-6.52], p< 0.053), respectively. Among contacts of patients with sputum culture positive PLNTB one secondary case and 16 new infections were identified.

CONCLUSIONS: Isochronous PTB is common in PLNTB patients. Routine screening of PLNTB patients for PTB is strongly recommended.

G3. IMPACT OF THE COVID-19 ON THE OUTCOME OF TB PATIENTS IN HAITI

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BACKGROUND: Haiti has the highest TB incidence in America, and has been affected by the covid-19 not because of the death and morbidity among TB patients, but mostly by disorganizing access to care and follow up of patients under treatment; it is known that the coverage rate was deeply reduced, but few is known about the outcome of these cohort of patients; to understand this, analysis of the outcome is needed that's what we propose to realize in order to better prepare other catastrophe and other high risk condition that could affect the patients in the country.

METHOD: Comparison of the outcome of the TB patients before during and after the peak of the occurrence of covid in 2018, 2019 and 2020

RESULTS:

Year	No Cases	Success	Lost To Follow up	DCD	Failure	Not Evaluated
2018	13744	11308 (78%)	1226(9%)	775 (5%)	112 <1%)	162 (1%)
2019	13305	10920(82%)	1195(9%)	607(5%)	114 (1%)	169 (1%)
2020	11043	9015(82%)	977 (9%)	667 (6%)	137(1%)	247(2%)

As we could see in the table above, the success rate has increase during the Covid-19 (2019-2020), though there no change in the nonsuccess outcome; however we observed an augmentation in the not evaluated case after the peak of covid in 2020

CONCLUSION: Contrary to the detection that was significantly affected by the covid-19, very few change were observed in the outcome of the TB patients in Haiti during this period; other deeper study are needed to better understand these observations

G4. INTOLERANCE TO ADVERSE EFFECTS AND LOST TO FOLLOW-UP IN THE TREATMENT OF TUBERCULOSIS IN THE HEALTH DISTRICT OF RICHARD-TOLL

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BACKGROUND: The health district of Richard-Toll in northern Senegal in West Africa has 195,000 inhabitants with166 patients including 11 patients with drug-resistant tuberculosis. With 27% of patients lost to follow-up, the objective of the study was to determine the causes.

MATERIALS AND METHODS: All patients included with the variables: age, sex, socioeconomic level, occupation, co-infection, level of knowledge about tuberculosis, degree of occurrence of side effects according to ANRS*. Data were analyzed with Rstudio software.

RESULTS: 84% of the patients had a low socio-economic level, the majority of whom were unemployed or had lost their jobs at the time of the onset of tuberculosis. 68% were in the age group (15-40) and sex ration of 0.94. Regarding the occurrence of the disease, 16% of the cohort with a good socioeconomic level and therefore a good nutritional status reported mild side effects of degrees 1 to 2, which did not prevent them from continuing the treatment. Of the 84% of patients with low socioeconomic status and deficiency malnutrition, the adverse events reported varied between grade 3 and 4 and there was more failure to comply with treatment and 98% of patients lost to follow-up with this group.

CONCLUSION: A good nutritional status would allow a better tolerance of side effects and reduce the number of patients lost to follow-up. Nutritional support for patients with low socioeconomic status should be effective.

G5. DOES LOCAL TRANSMISSION OR REACTIVATION OF REMOTE INFECTION EXPLAIN THE HIGH RATE OF TB IN FOREIGN-BORN WORKERS AT A MEAT PACKING PLANT IN ALBERTA?

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BACKGROUND: Brooks, Alberta (population 14,451 in 2016) has been identified as having an increased incidence of tuberculosis since 2013. This town has a large meatpacking plant that employs many foreign-born workers that developed active tuberculosis. We sought to understand what is driving the high rate of TB among foreign-born workers at the plant.

DESIGN/METHODS: All TB patients reported from Brooks in 2013-2021 were included. Demographic, contact tracing, and MIRU-VNTR data (all initial isolates of Mycobacterium tuberculosis in Alberta are DNA fingerprinted), was analyzed to identify secondary cases. Whole genome sequencing of MIRU-VNTR clusters is planned to further confirm transmission events.

RESULTS: There were 44 TB patients, giving an annual incidence of 34 per 100 000. Most (43/44 or 97.7%) were foreign-born; 22/44 (50.0%) worked at the meatpacking plant. One secondary case was found among two roommates, and another was found among medium-risk contacts that did not work at the plant. MIRU-VNTR typing of the 37 cultured isolates showed exact clustering only among the roommates and among 3 recent migrants who had no clear epidemiologic link, either representing false MIRU-VNTR clustering or an epidemiologic linkage not captured within our data.

CONCLUSION: The high rate of active TB in Brooks mainly represents reactivation of latent tuberculosis in the foreign born. Transmission resulting in secondary cases was limited and not linked to the meat packing plant. Efforts to reduce tuberculosis in this population should thus revolve around enhanced screening for latent tuberculosis.

G6. NONTUBERCULOUS MYCOBACTERIA: GEOGRAPHY PREDICTS PREVALENCE

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BACKGROUND: Nontuberculous mycobacteria (NTM) continue to cause increasing infections globally. However, due to scarce public health reporting, little is known about epidemiological and environmental risk factors for NTM. Virginia is one of the few states in the United States where NTM are reportable. Here, we describe the prevalence of the two major NTM groups statewide: Mycobacterium avium complex (MAC) and Mycobacterium abscessus complex (Mab).

DESIGN/METHODS: Virginia Department of Health data from 2021-2022 were obtained, including patient demographics, specimen source, and speciation. Cases were defined as any patient with at least one MAC or Mab isolate. Predictors of case rates were analyzed using regression analysis.

RESULTS: There were 519 cases identified; 455 (87.7%) were MAC and 64 (12.3%) were Mab. The statewide annualized case rate was 7.36 per 100,000 persons. Case rates were higher in the coastal plain region (9.15 per 100,000 persons) as compared to outside this region (5.28 per 100,000 persons, $p = 0.003$). However, the proportion of NTM that were Mab was similar inside and outside this region (12.1% and 12.5% respectively). In a multiple linear regression model, population density (β 2.429, 95% CI [0.148, 4.709], $p = 0.037$) and location within the coastal plain (β 3.000, 95% CI [0.519, 5.480], $p = 0.018$) were independently associated with case rate.

CONCLUSION: NTM is prevalent in Virginia, possibly due to a humid coastal region and dense urban areas. Future work should explore the impact of local environment on prevalence of individual groups and NTM overall.

G7. INVESTIGATING THE IMPACT OF CLOSING DISPARITIES IN TB INCIDENCE AND CASE FATALITY RATES ACROSS U.S.-BORN RACIAL/ETHNIC POPULATIONS IN THE UNITED STATES

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BACKGROUND: Despite advances in prevention and treatment, substantial racial/ethnic disparities exist in tuberculosis (TB) incidence and case fatality in the United States. We estimated the potential health impact of eliminating these disparities.

DESIGN/METHODS: Using National TB Surveillance System data, we estimated disparities, measured through age-specific TB incidence rate ratios (IRRs) and case-fatality ratios (CFRs) in 2019 for each U.S.-born racial/ethnic population, as compared to the non-Hispanic White population. We estimated population denominators using American Community Survey data and race-stratified life tables. We modeled TB trends over 2020–2035 for three scenarios: 1) continuation of current TB trends within each race/ethnic population (base-case); 2) elimination of IRR disparities; and 3) elimination of IRR and CFR disparities. We compared scenarios to estimate incremental TB cases and deaths prevented and quality-adjusted life years (QALYs) gained.

RESULTS: Among the non-White population under the base-case, we estimated 21,357 cases, 2,561 deaths, and 61,789 QALYs lost to TB over 2020–2035. Eliminating incidence disparities among non-White populations, we estimate 17,639 (82%; 17,639/21,357) fewer cases, 2,126 (83%; 2,126/2,561) fewer deaths, and 52,149 (84%; 52,149/61,789) QALYs gained in these populations. Eliminating incidence and case-fatality disparities among non-White populations, we estimate 2,305 (90%; 2,305/2,561) fewer deaths and 56,386 (91%; 56,386/61,789) QALYs gained. Estimated health benefits were greatest in the non-Hispanic Black population, with 9,412 cases averted, 1,470 deaths averted, and 31,722 QALYs gained with incidence and case-fatality reductions.

CONCLUSION: Eliminating U.S.-born racial/ethnic disparities in TB incidence and case fatality could avert over 80% of TB cases and 90% of TB deaths among non-White populations.

G8. CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WHO ARE INTOLERANT TO RIFAMPIN

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BACKGROUND: Rifampin forms the backbone of standard tuberculosis (TB) treatment. However, rifampin intolerance is relatively common at our tertiary referral hospital. The purpose of this study was to compare characteristics and outcomes between patients who received rifampin throughout treatment and those who were rifampin intolerant. Additionally, we described reasons for rifampin discontinuation and identified risk factors for rifampin intolerance.

DESIGN/METHODS: We conducted a retrospective cohort study of all patients with TB treated at our institution between January 2010 and August 2020. Patient demographics, clinical data, adverse events and clinical outcomes were abstracted. Rifampin intolerant patients were defined as those in whom rifampin was permanently discontinued due to adverse events; this group was compared with those who successfully received rifampin.

RESULTS: 829 patients were included in the study. 43% were female and 83% had pulmonary involvement. 76 patients (9%) were intolerant to rifampin. Patients with rifampin intolerance were significantly older (median age 67, IQR 50-77.5) compared with those who tolerated rifampin (median age 48, IQR 31-70, $p<0.0001$), and were more likely to have concurrent diabetes mellitus (37.3% of rifampin intolerant patients compared with 19% of patients who tolerated rifampin, $p<0.0001$). Of the rifampin intolerant patients, 15 (20.1%) were successfully challenged with rifabutin. Rifampin intolerance was most commonly due to transaminitis (25.3%), followed by rash (16%) and GI intolerance (8%). Median treatment duration was 274 days (IQR 160-361) in patients who tolerated rifampin, compared to 373 days (IQR 126-543, $p<0.001$) in those with rifampin intolerance. There was no difference in treatment outcomes between the two groups ($p=0.5$).

CONCLUSION: Rifampin intolerance is more common in older patients, and in those with concurrent diabetes mellitus. In patients who are intolerant to rifampin, rifabutin can often be successfully used.

G9. ACTIVE TUBERCULOSIS (TB) AND LATENT TB INFECTION (LTBI) EPIDEMIOLOGY IN ONTARIO PRIOR TO AND DURING THE FIRST TWO YEARS OF THE COVID-19 PANDEMIC: A PRELIMINARY ANALYSIS

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BACKGROUND: The impacts of the COVID-19 pandemic on TB prevention and care remain a concern in Ontario, Canada and globally. This analysis aims to describe and compare provincial TB and LTBI epidemiology in the first two years of the pandemic, compared to the pre-pandemic period.

METHODS: Active TB cases diagnosed between January 1, 2018 and December 31, 2021 were extracted from Ontario's integrated Public Health Information System. The overall incidence, days from symptom onset to diagnosis, proportion hospitalized, and proportion with a fatal outcome were calculated and compared for those diagnosed in 2018-19 versus 2020-21. The number of LTBI episodes reported, and the overall notification rate, were also determined for these two time periods.

RESULTS: The provincial incidence of active TB decreased slightly in the early pandemic period (2020-21) compared to the pre-pandemic period (2018-19), from 4.86 to 4.63 cases per 100,000 population. The difference in days from onset to diagnosis and the proportion with a fatal outcome between the two time periods were not statistically significant; however, a higher proportion of cases were hospitalized pre-pandemic (10.0%, 141/1,414) compared to during the pandemic (6.7%, 93/1,385) ($p<0.05$). The notification rate of LTBI decreased substantially during the pandemic, from 52.41 notifications per 100,000 population in 2018-19 to 28.51 in 2020-21.

CONCLUSION: This preliminary analysis helps build understanding of the potential impacts of the early phases of the COVID-19 pandemic in Ontario in 2020-21. Collaboration with public health and health system partners is needed to further characterize and address the pandemic's impacts on TB prevention and care.

G10. Tuberculosis Testing Patterns in South Africa to Identify Groups That Would Benefit From Increased Investigation: An Analysis of Laboratory Data 2012-2016

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BACKGROUND: The National Health Laboratory Service (NHLS) collects all public health laboratory test results in South Africa, providing an opportunity to identify groups, by age, sex, HIV, and viral suppression statuses, that would benefit from increased tuberculosis (TB) testing.

METHODS: Using NHLS data (2012-2016), we assessed levels and trends over time in the number of TB diagnostic tests performed (count and per capita) and TB test positivity. Estimates were stratified by age, sex, HIV status, viral suppression status, and province. We used logistic regression to estimate the odds of testing positive for TB by viral suppression status.

RESULTS: Nineteen million TB diagnostic tests were conducted 2012-2016. Testing per capita was lower among PLHIV with viral suppression than those with unsuppressed HIV (0.08 vs 0.32) but lowest among people without HIV (0.03). Test positivity was highest among young adults versus other age groups, males versus females of all age groups, and people with unsuppressed HIV. Test positivity was higher for males without laboratory evidence of HIV than those with HIV viral suppression, despite similar individual odds of TB.

CONCLUSION: Our results are an important national baseline characterizing who received TB testing in South Africa prior to the COVID-19 pandemic. People without evidence of HIV, young adults, and males would benefit from increased TB testing given their lower testing rates and higher test positivity. These findings provide a standard against which to assess changes during the COVID-19 pandemic and to guide future expansions of TB testing, which was substantially interrupted by COVID-19.

G11. EXPLORING THE RISK OF CARDIOVASCULAR DISEASE DUE TO LATENT TUBERCULOSIS INFECTION IN A LOW TUBERCULOSIS INCIDENCE SETTING: A POPULATION-BASED COHORT STUDY

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BACKGROUND: Latent tuberculosis infection (LTBI) has been associated with an increased risk of cardiovascular disease (CVD), but data is limited from low tuberculosis incidence settings. We aimed to explore the relationship between CVD and LTBI in British Columbia (BC) where ~90% of people with active tuberculosis are born outside of Canada.

DESIGN/METHODS: We developed a population-based retrospective cohort of immigrants in BC between 1985 and 2019. Approximately 62,000 participants had test results for LTBI including tuberculin skin test or interferon gamma release assay, with a median follow-up of 18 years (IQR: 12-25). The outcome was time from immigration to diagnosis with composite CVD events of heart disease or stroke. We fitted the Cox proportional hazards model, adjusting for potential confounders. Sensitivity analyses were conducted to explore the robustness of findings, including specific CVD events, dealing with competing risks and unmeasured confounding.

RESULTS: We observed an 11% higher risk of CVD in participants with LTBI (adjusted hazard ratio [aHR]: 1.11, 95% confidence interval [CI]: 1.02-1.21). Compared to the no LTBI group, the CVD risk was 21% higher if LTBI therapy was incomplete (aHR: 1.21, 95% CI: 1.07-1.36), while the risk was 4% higher if LTBI therapy was complete (aHR: 1.04, 95% CI: 0.94-1.16). Results were consistent in different sensitivity analyses.

CONCLUSION: LTBI is associated with an increased rate of CVD in a low tuberculosis incidence setting. The reduction in the rate of CVD in people completing LTBI therapy requires further investigation, but may be related to unmeasured health behaviours.