ABSTRACTS

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POSTER SESSION FACILITATORS

A. THE CHALLENGES OF DRUG-RESISTANT TB
Facilitator: Dr. Victoria Cook
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B. DIAGNOSTIC ADVANCES AND CHALLENGES IN TB CARE AND PREVENTION
Facilitator: Dr. Elizabeth Talbot
Dartmouth's Geisel School of Medicine, Hanover, NH, USA

C. EPIDEMIOLOGY OF TB TRANSMISSION AND MOLECULAR EPIDEMIOLOGY
Facilitator: Dr. Charlie Crane
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D. EPIDEMIOLOGY OF TB: PATIENTS, POPULATIONS, AND SURVEILLANCE
Facilitator: Dr. E. Jane Carter
Brown University, Providence, RI, USA

E. ENDING TB: THE DIAGNOSIS AND TREATMENT OF LATENT TB INFECTION
Facilitator: Dr. Lisa V. Adams
Dartmouth's Geisel School of Medicine, Hanover, NH, USA

F. NO LONGER NEGLECTED: ADDRESSING TB IN CHILDREN
Facilitator: Dr. Anna Mandalakas
Baylor College of Medicine, Houston, TX, USA

G. TECHNOLOGY AND mHEALTH SOLUTIONS TO TB CARE AND PREVENTION
Facilitator: Dr. Kevin Schwartzman
McGill University, Montreal, QC, Canada

ABSTRACTS FOR ORAL PRESENTATION

The Impact of Digital Health Technologies on TB Treatment Completion: A Systematic Literature Review

Dr. Dennis Falzon, World Health Organization, Geneva, Switzerland

Six Years of Monitoring TB Treatment with Video Directly Observed Therapy (DOT) in the U.S. and Mexico: How Did it Work?

Dr. Richard Garfein, University of California San Diego, La Jolla, CA, USA

Preliminary Results of National Surveillance of Childhood Tuberculosis in Canada

Dr. Ian Kitai, Hospital for Sick Children, Toronto, ON, Canada

Tuberculosis Cases and Contacts in Large, Urban North American City: Looking to Elimination

Ms. Teresa Leung, Toronto Public Health, Toronto, ON, Canada

Evaluating the Use of an Artificial Intelligence (AI) Platform on Mobile Devices to Measure and Support Tuberculosis Medication Adherence

Ms. Laura Shafner, AiCure, New York, NY, USA

Ethical Challenges in the Implementation of New Technologies: An Empirical Study of Stakeholder Perspective

Dr. Diego Silva, Simon Fraser University, Burnaby, BC, Canada

Table of Contents

A. THE CHALLENGES OF DRUG-RESISTANT TB

COMPLEX SYSTEMS: VISUALIZING MULTIDRUG-RESISTANT TUBERCULOSIS TREATMENT ADHERENCE IN A CAUSAL LOOP DIAGRAM

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BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) treatment adherence poses a complex public health challenge, due to the many important facilitators and barriers at multiple levels affecting each other over time. Interventions designed based on an incomplete understanding of this complexity are likely to fail. This paper extends prior attempts to describe adherence behaviors by presenting a broad, integrated systems diagram depicting the interactions most substantially affecting patient adherence to MDR-TB treatment.

METHODS: We engaged mixed stakeholder groups in urban Peru using System Dynamics methods to diagram the most important cause-and-effect connections determining MDR-TB treatment adherence over time. These causal loop diagrams were then validated and expanded based on a review of the scientific literature. Finally, expanded diagrams were reviewed with local stakeholders to ensure final versions continued to reflect local reality.

RESULTS: Stakeholders described that adherence was affected by adverse reactions to medications, psychosocial factors, and health care system barriers, among others. These factors vary in importance across three stages of treatment that were defined by patients. In many cases, the ripple effects triggered by treatment adherence (or nonadherence) circled back to both reinforce and undermine adherence over time ("feedback loops"). All stakeholder- diagrammed relationships were substantiated in the scientific literature. Additional relationships were added based on the literature, including financial difficulties, substance abuse, and gender effects. The final diagram had high face validity with stakeholders.

CONCLUSION: Future research is needed to validate and expand upon our initial model. However, the many feedback loops are important in shaping outcomes, and should be considered when designing intervention.

PSYCHOSOCIAL CHALLENGES OF MULTI-DRUG RESISTANCE TUBERCULOSIS PATIENTS AT ST. PETER TB SPECIALIZED HOSPITAL IN ADDIS ABABA

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BACKGROUND: Multidrug-Resistant Tuberculosis is a leading cause of high rates of morbidity and mortality, and increasing psychosocial challenges to patients, especially when co-infected with (HIV) in Ethiopia.

METHODS: A cross-sectional study was conducted at St. Peter TB Specialized Hospital, on 40 patients (25 males and 15 females) who are hospitalized for treatment. The patients were identified by using purposive sampling and made fill a questionnaire measuring their level of self-esteem, depression and stigma. Besides, data were collected from 16 participants, 8 care providers and 8 guardians, using semi-structured interview. The obtained data were analyzed using SPSS statistical program, descriptive statistics, and qualitative description.

RESULTS: (80%) of the respondents had suffered psychological challenges and social discriminations. (60%) of participants showed low level of self-esteem. The patients also reported that they experienced high self-stigma and stigma by other members of the society. The majority of the participants (75%) showed moderate and severe level of depression. In terms of sex there is no difference between the males and females in the level of depression and stigmatization by others and by themselves. But females showed lower level of self-esteem than males.

CONCLUSION: High level of depression, low level of self-esteem, stigmatization from by members of the community and self-stigmatization are highly encountered. There is no difference between male and female their level of depression and stigma due to sex. Patients encountered various psychological, social and medical problems during and after treatments.

EPIDEMIOLOGY, DRUG RESISTANCE AND OUTCOMES IN PREVIOUSLY TREATED TUBERCULOSIS PATIENTS WITH AND WITHOUT HIV AT THE KORLE-BU TEACHING HOSPITAL CHEST CLINIC IN ACCRA, GHANA

Bouton TC[1], Forson A[3,4], Kudzawu S[4], Kwara A[2]. [1]Alpert Medical School of Brown University, Providence, RI; [2]University of Florida College of Medicine, Gainesville, FL, USA; [3]University of Ghana School of Medicine and Dentistry; [4]Korle-Bu Teaching Hospital, Accra, Ghana.

BACKGROUND: Ghana has been identified by the WHO as one of the countries with the most severe burden of incidence rates per capita of HIV and TB co-infection. Like many countries, Ghana continues to rely heavily on the standardized five-drug Category II regimen for previously treated TB patients. With higher recurrence rates of tuberculosis in those with HIV co-infection, in addition to increased mortality, identifying modifiable risk factors for recurrence is especially important.

METHODS: A retrospective review of all patients with previously-treated TB diagnosed between 1/2010 and 7/2015 at Korle-Bu Teaching Hospital Chest Clinic in Accra, Ghana. Descriptive statistics were used to compare characteristics between those with HIV and those without.

RESULTS: HIV status was known at initiation of therapy in 94.35% of tuberculosis retreatment cases, of whom 23.9% were HIV positive. Overall mortality in this tuberculosis retreatment population was 19.25%, however in those with HIV it was 29.3%. Pan susceptible tuberculosis was found in 28.5% of HIV negative patients with available drug susceptibility testing, compared at least single drug resistance in 100% of isolates from HIV patients that were tested.

CONCLUSION: Testing rates for HIV in those undergoing retreatment for tuberculosis were high, however in those with HIV and TB co-infection mortality and resistance were also high. With especially poor outcomes and increased TB resistance seen in the HIV/TB coinfection population, our study serves to further highlight the importance of drug susceptibility driven, individualized regimens in these retreatment patients.

ISONIAZID-MONORESISTANCE AMONG TUBERCULOSIS PATIENTS, NATIONAL TUBERCULOSIS SURVEILLANCE SYSTEM — UNITED STATES, 1993–2014

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BACKGROUND: Isoniazid (INH) has been used for tuberculosis (TB) treatment for many years, but INH-monoresistance remains a persistent challenge in the United States (U.S.).

METHODS: We conducted multivariate analyses of the CDC National Tuberculosis Surveillance System from 1993–2014 and included culture-positive cases with initial drug susceptibility test (DST) results reported by 50 U.S. states or District of Columbia. We defined INH-monoresistance as culture-confirmed TB cases with resistance to INH and susceptibility to rifampin, pyrazinamide, and ethambutol. We excluded drug- susceptible cases that acquired drug resistance during therapy.

RESULTS: Of the 182,757 culture-confirmed cases, 8,133 (4.5%) were INH-monoresistant. Patients with INH- monoresistance had greater odds of being Asian (adjusted odds ratio [aOR] = 1.8; 95% confidence interval [CI]: 1.6–2.0]), non-Hispanic black (aOR = 1.2; 95% CI: 1.1–1.3), a correctional facility resident (aOR = 1.6; 95% CI: 1.3–1.8), having a previous TB diagnosis (aOR = 1.5; 95% CI: 1.3–1.7), or being foreign-born (aOR = 1.2; 95% CI: 1.1–1.3). INH monoresistance was associated with patients not completing therapy within one year (aOR = 2.0; 95% CI: 1.8–2.2), dying before or during therapy (aOR = 2.5; 95% CI: 2.0–3.1), being uncooperative or refusing treatment (aOR = 1.6; 95% CI: 1.1–2.4), or being lost to follow-up (aOR = 1.5; 95% CI: 1.2–1.9).

CONCLUSIONS: Treatment outcomes and individual patient characteristics may be contributing factors for the continued challenge of INH-monoresitant cases. This report highlights completion of therapy to ensure the reduction of TB drug resistance development.

IDENTIFICATION AND VALIDATION OF NEW MECHANISMS OF ISONIAZID RESISTANCE IN MYCOBACTERIUM TUBERCULOSIS

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BACKGROUND: Globally, ~14% of all tuberculosis (TB) cases are isoniazid (INH)-resistant, and ~10-12% of INH resistance is unexplained. The validation of novel INH resistance mechanisms can enhance the accuracy of rapid molecular tests for INH resistance including those for detection of both INH and rifampin resistance (i.e., multidrug resistance).

METHODS: We identified 13 M. tuberculosis clinical isolates from archived samples that were previously classified as INH resistant (INHR) by phenotypic testing but lacked mutations commonly associated with INH resistance. The MIC for INH was determined using a microdilution assay and whole genome sequencing (WGS) was performed to identify mutations associated with INH resistance.

RESULTS: Four strains were susceptible to INH while most exhibited low-level (4/13) or high-level (5/13) resistance. We identified numerous distinct mutations in the INH resistance-associated loci katG, ahpC, ahpD, fabG1, and fabG3 (but none in furA, inhA, or Rv1910c). One high-level INHR strain did not harbor mutations in any aforementioned loci. We performed functional genetics to determine if the katG V1A mutation confers resistance to INH. We confirmed the mutation was successfully introduced into the pansusceptible strain H37Rv by Sanger sequencing and found that it does indeed confer INH resistance.

CONCLUSION: A mutation discovered by WGS (katG V1A) was shown by functional genetics to confer INH resistance. Additional analyses will be conducted to determine the contribution of other mutations identified for INH resistance. Examination of isolates with unknown mechanisms of resistance by WGS could aid assay development by identifying novel resistance markers.

TEMPORAL DISTRIBUTION OF ACQUIRED RESISTANCE TO FLUOROQUINOLONES DURING TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS AND CHARACTERISTICS ASSOCIATED WITH EARLY ACQUISITION OF RESISTANCE TO FLUOROQUINOLONES

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BACKGROUND: We recently demonstrated acquired resistance (AR) to fluoroquinolones (FQ) in approximately 10% of multidrug-resistant tuberculosis (MDR-TB) patients during treatment. We sought to determine how fast such resistance emerged.

METHODS: Adults treated for MDR-TB with confirmed AR to FQ had baseline and serial monthly sputum cultures tested for susceptibility to FQ by the agar proportion method at CDC to identify the first isolate to be FQ- resistant. We classified AR in the first six months as "early" and after six months as "late," analyzing bivariate associations with clinical characteristics.

RESULTS: Fifty-nine patients acquired resistance to FQ in a median of three months (range 1–24; IQR 2–6), 45 (76%) in the first six months. Compared with patients with late AR, patients with early AR more often had four or fewer drugs tested locally for susceptibility (68.9% vs 42.9%, P=0.0039), more drug resistance at baseline when all drugs were tested at CDC (medians 8.0 vs 4.5, P=0.0008), and less DOT (9% vs 0% with no DOT, P=0.037). For comparison, among 489 patients with no AR to FQ, 36.2% had four or fewer drugs tested locally for susceptibility, 7.4% had no DOT, and the median number of drugs resistant at baseline was 4.0.

CONCLUSION: Three-fourths of acquired FQ resistance emerged within 6 months of beginning treatment. Characteristics associated with early AR to FQ in PETTS included number of drugs tested locally, extent of other drug resistance and DOT.

COMPORTAMIENTO DE LA DROGO RESISTENCIA EN MYCOBACTERIUM TUBERCULOSIS. CUBA, 2011 - 2015

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BACKGROUND: La resistencia desarrollada por Mycobacterium tuberculosis a las drogas constituye uno de los principales obstáculos en el control de la tuberculosis a nivel mundial. Por tanto, la realización sistemática de la vigilancia de la resistencia a drogas antituberculosas permite alertar oportunamente el hallazgo de aislamientos portadores de resistencia. El objetivo del presente estudio es describir el comportamiento de la resistencia a las drogas antituberculosas en los aislados de M. tuberculosis recuperados de pacientes con tuberculosis pulmonar en Cuba en el quinquenio 2011 - 2015.

METHODS: Se realizó un estudio prospectivo longitudinal. Se investigó la susceptibilidad de 1683 aislados de M. tuberculosis frente a isoniacida y rifampicina empleando el método de la nitrato reductasa. A los aislamientos multidrogorresistentes se les estudió la susceptibilidad a las drogas de segunda línea mediante el método proporcional y se les investigó el mecanismo molecular de resistencia.

RESULTS: Del total de aislados estudiados, 1412 pertenecían a casos nuevos y 271 a pacientes previamente tratados. El 95,5% de los aislamientos recuperados de casos nuevos fueron sensibles a isoniacida y rifampicina; en esta categoría de caso se detectaron 24 aislados con resistencia a rifampicina de los cuáles diez (0,7%) se revelaron como multidrogorresistentes. En cuanto a los aislamientos de pacientes previamente tratados, el
83,8% fue sensible a isoniacida y rifampicina y en 18 (6,6%) se detectó un comportamiento multidrogorresistente. En tres aislados de pacientes previamente tratados se identificó un comportamiento extremadamente resistente.

CONCLUSION: Se corrobora una baja prevalencia de aislamientos de M. tuberculosis multidrogorresistentes en Cuba.

ROUTINE NUTRITION SUPPLEMENT FOR MARGINALIZED POOR DRTB PATIENTS INCREASED TREATMENT ADHERENCE IN TWO POVERTY-STRICKEN DISTRICTS OF CHHATTISGARH STATE, INDIA

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BACKGROUND: Malnutrition and tuberculosis are the major concerns of underdeveloped regions of the world including India. The weight loss and waste caused during clinical course of TB & DRTB development with its associated complications further compromise the cachectic state.

With nearly half of its 28 million populations living below the poverty line, more than a fifth of them in every district live in extreme poverty with lowest Human Development Index in Chhattisgarh. Undernutrition and lower BMI with wasting among most of the diagnosed DRTB patients in vulnerable Rajnandgaon and Bilaspur districts critically hampered treatment adherence.

METHODS: With mobilization of local self-government funds by the program, 76 DRTB patients were provided nutritional food supplement in Rajnandgaon & Bilaspur districts during 2014-15. Enriched with energy, protein and micronutrient ingredients, monthly food boxes prepared and packed by accredited vendors, was given to the DRTB patients by local DOT providers. Treatment follow-up, counselling, weight and BMI monitoring was ensured.

RESULTS: 39 patients got cured and 21 competed treatment successfully. A marked improvement of ≥80% treatment adherence with 83% follow-up sputum tested Negative recorded. A cohort shows success of ≥78% with ≥51% Cure, ≤ 3% Death and 2% Default as recorded in 2012-13 against outcome of 28%, 20% and 25% respectively. A prospective plan is developed to serve all such cases in the state.

CONCLUSION: Addition of nutrition support can make an enormous difference to lives and livelihoods of poor DRTB patients by successfully curing them. Poverty and food insecurity being the key causes and consequences of poor adherence among most DRTB patients, it is essential that all such patients are linked to systematic planning for effective management of DRTB.

OUTCOMES AND COSTS OF MULTIDRUG-RESISTANT TUBERCULOSIS OUTPATIENT-ONLY CARE IN THE UNITED STATES

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BACKGROUND: Recent analyses of U.S. multidrug-resistant TB treatment practices and outcomes have not focused on patients treated only in outpatient settings.

METHODS: Of a population-based sample of 135 multidrug-resistant TB patients reported to CDC during 2005–2007, we describe characteristics and outcomes for 37 patients treated only in outpatient settings versus those with some inpatient care. We report odds ratios (OR) and multivariate logistic regression ORs (aOR) with 95% confidence intervals (CI) and costs in 2015 dollars.

RESULTS: Compared with patients having some inpatient care, patients aged 15-24 had greater odds of outpatient-only treatment than patients aged ≥ 25 (OR=2.8, CI=1.1-6.9). None with HIV, end-stage-renal disease, or cancer, and one diabetic had outpatient-only care. Patients with acid-fast-bacilli sputum smear-positive (OR=.24, CI=.10-.56), cavitary (OR=.26, CI=.11-.64), multilobe (OR=.19, CI=.08-.46), or miliary (0%) disease had lower odds of outpatient-only treatment. There was no significant association between sputum culture conversion or drug resistance and outpatient-only care. None of the 12 patients who died during treatment or two who experienced serious adverse reactions resulting in treatment discontinuation were treated in outpatient settings only. Excluding patients who died, there were no significant differences in treatment completion of outpatient-only and hospitalized patients (OR=0.57, CI=0.20-1.64), with outpatient-only treatment completion averaging $104,000 (median $79,000) versus $210,000 (median $167,000) for patients with some inpatient care.

CONCLUSION: U.S. multidrug-resistant TB patients treated entirely in outpatient settings were younger, had fewer comorbidities, and were less likely to die. They successfully completed treatment at half the cost as those with some inpatient care.

A COMPARISON OF METHODS TO ASSESS AND CLASSIFY DR-TB TREATMENT ADHERENCE

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BACKGROUND: Drug-resistant tuberculosis (DR-TB) treatment outcomes are impacted by the extent to which patients adhere to medications. There is controversy about how adherence should be defined and measured. The aim of this study was to assess the differences among three measures, and compare different cut-points for defining adherence.

METHODS: We used data from a cross-sectional study with 263 adults diagnosed with DR-TB and 86 of their healthcare service providers in Peru. Adherence was measured using three methods: adherence rate (percentage of prescribed dosages taken, reported in treatment logs), provider- reported categories (defined by the percentage of prescribed dosages taken), and patient- reported SMAQ (simplified medication adherence questionnaire). Agreement among measures were evaluated using Fisher's exact tests and Spearman's correlation coefficient rho. Correlation coefficients were compared by patient characteristic using Fisher's Z transformations. Different measures and cut-points for defining adherence were evaluated with logit regressions.

RESULTS: At a 90% cut-point, percentage of adherent patients was 64% using adherence rate, 56% with adherence categories, and 37% with SMAQ. We found a statistically significant relationship among the three measures (Fisher's exact p=0.000, Spearman's rho=0.35-0.58 with Prob>|t|=0.000). Adherence rate and adherence category had stronger relationships than either against SMAQ. Patient characteristics associated with adherence differed between 80% and 90% cut-points; both showed statistically significant associations with previous lost-to- follow-up and TB type.

CONCLUSION: Our evidence suggests that how we measure and define adherence could affect how we approach DR-TB treatment adherence barriers. Further research is needed to validate TB-specific adherence measures and prevent poor treatment outcomes before they occur.

Notes:

Include: Adults (18-65) with DR-TB – confirmed with microbiological test results or receiving prescribed treatment scheme for drug-resistance.

Exclude: patients whose adherence data in the 2 calendar-months prior to data collection is not complete (LTFU or people in treatment for less than 2 calendar-months)

SURVEILLANCE FOR BEDAQUILINE RESISTANCE IN MULTIDRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS (MDR TB) ISOLATES OBTAINED FROM TUBERCULOSIS PATIENTS IN THE UNITED STATES: 2015-2016

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BACKGROUND: The United States CDC has issued interim guidance for the use of bedaquiline (BDQ) in combination therapy for MDR TB. Two proposed mechanisms for reduced susceptibility of *M. tuberculosis* to BDQ are target-based resistance via the *atpE* gene, and efflux-based resistance via *Rv0678*.

METHODS: We determined BDQ minimal inhibitory concentrations (MICs) by broth microdilution of MDR TB isolates from US patients, regardless of BDQ treatment status, from June 2015 to June 2016. Isolates were evaluated for mutations in *Rv0678* and *atpE* by Sanger sequencing.

RESULTS: 112 MDR TB isolates (98 unique patients) were analyzed. MICs ranged from ≤0.008 - 0.5µg/ml; 99 isolates (88.4%) had MICs ≤0.06 µg/ml. Five isolates (4 patients) had elevated (≥0.25µg/ml) MICs. *Rv0678* was successfully amplified and sequenced in 103/112 isolates; 7 had either an insertion (2/7) or nonsynonymous substitution (5/7) mutation. Three of the 5 isolates with substitutions had elevated (0.25µg/ml) MICs. To our knowledge, the observed mutations have not been previously reported. In 68/112 isolates, *atpE* was successfully amplified; all were wild type. The 2 isolates with the highest MICs (0.5µg/ml; both from one patient) had no mutation in *atpE* or in *Rv0678*.

CONCLUSION: Most isolates tested were susceptible to BDQ (MIC ≤0.06µg/ml), while 5 (4.5%) had an MIC ≥0.25µg/ml. The clinical significance of the mutations identified is unknown. The mechanism of decreased BDQ susceptibility in the 2 isolates with MIC=0.5µg/ml is likely independent of the genes investigated. Molecular analysis of other implicated genes and optimization of our current assays may yield further insights into BDQ resistance mechanisms.

THE IMPACT OF ISONIAZID AND PYRAZINAMIDE MONO-RESISTANCE ON MORTALITY AMONG TUBERCULOSIS PATIENTS IN LOS ANGELES COUNTY, 2010-2014

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BACKGROUND: Isoniazid and pyrazinamide mono-resistant tuberculosis (TB) may be associated with poor treatment outcomes, but previous studies have found conflicting results. We assessed the impact of isoniazid (INH) and pyrazinamide (PZA) mono-resistance on mortality during TB treatment in Los Angeles County.

METHODS: We retrospectively reviewed drug susceptibility test (DST) patterns and treatment outcomes among TB cases reported to the Los Angeles County Tuberculosis Control Program from 2010 to 2014. All culture- confirmed TB cases with available DST results and an outcome of death or treatment completion were included. Multiple logistic regression was used to determine the association between INH or PZA mono- resistance and death while controlling for patient characteristics and use of directly observed therapy (DOT).

RESULTS: Of 2,346 TB patients included in the analysis, 163 (6.9%) had INH mono-resistance, 125 (5.3%) had PZA mono-resistance and 1,997 (85.1%) had drug-susceptible TB. During treatment, 24 (14.7%) INH mono- resistant, 25 (20.0%) PZA mono-resistant, and 214 (10.7%) drug-susceptible TB cases died. In the multiple logistic regression model adjusting for age, sex, race, non-injection illicit drug use, alcohol, immunosuppressive medication, underlying disease, HIV status, history of TB and use of DOT, patients with INH or PZA mono-resistance had higher odds of death than patients with drug-susceptible TB (odds ratio [OR] 2.01, 95% confidence interval [CI] 1.17, 3.45; and OR 2.90, 95% CI 1.65, 5.10, respectively).

CONCLUSION: Patients with INH and PZA mono-resistance were more likely to die than patients with drug-susceptible TB. Efforts are needed to improve treatment outcomes for INH and PZA mono-resistant TB patients.

B. DIAGNOSTIC ADVANCES AND CHALLENGES IN TB CARE AND PREVENTION

A PICTURE PAINTS A THOUSAND WORDS: FACILITATING THE VOICE OF INDIVIDUALS DIAGNOSED WITH TUBERCULOSIS (TB) IN TORONTO AND BARCELONA THROUGH PHOTOVOICE

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BACKGROUND: Photovoice is a participatory action research method that uses photography as a means for understanding and giving voice to the experiences of study participants. The resulting "photo novellas" have been used to support advocacy, and program planning for marginalized communities. An initial study was conducted in Toronto and then replicated in Barcelona utilizing identical methodology. The purpose of both studies was to provide an opportunity for individuals with tuberculosis (TB) to share their experiences through photos supported by written text. By sharing these images and text, we aim to increase the understanding and awareness of TB and improve services in Toronto and Barcelona.

METHODS: Participants were recruited by TB staff using pre-determined criteria. The majority of participants aged 18 -70, were born in TB endemic countries outside of Canada and Spain. Digital cameras and orientation were given to nine adults in Toronto and sixteen adults in Barcelona.

RESULTS: A total of 138 photographs with accompanying text were submitted. Through qualitative analysis, the images/texts were categorized into themes. The resulting themes of challenges, isolation, stigma, new beginnings and coping mechanisms were found in both Barcelona and Toronto. These themes were consistent despite differences in demographics and settings, contributing to the evidence that photovoice can be beneficial to TB programs globally.

CONCLUSION: The projects offered a creative and viable platform for individuals diagnosed with TB to express and share their experiences. Results from these studies will inform program planning, and the images/text shared on multiple platforms.

HEALTH SEEKING BEHAVIOURS ASSOCIATED WITH TUBERCULOSIS DIAGNOSTIC DELAY IN LIMA, PERU

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BACKGROUND: Early detection and diagnosis of tuberculosis (TB) is a global priority. Studies suggest that patients experience cough for several weeks prior to diagnosis, increasing periods of infectiousness. We aimed to determine behavioural factors associated with diagnostic delays among TB patients living in Lima, Peru.

METHODS: Data was collected from 105 TB patients being treated at public health facilities using a semi- structured interview guide in 19 districts of Lima in 2015. Behavioural factors associated with diagnostic delays were analysed using negative binomial regression.

RESULTS: The median number of days between symptom onset and the first positive diagnostic sample in public health facilities was 57 (interquartile range (IQR): 28-126). TB patients were significantly more likely to first self-medicate or use natural medicines than to visit formal health facilities (p=0.003) when they began to experience TB symptoms. The median number of visits to formal health facilities until the first positive diagnostic sample was collected was 2 (IQR: 2-3). Patients who first sought care at a private health facility had more visits to formal health facilities prior to diagnosis than those who first sought care from public or employer-insured health facilities (median 3 versus 2; Mann-Whitney test: p=0.02). Furthermore, seeking care at private health facilities had a positive effect on diagnostic delays in multivariable analysis adjusted for age and sex (p=0.05).

CONCLUSION: Diagnostic delay is prolonged and influenced by the type of care sought by individuals at symptom onset. TB case finding initiatives should target informal and private health facilities, where many TB patients first seek healthcare.

INTER-LABORATORY VARIABILITY AND UTILIZATION OF THE INTERFERON GAMMA RELEASE ASSAY IN SCREENING FOR LATENT TUBERCULOSIS INFECTION AT AN ACADEMIC MEDICAL CENTER: A RETROSPECTIVE REVIEW

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BACKGROUND: Previous studies have demonstrated a large number of pre-analytical factors which impact the results of QuantiFERON-TB Gold In-Tube (QFT-GIT) assay results and lead to variability. At Lifespan, the QFT-GIT was recently transitioned from Quest Laboratories to in-house testing. We sought to evaluate utilization of the test amongst various groups of providers in our hospital system and to evaluate for inter-laboratory variability following the transition.

METHODS: At our tertiary care referral center, the first three months of available in house QFT-GIT results were compared with the same three months in 2015 as well as a three-month summer period tested at Quest to evaluate for inter-laboratory variability and seasonal variability. Further review was completed to gain a better understanding of utilization of the test amongst the various subspecialty groups and to identify patient groups more likely to have indeterminate results.

RESULTS: The greatest percent of QFT-GITs were ordered by rheumatology at 22%. The other specialty areas with a high percent of tests ordered included internal medicine (13%), inpatient providers (13%), the TB clinic (12%) and the infectious disease clinic (10%). Notably, 25.4% of inpatient tests were indeterminate. Of QFT-GITs performed at the in-house lab, 4.8% were indeterminate compared to 6.4% performed at the Quest lab.

CONCLUSIONS: There was minimal inter-laboratory variability following the transition of the QFT-GIT from Quest to Lifespan. More work should be done to identify areas in our system that contribute to variability amongst tests and to identify specific groups that may be at increased risk of indeterminate results.

POST 2015: BARRIERS TO CARE ACCESS AND PROMPT TB DIAGNOSIS, A CROSS SECTIONAL STUDY

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BACKGROUND: Malawi is a low-income country with heavy Tuberculosis (TB) burden. TB is one of the top ten killer diseases in Malawi and a cause for public health concern. Although there is notable progress in TB control, diagnosis delay is a major problem which may result in higher tuberculosis infection rates and increased disease burden in the communities. Supported by Chinese government scholarship, the investigators developed the study mainly based on Chinese experience. Study aimed to investigate factors for diagnostic delay in the Northern region of Malawi.

METHODS: Cross sectional study using questionnaire interviews was conducted among 254 sputum positive TB patients in the northern region of Malawi. Statistical Package for Social Sciences (SPSS) version 16 was utilized in data analysis. Descriptive and analytical analysis was done to describe the study participants and to investigate the risk factors associated with patient delay.

RESULTS: The study revealed that it took 22 days in median for patients to arrive at a health facility for TB care from the onset of symptoms. Patients in debt status were at risk for delay; (adjusted odds ratio 9.17; 95 % CI 2.88 -29.17). Other risk factors for patient delay were lack of knowledge on TB, distance and waiting time at the care facility (adjusted odds ratios: 17.19,17.74, and 2.99 respectively with statistical significance).

CONCLUSION: Several factors influenced TB diagnosis delay. Population based studies to address knowledge gaps and improve awareness on significance of early diagnosis are needed. Addressing barriers in care access are critical in TB control.

HIGH-RESOLUTION PLASMA METABOLOMICS AND PUTATIVE MYCOBACTERIUM TUBERCULOSIS CELL WALL-DERIVED BIOMARKERS TO DISTINGUISH ACTIVE PULMONARY TUBERCULOSIS

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BACKGROUND: There are no peripheral blood biomarkers to reliably diagnose active tuberculosis (TB) disease. Using high-resolution metabolomics (HRM), we targeted *Mycobacterium tuberculosis (Mtb)* cell wall metabolites in plasma of patients with active TB disease to evaluate potential utility as diagnostic biomarkers.

METHODS: HRM analysis was performed on plasma from 17 active TB cases with a positive sputum smear for acid fast bacilli (AFB) and a positive sputum culture for *Mtb*, as well as 16 asymptomatic household controls with a negative AFB sputum culture. Detected metabolites were tested for accurate mass matches to previously described *Mtb* lipids. Metabolites were then tested for association with disease status using linear models for microarray data, fold- change analysis and classification accuracy. Selected metabolites were evaluated in an additional 56 patients with active TB disease.

RESULTS: For the 32,975 metabolites detected by HRM, 867 metabolites matched to previously characterized *Mtb* cell wall-derived lipids. Using a differential expression analysis, we identified four *Mtb* metabolites elevated in patients with active TB relative to household controls providing excellent classification accuracy (AUC of 0.95) for active TB. These included monoacyl-glycerophosphoinositol (Lyso-PI), monoacylated diacylglycerophosphoinositol-monomannoside (Ac1PIM1), diacylglycero-phosphoglycerol (PG) and monoacylglycerophosphoinositol-monomannoside (Lyso-PIM1) (each $p<0.001$ active TB vs household contacts). In an independent set of 56 active TB cases, at least one of the four metabolites was detected in all patients and at least two were detected in 47 patients (84%).

CONCLUSION: *Mtb*-derived cell wall lipid metabolites (Lyso-PI, Ac1PIM1, PG and Lyso-PIM1) may represent a plasma metabolomic signature that identifies active TB disease.

TUBERCULOSIS DIAGNOSTIC AND TREATMENT AVAILABILITY IN 14 HIGHEST BURDEN COUNTRIES

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BACKGROUND: Early diagnosis and rapid treatment initiation are critical for tuberculosis (TB). This requires delivery of tuberculosis care services where most patients seek initial care. In most countries, National Tuberculosis Programs are expected to have basic TB diagnosis at the primary care level. However, there is little published information on where exactly latent tuberculosis and multi-drug resistant tuberculosis (MDR-TB) diagnostic and treatment services are available in the highest burden countries.

METHODS: We addressed this gap by surveying local TB experts about key diagnostics and treatments in 14 countries that have been identified by WHO as having the highest burden of tuberculosis cases, MDR- TB, and HIV/TB co-infection.

RESULTS: Few countries have any tuberculosis diagnostic or treatment services available at lowest level, L0. Most countries have chest radiology available at or above L2 (district hospitals, 13/14, 93%) while smear microscopy is available starting at L1 (microscopy centers, 14/14, 100%). Drug susceptibility testing is mainly available at the tertiary (L3) level, with most countries having at least some capacity at L2 (11/14, 79%). Latent tuberculosis testing is mainly available at L2 (10/14, 71%) and above.

CONCLUSIONS: Our analysis shows that while most countries have invested in basic TB diagnosis (i.e. smears) and drug-sensitive TB treatment services at the L1 level and higher, availability of MDR and LTBI testing and therapy is quite limited at the decentralized levels.

As countries work towards universal health coverage, it is critical not only to strengthen TB services, but also to ensure greater integration with primary health care.

DIAGNOSTIC AND THERAPEUTIC CHALLENGES FOR DE NOVO MILIARY AND EXTRAPULMONARY TB IN A PATIENT ON ANTI-TNF THERAPY

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BACKGROUND: Anti-TNF-α therapies have made a significant impact on inflammatory disorders. However, TNF- α plays a central role in maintaining TB latency and patients on these therapies are often susceptible to difficult to recognize, rapidly progressing tuberculosis with serious and potentially fatal outcomes.

METHODS/RESULTS: A 30-year-old Philippine male (immigrated at age 7) with history of psoriasis on Humira® and methotrexate presented with night sweats, chills, dry cough, and spiking fever for two weeks. Earlier TB screening via γ-IFN release assay was negative. CXR was negative, however, CT scan showed multiple tiny pulmonary nodules associated with mediastinal and right paratracheal lymphadenopathy, hepatosplenomegaly and areas of hypodensity throughout the spleen, suspicious for coalescent granulomas. The differential diagnosis included miliary TB, FUO, fungal pneumonia and atypical pneumonia. Three sets of acid-fast bacilli sputum smears were negative. HIV Elisa, urine legionella antigen, hepatitis serology, basic autoimmune work-up, blood, stool and urine cultures were all unremarkable. Transbronchial biopsy results showed no malignancy or granuloma. BM biopsy showed scattered histiocytes within the interstitium, and special stains were negative of AFB and fungi. Based on the patient's endemic background and clinical diagnosis, he was started on empirical treatment for miliary TB. Therapy was complicated with elevated transaminases requiring discontinuation of TB therapy with outpatient follow up. The patient was persistently febrile and a new CT chest now revealed an enlargement of supraclavicular lymph nodes. Biopsy showed necrotizing granulomatous lymphoadenitis, and AFB stain for mycobacteria was positive. Once LFTs normalized, the patient was started on RIPE+B6 in a stepwise fashion with close LFT monitoring.

CONCLUSION: Detailed history and risk assessment for LTBI is crucial for patients prior to consideration of biological therapies. Despite negative screening tests for TB infection, treatment may be warranted as reactivation of TB may have potentially deleterious outcomes in these patients.

USING REDUCED MYCOBACTERIUM TUBERCULOSIS INOCULUM DENSITIES IN MGIT PYRAZINAMIDE SUSCEPTIBILITY TESTING TO PREVENT FALSE-RESISTANT RESULTS AND IMPROVE ACCURACY: A MULTI- CENTER EVALUATION

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BACKGROUND: The primary platform used for pyrazinamide (PZA) susceptibility testing of Mycobacterium tuberculosis is the MGIT culture system (Becton Dickinson). False-resistant results have been associated with the use of this system. We conducted a multi-center evaluation to determine the effect of using a reduced cell density inoculum on the rate of false-resistance.

METHODS: Two reduced inoculum densities were compared with that prescribed by the manufacturer (designated as "BD" method). The reduced inoculum methods (designated "A" and "C") were identical to the manufacturer's protocol in all aspects with the exception of the cell density of the inoculum. Twenty M. tuberculosis isolates, whose pncA gene had been sequenced and PZA Minimal Inhibitory Concentration determined, were tested in duplicate by nine independent laboratories using the three inoculum methods.

RESULTS: False-resistant results declined from 64 (21.1%) using the standard "BD" method to 17 (5.7%) using the intermediate ("A") inoculum and further declined to 8 (2.8%) using the most dilute ("C") inoculum method. The accuracy of the test results improved from 78.3% for the "BD" inoculum method to 90.5% and 94.1%, using the "A" and "C" methods, respectively. The percentages of resistant results that were false-resistant declined from 55.2% for the "BD" test to 28.8% and 16.0% for the "A" and "C" tests, respectively. Both test accuracy and precision were markedly improved using the two reduced cell density methods.

CONCLUSION: These results represent compelling evidence that the occurrence of false-resistant MGIT PZA susceptibility test results can be mitigated through the use of reduced inoculum densities.

FAST IMPLEMENTATION IN BANGLADESH: RESULTS AND LESSONS LEARNED.

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BACKGROUND: Bangladesh is one of 22 high tuberculosis (TB) burden countries. TB transmission in health-care facilities is driven by a large number of undiagnosed TB cases. FAST (Find cases Actively, Separate temporarily and Treat effectively) is an administrative TB transmission control strategy. We describe the results and challenges involved with the implementation of FAST as a TB transmission control strategy in Bangladesh.

METHODS: All patients admitted due to respiratory symptoms or with a history of lung disease to the three designated FAST hospital sites underwent Xpert MTB/RIF testing for pulmonary TB. FAST educational materials were developed and training sessions for physicians, nurses and laboratory technicians were held. Staff were assigned to discrete roles: cough monitoring, sputum specimen collection and delivery to the laboratory and result delivery to clinical providers.

RESULTS: 744/6710 (10.9%) patients who underwent Xpert MTB/RIF testing as part of FAST were diagnosed with unsuspected TB and 89/6710 (1.3%) were diagnosed with unsuspected MDR-TB. 245/1112 (22%) of patients admitted due to other lung diseases who had a prior history of TB were diagnosed with unsuspected TB. 31/682 (4.5%) of patients admitted with a known diagnosis of TB were found to have unsuspected MDR- TB. Major challenges for FAST implementation include staff shortages, diagnostic failure and supply-chain issues, simplifying reporting and reliance on external funding.

CONCLUSION: Although FAST implementation is resource intensive, it is feasible and revealed high rates of unsuspected TB in hospitals in Bangladesh. Ensuring key stakeholder engagement and laboratory capacity are important for sustainability and scalability.

THE POSSIBLE ASSOCIATION OF INTERLEUKIN-10 HIGH LEVEL IN PLASMA AND RECURRENT TUBERCULOSIS

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BACKGROUND: Interleukin-10 (IL-10) is one of the most important anti-inflammatory cytokines reported to suppress the protective immune response against tuberculosis. The present study aimed to assess the association between interleukin-10 and recurrent tuberculosis risk.

METHODS: The study was conducted at "Leo Daniello" Pneumology Hospital in Cluj Napoca, Romania. Twenty four patients with active pulmonary TB attending the hospital were included. The protocol for this study was approved by the Ethics Committee of Iuliu Hatieganu University of Medicine and written informed consent was signed by each patient. Venous blood samples were collected from patients before starting anti-tuberculosis treatment (ATT), after 3 months of ATT and after 6 months of ATT. Blood samples were directly centrifuged at 1000 x g for 15 minutes and then plasma were collected and stored at -20 °C until use. The plasma levels of IL-10 were quantified using a sandwich enzyme immunoassay kit according to the manufacturer's protocol. Of the 24 patients, 21 were available for re- evaluation 30 months after the end of treatment. All data were analyzed using GraphPad Prism version 5.0.

RESULTS: The results showed that Interleukin-10 levels in plasma of 24 tuberculosis patients at the end of treatment were correlated to recurrent TB rates. IL-10 level decreased until the end of treatment (ATT6) in 18 cases (Pattern 1) whereas it remained significantly higher in 6 cases (Pattern 2) even at the end of treatment. Follow-up of 30 months was performed in 21 cases; 7 had recurrence of TB, of which 5/6 had Pattern 2 and 1/15 Pattern 1. Other interesting results of our study is that the patients with abnormal chest X-Ray findings had higher IL-10 levels when compared to patients with normal X-Rays ($p=0.03$).

CONCLUSION: Other previous studies suggest that in tuberculosis, over expressed IL-10 during the chronic phase of the infection showed evidence of reactivation of tuberculosis with a highly significant increase in bacterial numbers within the lungs. These findings could be used in follow-up as clinical biomarker of the success of tuberculosis therapy.

DIAGNOSING TUBERCULOSIS IN HOSPITALIZED HIV-INFECTED INDIVIDUALS WHO CANNOT PRODUCE SPUTUM: IS URINE LIPOARABINOMANNAN TESTING THE ANSWER?

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BACKGROUND: Current diagnostic tests for pulmonary tuberculosis rely on generation of a sputum sample, but up to one third of HIV-positive individuals with suspected TB are unable to produce sputum.

METHODS: This study represents a post hoc sub-group analysis of data from a randomized, multi- center study. The study population consisted of hospitalized HIV-positive patients with suspected TB who were unable to produce sputum and who underwent urine testing with Alere Determine™ TB LAM Ag lateral flow strip test. The diagnostic utility of urine LAM for TB in this group was compared to the performance of urine LAM in patients who produced a sputum sample in the parent study.

RESULTS: There were a total of 187 patients in the "sputum scarce" cohort. In comparison to those who produced sputum, these patients had a younger age, a lower Karnofsky performance score, and a lower weight/BMI at admission. A greater proportion of sputum scarce patients were urine LAM positive, compared to those who produced sputum (31% vs. 21%, p=0.04). A higher proportion of sputum scarce patients died within 8 weeks of admission (32% vs. 24%, p=0.013). We estimate that 19% of HIV-positive, sputum scarce patients suspected of TB are correctly diagnosed with tuberculosis with the use of urine LAM testing, with a positive predictive value estimated at 63% (95% CI 43-82%).

CONCLUSION: Urine LAM testing can effectively identify tuberculosis in HIV-positive patients who are unable to generate a sputum sample for diagnostic testing.

RISK FACTORS ASSOCIATED WITH DIAGNOSIS DELAY OF PULMONARY TUBERCULOSIS IN INDIGENOUS PEOPLES ON THE PRAIRIES

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BACKGROUND: Despite the overall decline in tuberculosis (TB) incidence in Canada, rates among Indigenous peoples have not decreased since the late 1990s. On-going transmission associated with diagnosis delay has been identified as a major contributor to the persistence of TB in Indigenous communities. This study aims to estimate the duration of diagnosis delay and to identify its risk factors among Indigenous peoples on the prairies.

METHODS: Data was obtained from the Determinants of TB Transmission project, a seven-year (2006-2013) cohort study that described the epidemiology of pulmonary TB Canadian-born cases in Alberta, Saskatchewan, and Manitoba. Diagnosis delay was defined as the time from the onset of cough to the date of TB diagnosis defined as the start date of treatment. Descriptive statistics and logistic regression were used to identify risk factors associated with diagnosis delay.

RESULTS: One-hundred and fifty cases diagnosed in 2007 and 2008 were examined. The median diagnosis delay was 30 days (IQR: 3.5-60). Risk factors independently associated with longer diagnosis delay included having a household of less than six people (AOR: 2.54, 95% CI: 1.14-5.68) and a non-Indigenous mother tongue (AOR: 2.55, 95% CI: 1.01-6.50). Residing in a community with a working x-ray machine and technician was associated with shorter delay (AOR: 0.27: 95% CI: 0.11–0.63).

CONCLUSION: The reduction of diagnosis delay can potentially help mitigate transmission from TB cases. This study represents one of few studies investigating risk factors for diagnosis delay among Indigenous peoples in Canada.

C. EPIDEMIOLOGY OF TB TRANSMISSION AND MOLECULAR EPIDEMIOLOGY

A POPULATION BASED STUDY OF TRANSMISSION EVENTS ATTRIBUTABLE TO IMMIGRATION MEDICAL SURVEILLANCE REFERRALS VERSUS NON-REFERRALS IN CANADA

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BACKGROUND: In Alberta, foreign-born individuals accounted for ~90% of all TB cases in 2015. Programmatic activity to prevent these cases occurs within the national TB Medical Surveillance Program. We compared TB transmission resulting from "referrals" to the program versus "non- referrals".

METHODS: Foreign-born adults diagnosed with culture-positive pulmonary TB in Alberta between 2004-2013 were categorized as "referrals" or "non-referrals" and their contact lists assembled. The primary outcome was a transmission event (TST conversion or secondary case) among their contacts. Secondary cases were temporally linked contacts, and if culture-positive, had a TB isolate with an identical DNA fingerprint. Logistic regression analyses adjusted for clinical and sociodemographic variables.

RESULTS: 318 source cases (78 referral vs 240 non-referral) had a total of 4784 contacts. Referrals were in Canada for a shorter time (11 vs 29 months), had fewer contacts (3.5 vs 6), and were less likely to have cavitary (6% v 34%), smear-positive (22% vs 54%), or disseminated (0 vs 6%) disease. Referrals (6/78) were less likely than non-referrals to transmit (51/240), adjusted OR 0.290, 95% CI [0.115-0.730], p=0.0086. Fewer referrals (1/78) resulted in a secondary case vs non-referrals (12/240), though the difference was not statistically significant, p=0.18. 88% of all transmissions and 100% of secondary cases were attributable to source cases from sub-Saharan Africa or a country whose TB incidence was >150/100,000

CONCLUSION: Referrals were less likely to transmit. The surveillance system may be identifying cases earlier or surveilling TB phenotypes with lower transmission potential. To decrease transmission, we could target arrivals from countries with a TB incidence > 150/100,000.

PRIORITIZING TUBERCULOSIS GENOTYPE CLUSTERS FOR PUBLIC HEALTH ACTION IN THE UNITED STATES

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BACKGROUND: In the United States, 96% of all culture-positive tuberculosis (TB) cases are genotyped with spoligotyping and 24-locus MIRU-VNTR, and linked to case-based surveillance records within the TB Genotyping Information Management System (TB GIMS). When there is an unexpected concentration of genotype-matched cases in a county within a 3-year period, a log-likelihood ratio (LLR) statistic generates a high (LLR≥10) or medium (LLR=5–<10) alert. These alerts initiate TB GIMS email notifications, prompting a cluster assessment.

METHODS: CDC officials systematically assess cluster notifications each week to prioritize clusters for public health action; when patient characteristics suggest recent TB transmission, clusters are designated "Priority 1" (i.e., higher priority). We assessed differences in the proportions of cases with risk factors for transmission by priority level.

RESULTS: From January 1, 2015 to July 31, 2016, TB GIMS generated 89 (21%) high and 340 (79%) medium level alerts. Over half (58%) of the high alerts and one-quarter (25%) of medium alerts were assigned Priority 1. Patients in 138 higher priority clusters were more likely than patients in 291 lower priority clusters to be African Americans (39% vs. 30%), substance users (37% vs.
30%), incarcerated (7% vs. 3%), and to have TB with isoniazid resistance (8% vs. 3%), respectively.

CONCLUSIONS: A systematic cluster assessment process helps prioritize clusters that may warrant public health action. CDC has national guidance on genotype cluster assessment and prioritization forthcoming to empower frontline TB program staff to interpret and focus public health resources to interrupt TB transmission.

MOLECULAR EPIDEMIOLOGY OF TUBERCULOSIS IN BRITISH COLUMBIA, CANADA – A 10-YEAR RETROSPECTIVE STUDY

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BACKGROUND: Given the significant public health resources required for treatment, follow-up and contact tracing, it is important to understand the regional epidemiology of TB. Contributing greatly to this understanding has been genotyping of *Mycobacterium tuberculosis* (*Mtb*) using molecular methods – most commonly 24-locus Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats (24MIRU). Genotyping has significantly enhanced traditional contact tracing efforts and is a valuable tool for outbreak identification, surveillance and phylogenetic examination of TB.

METHODS: A total of 2,318 clinical *Mtb* isolates collected in British Columbia (BC), representing
99.5% of all culture-positive cases diagnosed from 2005 through 2014, were genotyped by 24MIRU. Genotyping results were combined with clinical and demographic information from BC's integrated Public Health Information System (iPHIS) to describe the molecular epidemiology of tuberculosis across the province.

RESULTS: 24MIRU analysis revealed 1,509 different genotypes, and identified 189 clusters (2–70 cases/cluster) with an overall clustering rate of 42.7%. Canadian-born individuals had increased odds of belonging to a genotype cluster compared to foreign-born individuals (OR 7.7, 95%CI: 6.2–9.7). Examining cluster composition, we found 15.5% of clusters were comprised exclusively of Canadian-born cases, 52.9% exclusively foreign-born cases, and 23.0% had both Canadian- and foreign-born individuals (8.6% contained ≥1 case of unknown origin).

CONCLUSIONS: While the high strain diversity detected indicates that many of BC's TB cases are likely due to reactivation of latent infections, there remain several pockets of endemic transmission in the province. Understanding how, where, and when transmission is occurring in BC will improve TB control efforts and permit effective allocation of resources.

EDUCATIONAL OPPORTUNITIES FOR MYCOBACTERIOLOGY TESTING PRACTICES

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BACKGROUND: Laboratorians within public health, clinical and reference laboratories performing mycobacteriology testing must be knowledgeable of biosafety requirements, growth-based and molecular testing methods, and interpretation of results. Limited continuing education opportunities exist for individuals new to testing or those needing refresher training.

INTERVENTION/RESPONSE: To address the need, Centers for Disease Control (CDC) and Association of Public Health Laboratories (APHL) developed an online curriculum for laboratorians. The curriculum was developed over three years and includes free modules on Laboratory Safety, Specimen Collection, Transport, Handling and Processing, AFB Smear Microscopy, Mycobacterial Culture, Identification, and Drug Susceptibility Testing of *Mycobacterium tuberculosis* complex (MTBC), Molecular Biology 101, Molecular Detection and Identification of Mycobacteria, and Molecular Detection of Drug Resistance in MTBC. The eleven modules are available as self-paced interactive learning and slides in PDF format for reference or group based trainings.

RESULTS: The modules are posted at aphl.org with usage monitored quarterly per module using Google Analytics. Interactive modules have been viewed 5,011 times, slide only format 5,175 times, and slides with notes 421 (added February 2016) times, respectively. Average total number of views per month is 80.

CONCLUSION: As more experienced staff near or reach retirement, maintaining technical proficiency in mycobacteriology testing becomes more difficult. This curriculum provides a resource for laboratorians to learn or review mycobacteriology testing practices at their own pace or within a group atmosphere. Maintaining a comprehensive and efficient laboratory system including a proficient workforce is critical to the overall prevention and control of tuberculosis in the United States.

THE EFFICIENCY OF MODERN METHODS OF DIAGNOSIS AND EPIDEMIOLOGICAL SURVEILLANCE OF DRUG-RESISTANT FORMS OF TUBERCULOSIS

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BACKGROUND: Tuberculosis (TB) is a significant global public health threat. In 2013, 9 million people fell ill with TB and 1.5 million people died from the disease – including 360,000 people coinfected with HIV. Globally in 2013, an estimated 480,000 people developed multidrug-resistant TB (MDR-TB), with extensively drug-resistant TB (XDR-TB) reported by 100 countries. There is slow progress in tackling drugresistant TB – 3 in 4 drug-resistant TB cases remain without a diagnosis, and only 97,000 patients were started on MDR-TB treatment last year. Between 2000 and 2013, an estimated 37 million lives have been saved through TB diagnosis and treatment.

METHODS: The studies were conducted in National Reference laboratory of the Republican specialized scientific-practical center of Phthisiology and Pulmonology in Tashkent. In research was used different types of materials such as: sputum, urine, surgical specimens and others collected from 354 patients. Males amounted to 213 (60%) and 141 women (40%). For the detection of Mycobacterium tuberculosis and drug resistance used polymerase chain reaction real-time (Xpert MTB/RIF).

RESULTS: From all the studies 354 patients, 113 cases (40%) showed TB positive results. Resistance to anti-TB drug rifampicin was observed in 38 patients, which amounted to (30%), a sensitivity of 75 patients (60%) and sensitivity is not determined in 12 patients (10%). The study has revealed that from among the identified positive results by PCR in the amount of 113 patients, 50 patients result microscopy showed a negative result.

CONCLUSION: Carried out modern methods of diagnostics (Xpert MTB/RIF) substantially reduces the time of the study, which verified the diagnosis of TB in 2 hours and reduces the formation of infectious aerosols into the environment compared to the culture method, which gives the opportunity to reduce the risk of infection of laboratory personnel.
Timely and quality diagnosis allows you to get information about the actual disease burden in the region, which can to improve treatment and implementation of preventive measures, including the task of ensuring infection control in health care institutions.

TUBERCULOSIS CASES AND CONTACTS IN A LARGE, URBAN NORTH AMERICAN CITY: LOOKING TO ELIMINATION

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BACKGROUND: To support our efforts toward the elimination of tuberculosis (TB), we examined the current epidemiology and clinical characteristics of pulmonary TB cases and their contacts in Toronto, Canada, a large urban centre where foreign-born residents account for half the population.

METHODS: Data were extracted from an electronic reporting database and contact line lists for pulmonary TB cases reported in Toronto from June 1, 2007 to May 31, 2012 and their respective contacts.

RESULTS: There were 960 pulmonary cases during this period, representing 64.9% of all TB cases in Toronto. The mean age at diagnosis was 47.1 years (range <1 to 99 years); 56.6% were male. The majority of cases (92.1%) were foreign-born. Over half (53.0%) of pulmonary cases were smear negative; eighteen percent had cavitary chest x-rays. Most cases (88.3%) were fully sensitive; 2.0% were multi-drug resistant. A total of 6,927 contacts were identified, averaging 7.2 contacts per case. The tuberculin skin test positivity rate was 43.0% overall (64.1% among foreign-born contacts). The proportion of converters and secondary cases was 4.9% and 0.8%, respectively; most were among household contacts.

CONCLUSION: As the majority of TB cases in Toronto were foreign-born and limited endemic transmission was observed, this suggests that local epidemiology is largely driven by global TB patterns.

TUBERCULOSIS TRANSMISSION IN OUTDOOR SMOKING AREAS: ASK THE QUESTION

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BACKGROUND: Strong interviewing techniques are essential to effective tuberculosis contact tracing. Tuberculosis exposure outdoors is thought to be low risk. We describe two investigations where asking "who is there when you smoke?" rather than "who do you smoke with?" would have discovered outdoor transmission within smoking groups.

RESULTS: The index case in the first cluster was smear 4+, cavitary and symptomatic. He worked in a retirement home kitchen and reported being a smoker who took breaks alone. Two subsequent genotypically-linked cases were diagnosed among workers in the same facility but different departments; neither were identified as contacts during the index case's follow-up. Further investigation showed that all three cases smoked together in the same outdoor smoking area.

The index case in the second cluster was smear 4+, cavitary and symptomatic. He had a history of shelter use and reported being a smoker but denied having regular smoking companions. Four years later, two genotypically identical cases were diagnosed who had not been identified as contacts of the index case. However, both could be placed in the same shelter during part of the index case's infectivity period. All three cases were heavy smokers who smoked in the same outdoor smoking area.

CONCLUSION: In both clusters, tuberculosis transmission leading to secondary cases occurred in outdoor smoking areas. The index cases did not view those in the same outdoor smoking area as social contacts at risk of acquiring tuberculosis, demonstrating the importance of asking the right questions for early identification and follow-up of contacts and secondary cases.

RISK FACTORS FOR RECENT TRANSMISSION OF TUBERCULOSIS AMONG FOREIGN- BORN PERSONS IN THE UNITED STATES, 2011–2015

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BACKGROUND: Homelessness, substance use, and incarceration are established risk factors for recent transmission (RT) of tuberculosis (TB) among U.S.-born patients but have not been well studied among foreign-born patients. We determined if these marginalizing conditions were associated with RT among foreign-born TB patients and assessed whether the associations differed between U.S.- and foreign-born patients.

METHODS: We estimated RT among cases with spoligotyping and 24-locus MIRU-VNTR genotyping results reported to the U.S. National TB Surveillance System during 2011–2015 using a field-validated, plausible source-case approach to classify TB attributable to RT. We used log-binomial regression to evaluate associations between RT and each condition by estimating adjusted prevalence ratio (aPR) and 95% confidence interval (CI), controlling for age and race/ethnicity.

RESULTS: Of the 35,020 TB cases in the analysis, 5,001 (14%) were attributable to RT, including 1,801 of 23,111 (8%) foreign-born cases. Among foreign-born patients, RT was positively associated with homelessness (aPR=1.7; 95% CI=1.4, 2.0), excessive alcohol use (aPR=1.5; 95% CI=1.3, 1.8), and illicit drug use (aPR=1.4; 95% CI=1.1, 1.7); RT was negatively associated with incarceration at diagnosis (aPR=0.4; 95% CI=0.3, 0.6). Aside from incarceration at diagnosis, which was not associated with RT among U.S.-born patients (aPR=1.0; 95% CI=0.9, 1.1), the associations did not differ meaningfully by nationality.

CONCLUSION: Improved strategies that target persons with marginalizing conditions are needed to control recent TB transmission regardless of nationality. Nationality-specific differences in the association between RT and incarceration should be explored further.

A COMPARISON OF METHODS FOR DETECTING TUBERCULOSIS TRANSMISSION — UNITED STATES, 2014–2015

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BACKGROUND: A log-likelihood ratio (LLR) statistic is used nationally to identify unexpected concentrations of genotype-matched tuberculosis (TB) cases within a county during a 3-year period. By comparison, a recently published field-validated plausible source-case method identifies genotype- matched cases that are attributable to recent transmission (RT).

METHODS: We evaluated TB cases reported to the National TB Surveillance System and identified LLR clusters that alerted during January 2014–September 2015. Clusters were categorized as "no alert" (LLR<5), "medium alerts" (LLR≥5 and <10), and "high alerts" (LLR≥10). We calculated the proportions of cases attributable to RT at each alert level and compared characteristics of patients in alerts by RT status using a χ^2 test.

RESULTS: Among 34,564 cases analyzed, 1,255 (4%) were in an LLR alert, and 4,949 (14%) were attributable to RT. Of all cases, 12% (4,154/33,309) of those identified in a no alert, 54% (449/828) in a medium alert, and 81% (346/427) in a high alert cluster were attributable to RT. Among cases identified in a medium or high alert, cases attributable to RT were more likely to be U.S.-born than foreign-born (75% vs. 63%, $p<.0001$). No other differences in demographic or social risk factors were detected.

CONCLUSION: The proportion of cases attributable to RT increased by alert level, supporting the use of LLR and plausible source-case methods for identifying TB transmission. Integrated use of methods to identify cases likely resulting from RT may allow TB programs to focus interventions on interrupting transmission at patient- and population-levels.

TUBERCULOSIS WHOLE GENOME SEQUENCING REPORT DESIGN STUDY

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BACKGROUND: Whole genome sequencing (WGS) of tuberculosis (TB) isolates accelerates TB diagnosis and the selection of appropriate treatment regimens. As part of the COMPASS-TB project, a collaboration between Public Health England (PHE) and the BC Centre for Disease Control to implement WGS in routine lab practice, we used formal information visualization methodologies to develop a simplified, intuitive report that clearly communicates genomic test results to the clinician.

METHODS: Expert consultation informed an inventory of tasks related to clinical and public health TB management. An online survey was administered to clinicians and public health professionals characterizing familiarity with WGS data and how this new data type could support management tasks. These results informed the design of eight prototype TB-WGS reports during a collaborative session with information visualization researchers. We are currently surveying our user group to evaluate their preferences amongst these prototypes.

RESULTS: In our first survey, seventeen responses were collected over one week. Participants predominantly reported involvement in clinical management (10/17) and worked in the UK (15/17). The genome-derived data most often used for clinical management included speciation, predicted drug sensitivity, and resistotype.

CONCLUSION: The next steps in the study will provide insight into users' design preference, informing the development of a finalized report that will support interpretation of complicated data and abide by standard reporting requirements and that will be used in PHE's new genomic pipeline for TB diagnosis.

A GENOTYPIC AND EPIDEMIOLOGIC ANALYSIS OF MASSACHUSETTS' MYCOBACTERIUM TUBERCULOSIS CASES FROM 2012-2015

Vindenes T[1], Jordan MR[1,2], Tibbs A[3], Stopka T[2], Johnson D[2], Cochran J[3]. [1]Tufts Medical Center; [2]Tufts University School of Medicine, Boston, MA; [3]Massachusetts Department of Public Health, Boston, MA, USA.

BACKGROUND: Massachusetts (MA) had an incidence rate 2.8 cases of tuberculosis (TB) per 100,000 individuals in 2015; although, TB in MA is on the decline, it's incidence remains far above the National TB Target for 2020 of 1.4 per 100 000. To reduce the TB incidence rate in MA, it is necessary to understand the local epidemiology of its transmission. This study generated a genotypic and epidemiologic analysis of Massachusetts TB cases from 2012-2015 and identified and described TB clusters in MA.

METHODS: This study used an existing TB case database which links de-identified patient demographic information with TB genotypes obtained from the CDC's TB Genotyping Information Management System database. Two or more cases with identical genotypes, which were close in space (within 50 kilometers) and time (3 years), were considered TB clusters.

RESULTS: 543/577 cases were genotyped. A total of 85 cases met the TB cluster criteria and a total of 32 clusters were identified. U.S-born individuals (p=0.003), homeless individuals (p=0.001) and those reporting illicit substance use (p=0.001) and alcohol use (p=0.001) were more likely to be in a TB cluster.

CONCLUSION: The identification of marginalized individuals more likely being in a TB cluster, highlights the overall public health approach required to combat TB. Findings from this study suggest that a public health approach including the testing of marginalized populations in MA for TB and providing cases with appropriate treatment may decrease overall TB incidence and support the State in achieving national 2020 TB targets.

THE MYSTIFYING APPEARANCE OF LATENT TUBERCULOSIS INFECTION

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BACKGROUND: This ethnographic research study focused on latent tuberculosis infection (LTBI) among Burmese Chin refugees who reside in the United States. Burma is one of the 22 high TB burden countries. In 2009, Burma was in the top three countries for notification of suspected LTBI per the CDC's Electronic Disease Notification system. The purpose of this study was to discover the Burmese Chin explanatory model (EM) of LTBI.

METHODS: Recruitment occurred in a Burmese Chin refugees' neighborhood in Phoenix, Arizona, a Refugee Women's Health Clinic, and community refugee events. Data were collected using participant observation, field notes, and semi-structured interviews. Data saturation was reached with eight participants. 15 participant interviews were analyzed using domain analysis, taxonomic analysis, and componential analysis.

RESULTS: Four main categories were derived guided by Kleinman's EM of Illness (1980): What is it?, How did I get it?, What do I call it?, and Expectations of treatment. The refugees' EM of LTBI revealed the definition of the illness, transmission, how it is named, and how it is treated. Responses varied in beliefs of how LTBI was acquired and transmitted. A language gap was revealed in how LTBI is named. Treatment was not fully comprehended during the medication regimen.

CONCLUSION: New knowledge of the EM of LTBI can help to inform culturally tailored interventions for Burmese refugees. Recommendations are to identify cultural navigators to achieve successful delivery of LTBI education and assist in TB program development. Future research includes an interdisciplinary intervention to deliver culturally relevant education and management of LTBI treatment.

CREATING A STANDARDIZED GENOMIC EPIDEMIOLOGY PIPELINE FOR TUBERCULOSIS IN CANADA - CHALLENGES AND OPPORTUNITIES

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BACKGROUND: Tuberculosis is a global pandemic with unequal distribution along lines of poverty. Programs depend on a robust understanding of microenvironments where transmission occurs. A macro perspective is critical given that disease is also driven by migration. Despite a growing global commitment to the use and sharing of public health data, specifically digitized genomics data, implementation is challenging. Contextual information is often lacking and its use may have ethical or privacy implications. Real-time monitoring is complicated by lack of standardization and inadequate metadata. Translating metadata to end-users is limited. Ontologies provide a framework for integrating data. Ontologies are well-defined, standardized vocabularies interconnected by logical relationships facilitating queries, increasing interoperability between systems, integrating isolated databases and resolving semantic ambiguity. Uptake of genomic epidemiology ontology could contribute positively to TB elimination in Canada. Statement of Hypothesis: Currently used contextual information descriptors are highly variable.

METHODS: The National Center for Biotechnology Information Sequence Read Archive (NCBI SRA) was searched using terms: "Tuberculosis" and "Canada."

RESULTS: A total of 471 genetic sequences from Canada were found. Submitters were from BC, Manitoba, Ontario and Quebec. Significant variability was observed with respect to the granularity of data and use of standardized language.

CONCLUSION: Available genomics data for TB in Canada is subject to significant variability with respect to deposited contextual information - highlighting the needs for standardized data reporting. Our findings will play a key role in shaping the development of improved ontologies and data standards critical for data integration and effective TB genomic epidemiology.

D. EPIDEMIOLOGY OF TB: PATIENTS, POPULATIONS, AND SURVEILLANCE

KNOWLEDGE OF TUBERCULOSIS AMONG 6109 PATIENTS IN A NGO-SUPPORTED DOTS PROGRAM IN INDIA

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BACKGROUND: Improving patient knowledge of tuberculosis (TB) is a salient component of TB control strategies. Patient knowledge of TB encourages infection prevention and improves treatment adherence. The aims of this study were to assess the rate and identify predictors of patient TB knowledge before and after directly observed treatment (DOTS).

METHODS: A matched patient-counsellor dataset comprising 6,109 TB patients undergoing DOTS with support from the NGO OpASHA was collected in nine Indian cities from March 2013 to September 2014. At the beginning and end of DOTS, patients were asked about their knowledge of TB symptoms, transmission and treatment.

RESULTS: Patients beginning DOTS (n=3,467) answered 55.0% (54.4%, 55.6%) of knowledge questions correctly. For individual questions, 52.5% (50.8%, 54.2%) knew that cough was a symptom of TB, 67.2% (65.6%, 68.7%) knew that TB was communicable, and 87.3% (86.1%, 88.4%) knew that medication should be continued even when symptoms subside. Patients at the end of DOTS (n=4,693) answered 59.4% (58.9%, 59.9%) of knowledge questions correctly. At entry into DOTS, patient knowledge was significantly predicted by demographic information including literacy, employment, family history of TB, and education.

CONCLUSIONS: The overall knowledge of TB among TB patients is moderate and improves only slightly over the course of the treatment. Some of the key facts about TB (e.g. length of treatment), are being conveyed efficiently to patients, while others (e.g. common TB symptoms) are not. Reinforcing communication on vital information for patients is critical to improving outcomes.

CASE STUDY KANANGA, RDC: CHALLENGES AFTER TESTING AN EPIDEMIC IN URBAN

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BACKGROUND: Kananga, a town with 1061 million inhabitants in West Kasai, faces a tuberculosis (TB) epidemic among illicit drug users and the homeless that began during the beginning of this century. Since May 2006, a portable radiographic screening program was implemented for the management of the epidemic in 2011, which resulted in a decrease in the annual number of TB cases reported among those groups at risk. DNA showed reduction of transmission between these populations (published in 2013).

METHODS: Description of TB trends, the recent transmission, efficiency and return on assets case detection during a study period.

RESULTS: Comparing May 2006-2011 (during epidemics and post-hatching) the annual average of reported TB cases among illegal drug users and homeless people decreased 19.5 representing 12.6% against 4.7% in the number total TB cases in Kananga. The proportion of TB cases attributable to recent transmission reduced by 80% in 2006 to 45% in 2011 at the outbreak management and average post-hatching of 38% management.

CONCLUSIONS: Screening for TB among illicit drug users and the homeless in Kananga and social interventions such as supportive housing projects and small-scale detoxification, have had a significant impact on TB incidence and recent transmission among these groups risks.

CORRELATION POSITIVITY OF NONTUBERCULOUS MYCOBACTERIA (NTM) AND SEVERITY PULMONARY TUBERCULOSIS PATIENTS

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BACKGROUND: The research aims to detect correlation between Non tuberculous Mycobacteria and the severity of pulmonary Tuberculosis patients and to find out what spesies of NTM is detected in patients with pulmonary TB.

METHOD: This study was conducted 40 isolat Mycobacteria at laboratory Clinical Microbiology Soetomo Hospital, Surabaya Indonesia, from patient TB .Colonies were then examined using immunochromatographic antigen MPT 64, then a molecular test was performed using PCR and sequencing.

RESULTS: The result showed from 40 samples were used, 20 isolat were NTM and 20 M.tuberculosis complex. Sequencing of 20 samples were positive by PCR 116SrRNA, and detected Mycobacterium kansasii (30%), Mycobacterium gordonae (5%), Mycobacterium parascrofulaceum (2,5%), Mycobacterium simiae (2,5%) Mycobacterium avium (2,5%), Mycobacterium terrae(2,5%). Clinical severity by Bandim TB score from patients medical record showed a significant correlation between positivity of NTM detection and the severity among Tuberculosis patients , with p value =0,03.

CONCLUSION: This finding suggest that NTM infection detection is correlated with disease severity of pulmonary TB.

SEVERE ADVERSE EVENTS (HOSPITALIZATION OR DEATH) ASSOCIATED WITH TREATMENT FOR LATENT TUBERCULOSIS INFECTION, UNITED STATES, JANUARY 2004–AUGUST 2016

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BACKGROUND: Treatment for latent tuberculosis infection (LTBI) is key to eliminating tuberculosis (TB) in the United States. Isoniazid (INH) has been the primary LTBI treatment for many years. In 2011 CDC recommended another option for LTBI treatment: 3 months of INH and rifapentine (RPT) or 4 months of rifampin (RIF). Although rare, severe adverse events (SAEs) (hospitalization or death) have been associated with LTBI treatment.

METHODS: In 2004, CDC initiated the National Surveillance for Severe Adverse Events (NSSAE) Associated with Treatment for LTBI. An SAE was defined as a drug-associated reaction occurring after ≥1 LTBI treatment dose resulting in hospitalization or death. CDC conducted comprehensive onsite reviews of SAEs upon invitation by medical providers through their health departments. We analyzed NSSAE reports from January 2004–August 2016.

RESULTS: Health departments reported 66 SAEs among recipients of INH-only (n=44), INH-RPT (n=20), RIF (n=1) and INH/Levofloxacin (n=1) for LTBI. Among INH-only recipients, seven died; five, including one child, underwent liver transplantation. Among INH-RPT, RIF, and INH/Levofloxacin recipients, length of hospitalization ranged 1–20 (median: 3) days; no liver transplants or deaths were reported. The RIF recipient had an acute kidney injury but recovered after three hemodialysis treatments.

CONCLUSION: Liver failure and death can occur among INH recipients. Medical providers should be vigilant about SAEs associated with any LTBI treatment. Patients should stop medication and seek medical attention promptly at onset of any adverse sign or symptom. To capture all LTBI-treatment- associated SAEs, providers should continue to report SAEs through health departments (email: LTBIdrugevents@cdc.gov).

INSIGHT TOWARDS TB ELIMINATION FROM WASHINGTON STATE

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BACKGROUND: While effective, current overseas TB screening applies to a small fraction of all persons entering the US. Expanding overseas screening and enhancing post-immigration follow-up may reduce TB burden among high-risk populations, bringing further progress towards TB elimination. To better target such efforts, this study analyzed foreign-born (FB) persons diagnosed with pulmonary TB in Washington State (WA).

METHODS: Cases of pulmonary TB diagnosed among FB persons in WA from 2009 through 2014 were stratified by overseas screening status based on visa type. Cases were described and compared across strata on key demographics, time from arrival to diagnosis, select TB risks, and technical instructions (TIs) governing TB screening at time of immigration.

RESULTS: On average the full cohort of 661 cases were diagnosed at 47.7 years of age, 12.8 years following arrival. The majority (54.3%) received overseas TB screening, while 22.8% did not. Differences among strata included age at diagnosis, and time from arrival to diagnosis. Overall, the majority (76.9%) immigrated to the US before introduction of TIs using culture and directly-observed therapy. Of the 151 persons not screened, most (53.6%) entered the US with no official immigration status or under US visa waiver.

CONCLUSION: Experience in WA suggests expanding overseas screening to nonimmigrant risk groups may reduce the burden of TB in the US FB population. Additional gains are possible through enhanced domestic screening and treatment among FB persons entering the US without benefit of overseas screening. Domestic TB screening among high-risk FB persons should be considered irrespective of years since arrival.

COMPREHENSIVE CARE FOR HIV/TB COINFECTION IN A MEXICAN BORDER CITY: PROYECTO CuVIT

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BACKGROUND: In Mexico, tuberculosis is the leading cause of death among persons with HIV (PWHIV) and Baja California has the highest HIV/TB mortality rate of the country. Given that Mexico universally vaccinates newborns with BCG, which causes false-positive tuberculin skin test results, prevalence of M. tuberculosis (Mtb) infection among PWHIV is unknown. This study provides the first estimates of Mtb infection and demonstrates the viability of routine TB testing in HIV clinics of Tijuana, Mexico.

METHODS: We conducted a cross-sectional study in 2015. Participants aged > 18 years, diagnosed with HIV < 6 months prior and CD4+ count >100 cell/mm3 were eligible for the study. Participants completed a survey and serologic testing using interferon-gamma release assay (IGRA) for Mtb. Multivariable logistic regression model was performed to identify factors associated with Mtb infection.

RESULTS: Among 92 participants enrolled, mean age was 31.7 (SD= 9.8), most were male (n=70; 77%) and 17% (n=15) reported using drugs in the last 6 months. Prevalence of Mtb infection was 34% (n=33). The final multivariate model, Mtb infection was independently associated with having >500 CD4+ cell/mm3 count [Adjusted Odds Ratio (AOR)=10.12, 95% Confidence Interval (CI)=1.72-59.4], having full or part-time job (AOR= 0.22, 95% CI= 0.06-0.76), and using methamphetamine (AOR=21.25, 95% CI=1.83-245.54).

CONCLUSION: The study found that one-third of newly diagnosed PWHIV had Mtb infection. These findings suggest that routine TB screening in HIV/AIDS clinics should be implemented, as a way to identify and treat, and offer preventive treatment for persons at high risk for TB.

EVALUATION OF THE CEPHEID HIV-1 VIRAL LOAD ASSAY IN INDIA

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BACKGROUND: Viral load (VL) is the preferred ART monitoring approach for HIV-positive patients. However, more affordable, technologically simpler assays are needed. The Xpert HIV-1 Viral Load assay (Cepheid, Sunnyvale) is a new, automated molecular test, and can leverage the GeneXpert systems that are widely being used for TB. We assessed the correlation between the VLs obtained from Xpert in comparison to a current reference standard – the COBAS TaqMan HIV-1 assay.

METHODS: Known HIV-positive adults receiving care at Attavar Hospital in Mangalore, India were enrolled into the study between July and September 2016, irrespective of ART status. Patient plasma was used to run the Xpert VL assay at Kasturba Medical College, Mangalore, while samples were shipped to a reference laboratory in Mumbai for the TaqMan assay.

RESULTS: To date, 158 samples have been collected and included in the study. Of those, 137 returned valid results by both Xpert and TaqMan. Of those 137 results, 46 had quantifiable VLs. The HIV-RNA values quantified by both assays were highly correlated (Pearson r = 0.9926 (95% CI 0.9865, 0.9959)). Of the total Xpert assays performed, 14% were invalid/errors, primarily because of a suboptimal cartridge lot. Turn-around-time was less than one day for Xpert compared to 7-10 days for TaqMan.

CONCLUSION: Our study showed Xpert performed extremely well in comparison to the TaqMan assay, and greatly reduced time to results. However, our results show a higher than expected invalid/failure rate for Xpert. Further work is necessary to improve the supply chain for and quality of Xpert cartridges in India.

ESTIMATES OF ACTIVE TUBERCULOSIS AND LATENT TUBERCULOSIS INFECTION AMONG FOREIGN- BORN UNDOCUMENTED PERSONS IN THE UNITED STATES, 2014

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BACKGROUND: Of the 9,412 tuberculosis (TB) patients in the U.S. in 2014, 66% were foreign-born. Foreign-born persons without legal authorization for U.S. residence (undocumented) comprise approximately 3.4% of the population, and may be both medically underserved and at risk for TB. We estimated the number of undocumented persons with active TB and latent TB infection (LTBI) in the U.S. and California in 2014 to inform TB prevention efforts in this vulnerable population.

METHODS: We estimated the number of undocumented persons with TB by applying 2014 country-of-origin-specific TB rates to 2014 estimates of the undocumented population from the Center for Migration Studies (1). Country-of-origin- specific TB rates were calculated using reported TB cases from CDC and denominators from the American Community Survey, 2014. For LTBI estimates, LTBI prevalence by race/ethnicity in the foreign-born population, published from NHANES 2011-2012 (2), were applied to the undocumented population estimates in 2014.

RESULTS: There were an estimated 1,455 undocumented persons with TB (15% of all TB patients; 23% of foreign-born TB patients) and 1,766,252 (14% of 13 million) with LTBI in the U.S. in 2014. In California, there were 326 undocumented persons with TB disease. Of the estimated 2.4 million persons with LTBI in California, 427,316 (18%) were undocumented.

CONCLUSION: A substantial number of persons at risk for TB in the U.S. and California may be undocumented and thus medically underserved and without health insurance. Public health programs should develop strategies to prevent TB and ensure rapid TB diagnosis and treatment among undocumented persons.

KNOWLEDGE OF HAITIAN DIABETICS ABOUT TUBERCULOSIS

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BACKGROUND: Haiti has the highest TB incidence in America, and diabetes is also one of the most prevalent non communicable diseases affecting the Haitians. While the link between diabetes and TB is well established, very little is known about Haitian diabetic patients' knowledge of TB; a disease that represents a permanent risk for their health. The objective of this survey was to increase diabetic patients' awareness about TB.

METHODS: From Sept 13th to 17th, at the special diabetes clinic of Port-au-Prince, 52 diabetic patients 15 years of age and older were interviewed, using a questionnaire approved by the program committee after a verbal consent agreement. Epi-info was used to build the questionnaire and for analysis.

RESULTS: 53% of patients were men, mean age 43, 38% completed primary school, 25% secondary, and 15% were illiterate. The mean time on diabetic treatment was 10 years. 94% reported hearing about TB, most of them through Health centers and radio. 65% knew that coughing is the main sign of TB, and 63% knew its method of transmission. 60% knew that diabetes should not stop their TB treatment, 49% knew that TB treatment is free, and 45% knew that there is a vaccine against TB and knew of the NTP. 75% knew TB is curable and 65% knew that it kills; only 28% thought there is a link between Diabetes and TB. The association between education level and knowledge of TB was noted.

CONCLUSION: With this survey, we have discovered that Haitian diabetics have limited knowledge of TB; while this study can be used as baseline data, further complete studies are required to assess the full scope of their knowledge and awareness of TB.

DETECTION OF ACTIVE TB AMONG IMMIGRANTS REFERRED FOR POST-LANDING MEDICAL SURVEILLANCE FOR TUBERCULOSIS IN ONTARIO, 2010 TO 2014

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BACKGROUND: Immigrant applicants to Canada must undergo radiographic screening for tuberculosis (TB). Those assessed as having inactive pulmonary TB are referred to provincial/territorial public health authorities for post-landing TB medical surveillance (TBMS). This analysis was undertaken in order to measure the outcomes of TBMS in Ontario, specifically the detection of active TB.

METHODS: Data were extracted from Ontario's electronic reportable disease database to quantify the number of TBMS referrals received in Ontario between 2010 and 2014, stratified by age, sex, public health unit (PHU), and country of birth. For each of these variables, the yield of active TB case detection attributable to TBMS (i.e., diagnosed within two years of starting TBMS) was determined.

RESULTS: Ontario received 12,585 TBMS referrals between 2010 and 2014. Among those medically assessed (n=10,003), the yield of active TB case detection attributable to TBMS was 1.6% (158 cases). This represents 5.7% (158/2,779) of all foreign-born TB cases reported in Ontario during this period. There were no significant differences in the yield of active TB by age, sex, or PHU, however, immigrants referred for TBMS were significantly more likely to be subsequently diagnosed with active TB if born in a high TB incidence country (≥30 cases per 100,000 population).

CONCLUSION: Despite the relatively high volume of referrals received, the current approach to post- landing medical surveillance detects only a small proportion of active TB among immigrants in Ontario. An evidence-informed risk-based approach to TBMS should be considered to maximize existing resources aimed at the detection of active TB among immigrants.

EVALUATION OF THE TB REGIONAL TRAINING AND MEDICAL CONSULTATION CENTERS (RTMCCS)

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BACKGROUND: The CDC Division of Tuberculosis Elimination conducted an evaluation of the TB Regional Training and Medical Consultation Centers (RTMCCs). The evaluation focused on TB programs' satisfaction with current RTMCC activities, suggestions for improvement, and ideas for future activities.

METHODS: All CDC-funded TB programs were invited to participate in telephone interviews. The questionnaire included qualitative and quantitative questions with clarifying probes. The questions were emailed to TB controllers prior to interviews to allow them to prepare for the discussion and to invite appropriate colleagues to participate. Interviews were conducted by a member of the CDC RTMCC project team and were approximately 1 hour in duration. Interviews took place from December 2015 to May 2016. Sixty TB programs were interviewed.

RESULTS: Overall satisfaction with RTMCCs meeting programs' needs was positive (4.4 on a scale of 1-5, with 1 being very dissatisfied and 5 being very satisfied). A total of 54 programs (90%) indicated there would be a negative impact if the RTMCC training and education services were not available, and 45 (75%) indicated there would be a negative impact if the medical consultation services were not available. When asked which RTMCC activity is the most important, 43% of programs stated medical consultation; 40% stated training, education, or products; and 15% stated all/combination of services.

CONCLUSION: Overall, TB programs are satisfied with the current services provided by the RTMCCs and see a need for them to continue. Information from the evaluation will be used to help RTMCCs develop their work plans and better serve their project areas.

CO-MORBID ILLNESSES IN PULMONARY TUBERCULOSIS PATIENTS IN A TERTIARY CARE HOSPITAL KANCHEEPURAM

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BACKGROUND: The aim was to find out the demographic profile of different comorbid illnessess and unhealthy habits in the pulmonary tuberculosis patients who attended the outpatient department of Pulmonary medicine, SRM Hospital and Research Centre, Kattankulathur, Kanchipuram district between November 2014 and March 2016.

METHODS: SRM Medical college and Hospital, a tertiary care centre surrounded by 151 villages and hamlets. Every day about 30-50 patients visits the pulmonary medicine department in this tertiary care centre for treatment. About 1565 patients were suspected for Pulmonary Tuberculosis by clinical examination, as per RNTCP guidelines two sputum samples(early morning and spot sample) from 1565 patients were collected in the Microbiological laboratory. All the 3125 samples were screened for Acid Fast Bacilli (AFB) by Ziehl-Neelsen (ZN) method. All AFB smear positive sputum samples were cultured in Lowenstein Jensens (LJ) medium after the decontamination using modified Petroffs method. The demographic details of the patients such living place, occupation, social status, disease contact, family history of TB with a questionnaire and the details of clinical investigations after the consent. The prevalence of co morbid illnesses such as Hypertension, Diabetes, Chronic obstructive Pulmonary Disease (COPD), Renal failure, Cancer and HIV in pulmonary TB patient and analysed the association with their demographic profile.

RESULTS: Out of 1565 patients, 140 patients were smear positive, among the 140 sputum samples processed 104 (74.28%) were positive for Mycobacterium species cultured on LJ medium. Out of 104 Mycobacterial isolates, 102 (98%) were M. tuberculosis and 2 (2%) were Non Tuberculous Mycobacterium (NTM) which were Para nito benzoic acid (PNB) positive The demographic profile of patients showed that the co morbid illnesses of the TB patients were Hypertension(12%), Diabetes Mellitus(34%), COPD(9 %), renal failure(3%) , cancer 5% , HIV 2% and Unhealthy habits like smoking and drinking alcohol(17%) and disease transmission from the family(5%). The mortality rate was around 2%.

CONCLUSION: Diabetes Mellitus and unhealthy habits like smoking and alcohol consumption are one of the most common source leading to immunocompromised status that aggravate the Tuberculosis infection.

INCREASE IN PROPORTION OF FOREIGN-BORN PERSONS WITH TUBERCULOSIS WHO HAVE LIVED IN THE UNITED STATES ≥10 YEARS, 1993–2015

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BACKGROUND: Although the United States has been successful in substantially reducing the incidence of tuberculosis overall, that success has disproportionately benefited U.S.-born persons. From 1993 to 2015, foreign-born (FB) persons constituted an increasing percentage of overall U.S. TB cases, rising from 29.5% to 66.5%. Notably, a large proportion of FB U.S. TB cases has lived in the United States ≥10 years.

METHODS: We analyzed data from the 1993–2015 U.S. National Tuberculosis Surveillance System to characterize TB among FB persons in the United States ≥10 years compared to those here <10 years and used chi-square tests to detect significant differences between groups.

RESULTS: The proportion of FB U.S. TB cases that had arrived ≥10 years before diagnosis increased from 27.8% during 1993–2006 to 46.0% during 2013–2015. During 2007–2015, FB U.S. TB cases that had lived in the United States ≥10 years had significantly greater odds than more recent arrivers of being ≥45 years of age, being sputum-smear positive (p=<0.0001, respectively), having only extrapulmonary TB (p=0.002), or reporting a previous episode of TB disease (p=0.05). FB TB cases here ≥10 years also had greater odds than more recent arrivers of having diabetes (p<0.0001) or being homeless during the year before TB diagnosis (p<0.0001).

CONCLUSION: Foreign-born TB cases in the US ≥10 years are associated with older age, extrapulmonary TB, diabetes, and being homeless. Targeting FB persons in the US ≥10 years with certain risk factors for screening and diagnosis will advance elimination efforts.

CLINICAL REVIEW OF TUBERCULOSIS CASES IN SOLID ORGAN TRANSPLANT RECIPIENTS, 2005 TO 2015

Wong J[1,2], Wachte S[1,2], Irwin L[3], Hoang L[4], Morshed M[4], Gardy J[1,2], Guthrie J[1,2], Wright A[2], Gill J[2], Cook V[1,2], Johnston J[1,2]. [1]BC Centre for Disease Control; [2]School of Population and Public Health, University of British Columbia; [3]BC Transplant; [4]BC Centre for Disease Control Public Health Laboratory, Vancouver, BC, Canada.

BACKGROUND: The risk of active tuberculosis (TB) is known to be elevated among solid organ transplant (SOT) recipients. However, little is known about the epidemiology of TB among SOT recipients in British Columbia (BC). The objectives of this study were to describe the epidemiology and clinical outcomes of SOT recipients diagnosed with TB.

METHODS: We identified all cases of TB diagnosed in BC between January 2005 and June 2015 who had transplant reported as a risk factor which was linked with BC Transplant to collect transplant details and clinical outcomes. Charts of individuals diagnosed with TB after transplant were reviewed and descriptively analyzed. Diagnosis rate was estimated using the population of SOT recipients followed by BC Transplant for two time-points and extrapolated.

RESULTS: We identified 22 cases of TB among SOT recipients, for an estimated diagnosis rate of 0.7%. The median time from transplant to TB diagnosis was 684 days. The majority of cases was male, lived in Greater Vancouver, was born in a country with a high-incidence of TB, and received a kidney transplant. Only 4 cases had any record of screening prior to transplantation. As of August 2015, the outcomes of 20 individuals were known: 13 were successfully treated for TB, 3 had ongoing treatment, and 4 had died prior to completion of TB treatment for a mortality rate of 20%.

CONCLUSION: SOT recipients who are infected with TB have a high mortality rate, underscoring the importance of TB prevention strategies in this population including TB screening prior to transplantation.

E. ENDING TB: THE DIAGNOSIS AND TREATMENT OF LATENT TB INFECTION

INDETERMINATE QuantiFERON GOLD TEST RESULTS AND THE NEED OF PRE-ANALYTICAL TEST EDUCATION

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BACKGROUND: The QuantiFERON Gold-in-tube (QFT-G) assay is used to identify individuals with latent tuberculosis infection (LTBI) and gives quantitative and qualitative results of positive, negative or indeterminate results (that cannot be interpreted clinically). Several factors such as immunosuppression status and pre-analytical factors (too little or too much blood in the QFT-G tube and not shaking the tube after blood collection) have been suggested to be significantly associated with indeterminate QFT-G result.

METHODS: Medical records of patients who had indeterminate QFT-G results between 01/2015-05/2016 were retrospectively reviewed for medical unit the blood draw done, demographics and ICD-9/10 diagnosis codes. The mitogen and nil control values were stratified by immunosuppression and compared using Kruskal-Wallis test.

RESULTS: For the 175 QFT-G indeterminate results, 65 (37.1%) of the patient had ICD-9/10 diagnosis codes indicating immunosuppression. The mean and standard deviation values between normal and immunosuppressed patients for the mitogen control were: 0.217±0.218 and 0.264±0.481 (p=0.378) and the nil control: 0.079±0.190 and 0.158±0.502 (p=0.142), respectively. Accounting for medical units, 53.7% (94/175) of the indeterminate QFT-G test results in the period investigated were in patients from 11 of the 42 units.

CONCLUSION: There was no significant difference between the interferon-gamma measured in the mitogen control between normal and immunosuppressed patients, indicating that pre-analytical factors, not immune health may be the cause of indeterminate QFT-G results. An educational intervention focusing on blood collection and handling that targets nurses in medical units with high indeterminate rates for the QFT-G may reduce the rate of indeterminate QFT-G at HMH.

POST-IMMIGRATION SCREENING FOR LATENT TUBERCULOSIS INFECTION IN CANADA: A COST-EFFECTIVENESS ANALYSIS

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BACKGROUND: In Canada, most TB cases occur through reactivation in immigrants. To accelerate TB elimination efforts, new screening and treatment strategies for TB prevention are needed. The current TB surveillance system in Canada, based on active disease identification, flags 2% of new immigrants at increased risk for TB for post-immigration follow-up, which may include screening for latent TB infection (LTBI). We evaluated outcomes if this system was expanded to flag all new immigrants or targeted to specific TB incidence subgroups.

METHODS: A discrete event simulation model evaluated expanding post-arrival surveillance in the 2014 cohort of 260,600 migrants. The model used a ten-year time horizon, 5% discount rate, and evaluated screening with TST or IGRA and treatment with isoniazid or rifampin. Universal LTBI screening and targeted LTBI screening, stratified according to TB incidence from country of origin, were compared to the current system. Discounted TB cases, costs, and quality adjusted life years (QALYs) were reported.

RESULTS: Detailed results are reported in **Table 1**. In the current system, 517 cases of TB occurred over a ten-year period. No strategy was cost-effective; however, if we had to target screening, an IGRA followed by treatment with isoniazid in migrants from countries with >99 TB cases per 100,000 persons was the most cost-efficient. This strategy had an incremental cost of $314,311 per TB case prevented and $1,426,055 per QALY gained.

CONCLUSION: Expanding the TB surveillance system is cost-prohibitive. Pre-immigration LTBI screening and/or treatment and risk-based targeted screening recommended in Canadian guidelines are two alternatives that must be evaluated.

Table 1. **Results of expanding the post-arrival TB surveillance system in Canada to include all new migrants or only migrants from select TB incidence thresholds**

Factor	Reference (No Screening)	TST/9INH	TST/4RIF	IGRA/9INH	IGRA/4RIF	SEQ/9INH	SEQ/4RIF
Post Arrival Screening of All New Migrants							
TB Cases	517	483	495	450	467	487	497
Population QALYS	1,617,664	1,617,663	1,617,649	1,617,670	1,617,662	1,617,659	1,617,632
Population Costs (2016 CAD)	11,883,360	39,037,880	31,037,460	43,676,560	35,337,360	32,548,940	28,692,060
Incremental Cost per TB Case Prevented	Reference	761,669	881,317	476,946	476,122	694,283	868,860
Incremental Cost per QALY Gained	Reference	(40,876,011)	(1,314,020)	5,276,852	(19,754,412)	(4,185,741)	(537,501)
Post Arrival Screening of Only Migrants From >30 Cases per 100,000							
TB Cases	517	486	495	452	468	489	499
Population QALYS	1,617,664	1,617,645	1,617,644	1,617,657	1,617,670	1,617,643	1,617,633
Population Costs (2016 CAD)	11,883,360	31,428,360	25,538,800	35,337,360	29,004,780	27,180,580	24,183,680
Incremental Cost per TB Case Prevented	Reference	628,871	638,274	361,912	350,385	543,752	698,916
Incremental Cost per QALY	Reference	(1,039,382)	(684,392)	(3,719,547)	2,754,494	(758,357)	(403,264)
Post Arrival Screening of Only Migrants From >99 Cases per 100,000							
TB Cases	517	495	504	465	482	498	509
Population QALYS	1,617,664	1,617,639	1,617,627	1,617,675	1,617,638	1,617,644	1,617,635
Population Costs (2016 CAD)	11,883,360	25,095,780	21,056,480	28,092,680	23,662,480	22,541,900	20,352,860
Incremental Cost per TB Case Prevented	Reference	628,779	750,281	314,311	337,462	572,041	1,022,100
Incremental Cost per QALY	Reference	(535,080)	(249,624)	1,426,055	(459,721)	(546,544)	(298,926)
Post Arrival Screening of Only Migrants From >199 Cases per 100,000							
TB Cases	517	510	516	492	502	512	518
Population QALYS	1,617,664	1,617,647	1,617,633	1,6176,37	1,617,655	1,617,628	1,617,627
Population Costs (2016 CAD)	11,883,360	19,206,220	16,912,940	21,134,660	18,528,660	17,903,220	16,600,220
Incremental Cost per TB Case Prevented	Reference	1,105,247	4,715,692	365,025	438,696	1,238,443	(4,295,398)
Incremental Cost per QALY	Reference	(440,899)	(163,282)	(353,628)	(749,744)	(167,105)	(129,783)

Total population consists of 260,600 new migrants.
All costs from a healthcare system perspective.
Numbers in parentheses represent negative values.
TST: Tuberculin skin test; IGRA: interferon-gamma release assay; SEQ: sequential testing, where a single negative equates to a negative result; 9INH: 9 months of isoniazid therapy; 4RIF: 4 months of rifampin; TB: Tuberculosis

COMBINING THREE TESTS TO MEASURE PREVALENCE OF LATENT TUBERCULOSIS INFECTION IN 11,000 HIGH RISK PERSONS IN THE UNITED STATES

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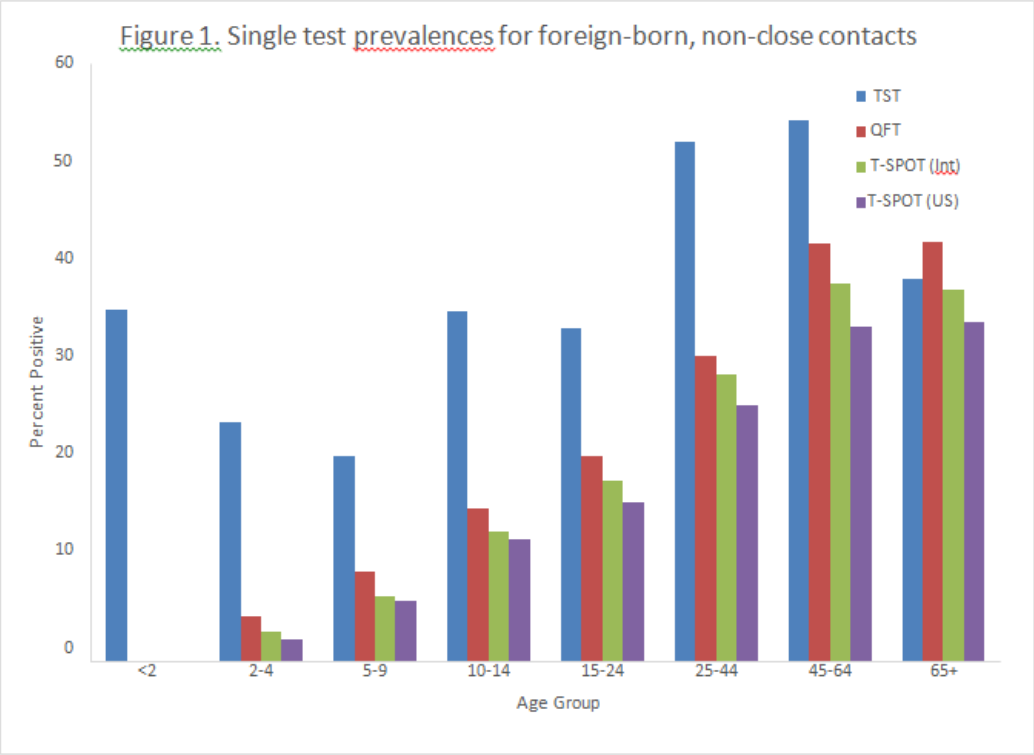
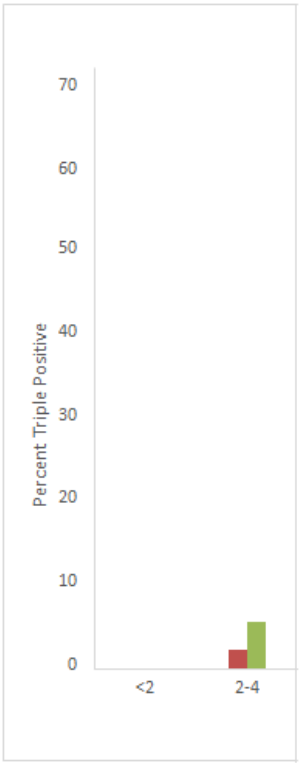
BACKGROUND: Over 85% of tuberculosis (TB) in the United States arises in people with untreated latent tuberculosis infection (LTBI). The tuberculin skin test (TST) and blood-based interferon gamma release assays (IGRA), QuantiFERON Gold In-Tube (QFT) and T-Spot.TB (TSPOT), are approved to diagnose LTBI. The Tuberculosis Epidemiologic Studies Consortium, a research partnership between CDC and 10 U.S.sites, compared the three tests in persons at highest risk for progression to TB.

METHODS: Between July 2012 and September 2014, persons of any age at high risk for TB or LTBI (TB contacts, foreign-born from high-prevalence countries, HIV-infected) were interviewed about demographics, symptoms, and risk factors; and simultaneously tested using QFT, TSPOT, and TST. Analyses assessed agreement between the tests.

RESULTS: Of 11,962 participants analyzed, 6284(53%) were male, 9,287(78%) 15-64 years old, and 516(4%) <5 years old. Participants included 9,643(81%) foreign-born, 1,052(9%) contacts, and 1,372(11.5%) HIV-infected. LTBI single test prevalence by IGRAs but not TST increased with age (<65 years old) among the foreign-born, as did the probability of having all three tests positive. (Figure 1 & 2) LTBI prevalence was lowest among US-born HIV- infected by any test (2.2-7.8%). Agreement between TST and IGRAs was lowest among foreign-born children <5 (Kappa 0.11-0.20) and highest among US-born ≥65 years old (Kappa 0.57-0.62).

CONCLUSION: IGRAs appear to perform better than TST for LTBI testing among foreign-born persons, especially children. Ongoing follow-up of U.S.-born HIV-infected persons without additional risk factors will help resolve the question of whether they should be routinely tested.





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POLICY IMPACT OF USING SHORTER REGIMENS FOR TREATMENT OF TB INFECTION IN NEW YORK CITY TB CLINICS

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BACKGROUND: In 2015, the New York City (NYC) Health Department changed its policy to more widely use two available shorter treatment regimens for treatment of tuberculosis (TB) infection: 1) 4-months daily rifampin (4R), and 2) 3-months once-weekly isoniazid and rifapentine by directly observed therapy (3HP), in four NYC TB clinics.

METHODS: Patients diagnosed with TB infection in January-June 2015 were preferentially offered 3HP and/or 4R by a physician as clinically indicated. 9H was offered if patients were ineligible for or refused either of the shorter treatment regimens. Treatment outcomes were assessed.

RESULTS: Among 649 patients eligible for treatment for TB infection, 449 (69%) initiated treatment; 394 (88%) on one of the shorter treatment regimens (125 (28%) on 3HP, 269 (60%) on 4R) and 55 (12%) on 9H. Of the remaining patients, 157 (24%) refused treatment, and 43 (7%) were lost. Compared to patients on 9H, treatment completion was higher among patients on 3HP or 4R (79% for 3HP and 70% for 4R vs. 49% for 9H). Discontinuation of treatment due to side effects occurred in seven patients; three on 4R and two each on 9H and 3HP. The most common side effects were skin rash and high liver enzymes.

CONCLUSION: The majority of patients on treatment for TB infection accepted one of the shorter treatment regimens. Tolerability of the regimen and increases in treatment completion were observed. Wider use of shorter treatment regimens by non-health department providers may extensively improve treatment completion for TB infection in NYC and advance progress towards TB elimination.

VARIABILITY BY MANUFACTURER LOT NUMBER AS A POSSIBLE CAUSE FOR FALSE-POSITIVE QUANTIFERON-TB GOLD IN-TUBE (QFT) AND T-SPOT.TB (T-SPOT) RESULTS DURING SERIAL TESTING OF HEALTH CARE WORKERS (HCW)

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BACKGROUND: A tuberculin skin test (TST), QFT and T-Spot comparison study among 2,122 U.S. HCW detected 21 (0.9%) TST conversions after 3 serial repeats. QFT and T-Spot conversions were 6- to 9-fold more common (138 (6.1%) and 177 (8.3%), respectively). After review all conversions were deemed likely false-positive.

METHODS: Using data for 1968 HCW with triple-negative baseline results, we calculated conversion rates for QFT and T-Spot. We censored results after HCW conversion and excluded 188 QFT and 160 T-Spot assays in lots with < 50 results.

RESULTS: For QFT, there were 98 (2.00%) conversions for 4, 899 assays within 9 lot numbers with 145 to 1,201 tests. Site variation was 2.7-fold: 12 (1.03%), 28 (2.34%), 22 (1.80%) and 36 (2.74%) for sites in NY, MD, TX and CO. Conversions by lot ranged 4-fold from 3/342 (0.88%) to 28/732 (3.83%). Conversions also varied as high as 5.6-fold within lots across sites. For T-Spot there were 152 (3.23%) conversions for 4, 710 tests within 9 lots with 72 to 680 tests. Site variation for T-Spot was 9.7-fold: 22 (1.90%), 95 (8.41%), 24 (2.07%) and 11 (0.87%) for sites in NY, MD, TX and CO. Conversions by T-Spot kit lot number ranged from 0/150 to 28/334 (8.4%), and variation within lots was over 10-fold for lots with over 100 assays per site.

CONCLUSION: Analyses suggest variation by site and manufacturer in 2008-11 contributed to a 6- to 9-fold higher false-positive conversion rate for IGRAs compared to TST in the overall study.

TUBERCULOSIS ELIMINATION USING TARGETED TESTING FOR LATENT TUBERCULOSIS INFECTION

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BACKGROUND: After two decades of declining incidence, progress towards tuberculosis (TB) elimination in the US may have stalled. Texas is one of four states that reported more than 500 TB cases in 2015. State focus on treatment of new cases and their contacts with latent infection (LTBI) translates into limited resources for targeted testing and treatment of populations at risk for LTBI not associated with an active case.

METHODS: Funding through the US Medicaid Waiver program has allowed us to develop a project aimed at identifying and treating LTBI in a 20 county area of Texas with a population of over 2.6 million. Providers in the project use interferon gamma release assay (IGRA) blood testing to screen populations at high risk for TB, including homeless, foreign-born, immune-compromised, healthcare workers, and diabetics. Implementation includes enrollment of clinics and settings serving high risk populations; training for providers about TB disease and LTBI, including treatment; and collection of data to assess project impact and outcomes. Challenges include convincing people who are not feeling ill to start and complete treatment and encouraging providers to expend incorporate identification and treatment of high-risk patients into their protocols.

RESULTS: Twenty sites have used IGRA testing to screen over 5,000 at-risk individuals, 435 of whom had a positive IGRA. One hundred and eighty one of these have LTBI. Ninety-nine have started treatment and 49 have completed treatment.

CONCLUSION: Strategies to engage persons with confirmed LTBI into treatment need to be developed and implemented.

OUTREACH TO LA COUNTY CIVIL SURGEONS TO IMPROVE LTBI TESTING AND TREATMENT AMONG PERMANENT RESIDENCY APPLICANTS: PRELIMINARY RESULTS FROM A PILOT PROJECT

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BACKGROUND: Approximately 600,000 foreign-born persons living in the United States are screened for tuberculosis (TB) each year by civil surgeons as part of the application process for permanent residency. Public health outreach for latent TB infections (LTBI) treatment in this population is limited. We describe preliminary experience from a pilot project to improve LTBI treatment among green card applicants in Los Angeles County (LAC).

METHODS: Project activities have included: 1) outreach to LAC civil surgeons via telephone, fax, mail and email; 2) education workshop for civil surgeons with a focus on LTBI testing, treatment, and referral; and 3) LTBI surveillance and telephone survey of applicants at 5 pilot clinics.

RESULTS: We found that most civil surgeons do not treat LTBI nor refer applicants for treatment. While many civil surgeons expressed interested in using interferon-gamma release assays (IGRAs), most use only the tuberculin skin test for TB screening. The high cost of IGRAs is a major barrier for adopting IGRA-based screening. Sixty-nine civil surgeons attended the workshop, and participant evaluations were highly favorable. While most LTBI positive applicants knew about their LTBI status, many did not know that LTBI could be treated. Most applicants reported willingness to take shorter course LTBI treatment (12 weekly or 4-month daily regimens), if recommended by a provider.

CONCLUSIONS: Our preliminary experience has highlighted opportunities and barriers for improving LTBI testing and treatment among permanent residency applicants. Ongoing activities include providing lower cost IGRA options for civil surgeons and a telephone-based LTBI treatment support intervention.

LATENT TUBERCULOSIS INFECTION SCREENING AMONG FEDERAL INMATES: 1998 TO 2014

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BACKGROUND: Screening for latent tuberculosis infection (LTBI) among federal inmates is a significant public health program to prevent TB transmission in this closed environment.

METHODS: Inmates are offered a baseline 2-step tuberculin-skin test (TST) assessment on admission and ongoing follow up throughout incarceration. Inmates with a positive TST may have further testing with interferon-gamma release assay (IGRA).

RESULTS: Participation in screening on admission is very high (n=4,210 or 86% in 2014). The proportion of inmates with a positive TST on admission was 10.4% (n=324) in 2009 and has trended upwards to 15.4% (n=504) in 2014. Among inmates with repeat TST the proportion who converted to TST positive has trended downwards from 1.5% (n=93) in 2007 to 0.7% (n=50) in 2014. The overall proportion of inmates who are TST positive has remained stable at 18.7% in 2007 and 16.9% in 2014. Foreign-born inmates were more likely to have a positive TST (47.1%) compared to Canadian-born inmates (10.2%) or inmates of Aboriginal ancestry (18.9%). TST status was not associated with HIV status. Of 784 TST positive inmates who had IGRA testing, 24% (n=188) had positive results.

CONCLUSION: Screening for latent TB infection continues to identify inmates TST positive inmates on admission and throughout incarceration. TST conversions appear to be declining, possibly indicating reduced transmission between 2007 and 2014. Consistent with the epidemiology of TB in Canada, foreign-born inmates have the highest TST positive rate. One quarter of inmates had concordant IGRA results.

TUBERCULOSIS IN NEW HAMPSHIRE: NEW APPROACHES TO REVEAL THE RESERVOIR OF INFECTION

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BACKGROUND: New Hampshire (NH) is a low-incidence state committed to tuberculosis elimination, which includes the identification and treatment of latent tuberculosis infection (TBI). We used geospatial analysis of Interferon Gamma Release Assay (IGRA) results to identify areas with TBI to target resources and interventions.

METHODS: We created a dataset of NH residents diagnosed from 2011 through 2015 with active tuberculosis disease (TB) or TBI, which we defined as any positive T-SPOT.*TB*® (Marlborough, MA) (T-SPOT) result. By mapping according to our state public health regions, we compared residential locations of those diagnosed with TB and TBI.

RESULTS: We identified 59 TB and 72 TBI patients. 78% of TB and 64% of TBI patients resided in southeastern regions, where 60% of the state population resides. Unexpectedly, 31% of TBI patients lived in regions which contained only 7% of TB patients. Our highest TB rate (2.1/100,000 population) and second-highest TBI rate (1.5/100,000 population) were observed in a high-population density region. Two of our three highest TBI rates (3.43/100,000 population and 1.38/100,000 population) were observed in regions with very few TB patients (n=1 and n=0, respectively).

CONCLUSION: Mandatory reporting of positive IGRA results and innovative use of geospatial analysis allowed us to identify locations in our state with TBI reservoirs so we can best allocate resources for TB elimination. As expected, high rates of TB and TBI were identified in high-population areas; however, some regions with low TB rates were unexpectedly identified with significant TBI populations.

TREATMENT COMPLETION FOR TUBERCULOSIS INFECTION IN A MOBILE POPULATION AS BRIDGE CASE MANAGEMENT INTENSIFIES

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BACKGROUND: The non-profit Migrant Clinicians Network (MCN) offers Bridge Case Management (BCM), an innovative care continuity and coordination service for individuals with tuberculosis (TB) or undergoing other high-value interventions. This study assessed which personal and health system characteristics are associated with treatment completion for TB infection in a vulnerable population as BCM intensity increases.

METHODS: This study included case management data on all patients (n =143) receiving BCM for TB infection, 2005-2012. Kaplan-Meier curves elucidated overall survival rates. Multivariate Cox proportional hazards analysis determined the magnitude and direction of characteristics significantly associated with treatment non-completion; multivariate logistic regression reinforced key findings.

RESULTS: Overall TB infection treatment completion was 62.9% (95% CI: 54.1%-70.5%) and the majority of those who did not complete treatment consumed at least three months' worth of medicine. An increase of one BCM call to a clinician regarding a patient's care decreased the hazard of non-completion by 5.3% (95% CI: 1.3%-9.1%). Conversely, living in farmworker camps had 2.2 times the odds (CI: 1.0-4.7) of non-completion compared to living in a home and self-identified alcohol abuse predicted non-completion perfectly. The type of referring organization was not a significant predictor of non-completion.

CONCLUSION: BCM offers clinicians an effective way to ensure care continuity for patients who relocate, including bi-directional communication with treating clinicians. BCM increased treatment completion for TB infection. Using shorter regimens will likely improve outcomes further. Given this and previous evidence, all mobile patients at high-risk of TB activation, especially farmworkers, should be enrolled in a BCM-type program.

PREVALENCE OF LATENT TUBERCULOSIS INFECTION IN SYRIAN REFUGEES TO CANADA

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BACKGROUND: In the past year, Canada has accepted more than 25 000 Syrian refugees. Prior to arrival they underwent standard immigration medical examinations that included, in those 11 years of age or older, a chest radiograph to screen for pulmonary tuberculosis (TB). Canadian Collaboration for Immigrant and Refugee Health recommends to additionally screen refugees from high prevalence groups for latent tuberculosis infection (LTBI). The prevalence of TB in this population was uncertain as conflict and displacement has been shown to increase TB. A refugee clinic in Edmonton, the New Canadians Clinic (NCC), presented a unique opportunity to estimate prevalence of TB and LTBI in Syrian refugees arriving to Canada.

METHODS: 100 consecutive Syrian refugees, mean age 22 years (range five to 48 years) seen at the NCC in January 2016 were screened for TB and LTBI. To facilitate screening of this condensed cohort, an interferon-γ release assay (IGRA) was added to the standard testing protocol offered to all refugees at the NCC. Patients with a positive IGRA were referred to Edmonton Tuberculosis Clinic (ETBC) for evaluation and, if appropriate, offered prophylaxis.

RESULTS: No cases of active TB were found. Valid IGRAs were measured in 99 of 100 individuals and nine, 9% (five male, four female; age range six to 41) were IGRA positive. Eight of nine patients attended follow up appointments at the ETBC and began LTBI prophylaxis.

CONCLUSION: 9% prevalence of LTBI was higher than expected, however not high enough to warrant a widespread screening program at this time.

HIGH PREVALENCE OF LATENT TUBERCULOSIS INFECTION AMONG GREEN CARD APPLICANTS IN LOS ANGELES COUNTY CIVIL SURGEON CLINICS

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BACKGROUND: One-third of world's population is infected with Mycobacterium tuberculosis, and it remains prevalent among many US immigrants. Green card applicants currently living in the United States are screened for tuberculosis (TB) by licensed civil surgeons, but little is known regarding latent tuberculosis infection (LTBI) prevalence in this population.

METHODS: We collected demographic information and tuberculin skin test results from immigration-related medical examination forms from four civil surgeon clinics in Los Angeles County. We defined LTBI as induration ≥10 mm with no radiographic evidence of TB disease. Countries other than Canada, Australia, New Zealand, or Western and North European were defined as having elevated TB burden. Two-sided chi-squared tests were used to determine differences in LTBI prevalence by patient characteristics.

RESULTS: Since November 2015, TB screening data for 144 patients were reported. Of these, 86 (60%) were female and median age was 33 years old (range: 3 – 75 years). Most patients were from Western and Northern Europe (31%) or Asia (31%), and 83 (58%) were from countries with elevated TB burden. Overall, 35 (24%; 95% confidence interval=0.18, 0.32) tested positive for LTBI. LTBI prevalence was not significantly different across gender (p-value=0.55) or age group (p-value=0.13). However, LTBI prevalence was significantly different between patients from elevated versus low TB burden countries (33% versus 13%, respectively; p-value=0.01).

CONCLUSIONS: LTBI prevalence is high among green card applicants from high TB burden countries. Public health outreach to treat LTBI in this population is necessary.

BARRIERS TO ADOPTION OF A TWELVE WEEK ISONIAZID/RIFAPENTINE REGIMEN FOR THE TREATMENT OF LATENT TUBERCULOSIS INFECTION IN TWO U.S. FEDERAL HEALTHCARE SYSTEMS

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BACKGROUND: Latent tuberculosis infection (LTBI) treatment is a cornerstone of tuberculosis (TB) elimination. Weekly isoniazid (INH) and rifapentine (RPT) for 3 months (3HP) has improved completion rates. Although many TB programs use 3HP, a 3HP uptake assessment in national health systems hasn't been performed. We examined 3HP adoption in the Indian Health Service (IHS) and the Veterans Healthcare Administration (VHA). Both systems use a common VistA-based electronic health record (EHR).

DESIGN/METHODS: IHS/VHA RPT dose data, a surrogate for 3HP use, was analyzed for federal fiscal years 2012–2015. To assess 3HP use barriers, we surveyed key providers in the 12 IHS administrative regions and the 21 Veterans Integrated Service Networks (VISNs).

RESULTS: Both agencies ordered RPT <30 days after the 2011 MMWR publication of 3HP guidelines. Orders were subsequently received from 20 of 21 VISNs and the eight largest IHS regions. Forty-seven IHS sites (10 of 12 regions) and 46 VHA providers (16 of 21 VISNs) returned surveys. While more VHA than IHS sites had in-house LTBI consultation resources available (100% vs 48%), only 58% of VHA and 26% of IHS respondents could confirm 3HP provider education. A minority (48% IHS, 39% VHA) of respondents identified DOT structures available for 3HP administration. Even fewer (20% IHS, 25% VHA) sites incorporated TB medication dosing guidance into the EHR.

CONCLUSIONS: Segments of both systems adopted 3HP immediately after the release of CDC guidelines. However, implementation isn't uniform. A lack of provider education, DOT services, and EHR LTBI medication guidance may be barriers to broader 3HP use.

F. NO LONGER NEGLECTED: ADDRESSING TB IN CHILDREN

AN EVALUATION OF WINDOW PERIOD PROPHYLAXIS REFERRALS IN A PEDIATRIC TB CLINIC

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BACKGROUND: Window period prophylaxis (WPP) treatment is prescribed as standard of care in the Pediatric Tuberculosis (TB) Clinic in Winnipeg, Manitoba for children ≤5 years old identified through Public Health (PH) contact investigation. Models and theories support WPP, but the evidence for its use is inferential.

METHODS: We received 788 referrals for WPP (2006-2015) and reviewed patient demographics (age, sex, type and duration of contact, residence), case details (disease site, sputum bacteriology and sensitivity, radiographic findings, symptoms, resistance), referral process (timing and access to clinic), treatment compliance, the barriers to providing WPP, and the rate of PPD conversion/reversion.

RESULTS: Most referrals from Public Health did not include necessary details to make appropriate risk assessment for disease. There were 10 missed opportunities for WPP, 3 of whom had primary
TB disease at referral, while 7 had Latent TB infection (LTBI). Of the 788 referrals, there were 9 eventual conversions (LTBI, 1.1% conversion rate). Three cases of primary TB were diagnosed during their initial assessment for WPP treatment. Risk factors for conversions were age young age, delayed referral and multiple exposures. Over the years we also noted PPD reversions.

CONCLUSION: To better utilize and prioritize valuable PH resources it important to be able to access specific case details to improve risk stratification of referrals and timely referrals. We recommend the prioritization of children <36 months old for WPP and/or those who have had multiple exposures to active TB cases. More studies are needed to clarify the role of BCG related reactions in this young population.

ASSOCIATION OF FACTORS WITH SUCCESSFUL TREATMENT OUTCOME OF CHILDHOOD TUBERCULOSIS IN BARANGAY COMMONWEALTH, QUEZON CITY: A 2-YEAR RETROSPECTIVE STUDY

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BACKGROUND: Tuberculosis remains a public health concern worldwide. Reports on the association of factors of childhood tuberculosis with treatment outcome are limited in the Philippines. This retrospective cohort study aims to determine the association of factors of childhood tuberculosis with successful treatment outcome.

METHODS: Medical records including TB registry, treatment cards and profile of children 0-14 years old with tuberculosis treated from January, 2013 to July 15, 2015 at National Government Center, Doña Nicasia and Commonwealth Health Centers of Barangay Commonwealth, Quezon City were reviewed. Socio-demographic, anthropometric and clinical data were extracted. The association of these data with treatment success was analyzed by univariate and multivariate logistic regression.

RESULTS: There were 267 subjects. Children were mostly 4 years or younger (157, 59%), belonged to families along poverty threshold (135, 54%). Majority gained weight after treatment (223, 84%). Two hundred fifty nine (97%) completed treatment. Three (1%) were cured. Five (2%) defaulted. No cases of death or treatment failure were reported. Weight gain ($p=0.001$) and absence of comorbidity such as ATP ($p=0.015$), scabies ($p=0.015$), parasitism ($p=0.019$), hearing defect ($p=0.000$) and brain cyst ($p=0.000$) were significant factors independently associated with treatment outcome. Weight gain was significantly associated with treatment success ($p=0.042$).

CONCLUSION: Weight gain is a factor of a successful treatment in childhood tuberculosis. Children who gained weight after treatment were more likely to have a successful treatment outcome.

RISK FACTORS FOR IGRA POSITIVITY AMONG CHILDREN PRESENTING FOR PRIMARY CARE IN A U.S. SAFETY-NET CLINIC SYSTEM.

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BACKGROUND: Since 2011, Quantiferon-TB Gold® (QFT) has been used for pediatric (≥2 years) latent tuberculosis screening in primary care clinics at Denver Health, an urban US safety-net hospital/clinic system which contains a high proportion of pediatric patients who meet current guidelines for screening based on patient or family origin from TB endemic countries, particularly Latin America. Having previously described a QFT positivity rate of 2.1% in our pediatric clinic population, we undertook a case-control study to identify demographic factors associated with positive QFT testing.

METHODS: All pediatric QFT's performed in our lab between 1/5/2011 and 8/19/2014 were identified. Patients with positive tests were matched 1:1 for age, primary language and specific clinic with negatives. Odds ratios and 95% confidence intervals were calculated for demographic characteristics, and statistically evaluated using Chi-square tests.

RESULTS: 79 positive tests were identified and matched. Two factors were statistically associated with positive testing: being born/travelled/lived in a TB endemic country (OR 2.09 (95%CI 1.02-4.32), p=0.03) and Self-Pay/Uninsured insurance status (OR 3.24 (95% CI 1.42-7.64), p=0.002). Neither residence in a household with at-risk family members (immigration from TB endemic country, prison exposure), nor self-identified race or ethnicity were associated with positive testing.

CONCLUSIONS: An understanding of the relative importance of risk factors for pediatric tuberculosis infection in primary care settings in the US, and prioritization of children with history of birth or extended travel/living in TB endemic countries, or those ineligible for insurance, may allow more targeted identification of patients for routine screening and improve resource utilization.

QUANTIFERON-GOLD TB® PERFORMANCE FOR TUBERCULOSIS INFECTION SCREENING IN CHILDREN 18 TO 24 MONTHS OLD

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BACKGROUND: Interferon-gamma releasing assays including Quantiferon-Gold TB® (QFT) are preferred over TST in BCG-vaccinated adults and older children but there is insufficient evidence in children under
2 years old. Testing concerns in this age group include potentially high rates of indeterminate results due to poor mitogen responsiveness and difficulty with phlebotomy. Though not laboratory approved, since introduction of QFT in Denver Health Clinics (serving a low-income population in Denver, USA), 27 tests were performed inadvertently on children < 2 years.

METHODS: Medical records of all patients < 2 years with QFT between 1/5/2011 and 8/19/2014 were reviewed. Laboratory values for nil, mitogen and TB antigen tubes were assessed.

RESULTS: Patients ranged from 18.5 to 23.9 months (median 21.9) and were 41% male. All were tested for routine TB screening; none were contacts of an active case. Of the 27 QFT results, 26 were negative, 1 positive and none indeterminate. Mitogen reactions ranged from 1.187 to <10 IU/ml; 16/27 reached the >10 maximum threshold. The one positive had a Tb antigen response of 0.66 IU/ml, nil response of
0.13 and mitogen of >10. No patient in the cohort developed evidence of tuberculosis infection or active disease as of 9/1/2016.

CONCLUSION: Low rates of indeterminate results and robust mitogen results suggest that these factors may not be significant barriers to utilization of QFT in children 18-24 months. Though specific details were unavailable, phlebotomy was also clearly not insurmountable in these cases. These results add incrementally to our understanding of TB diagnostic tools in the very young.

STRATEGIES TO IMPROVE DETECTION OF OUTBREAKS OF TUBERCULOSIS INVOLVING PEDIATRIC CASES — UNITED STATES, 2015

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BACKGROUND: Because culture-negative tuberculosis cases cannot be genotyped, genotype-based alerting mechanisms to identify potential tuberculosis outbreaks exclude most pediatric tuberculosis cases. We evaluated 3 potential strategies to identify transmission chains involving children.

METHODS: Our study population was U.S. counties or county-equivalents with ≥2 tuberculosis cases in persons under age 15 years during 2015. We enumerated the jurisdictions with a pediatric tuberculosis proportion above the national average of 5%, those with a pediatric tuberculosis proxy rate (i.e., jurisdiction's overall case rate multiplied by pediatric proportion) above the 2014 national rate of 0.8 cases/100,000 children, and those with a >0.3 case increase in mean number of pediatric cases per calendar quarter when comparing the most recent 3 quarters to the most recent 8 quarters (i.e., above the median increase nationally among jurisdictions with ≥2 pediatric cases).

RESULTS: Among the 91 jurisdictions with ≥2 pediatric tuberculosis cases, 68 (74%) had >5% pediatric cases, 18 (20%) had a pediatric tuberculosis proxy rate >0.8/100,000, and 58 (64%) had a >0.3 case increase in the quarterly moving average. Sixteen jurisdictions, including one with a known outbreak involving pediatric cases, were identified by all strategies; 36 were identified by two; and 24 were identified by only one strategy.

CONCLUSION: Three strategies identified jurisdictions with greater than national concentrations of or increases in pediatric tuberculosis cases; however, different strategies identified different locations. Further optimization and combination of these strategies could provide a method to detect transmission chains involving children that could supplement other genotype-based alerting mechanisms and help direct tuberculosis control efforts.

T-SPOT.TB PERFORMANCE IN ROUTINE PEDIATRIC PRACTICE IN A LOW TB BURDEN SETTING

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BACKGROUND: The T-SPOT.TB is an interferon-gamma release assay (IGRA) that measures immunologic response to tuberculosis infection (TBI). Due to conflicting and limited data, IGRAs are recommended only in children >2 years of age. We analyzed T-SPOT.TB results to determine the prevalence of categorical results and their associations with key variables.

METHODS: Oxford Immunotec provided de-identified cross-sectional results for 44,289 children <17 years of age from 2010-2015. Associations between test outcome and demographics were estimated by bivariate analysis and logistic regression.

RESULTS: Tests were not performed in 1.3% (592/44,289) due to technical error, with no associated patient characteristics. Invalid tests due to low mitogen responses were uncommon (0.2%, 86/44,289) and not associated with patient characteristics. Invalid tests due to robust nil responses were uncommon (0.4%,168/44,289) and associated with younger age and HIV clinic draw site. Positive responses, versus negative responses, were more likely in samples from older children ($p< 0.0001$) and public health draw sites ($p's\leq 0.0001$). Younger children had higher odds of borderline than negative results ($p< 0.0001$), but no difference in the odds of positive versus borderline results.

CONCLUSIONS: Immature immune responses in younger children may have resulted in rare invalid results due to robust nil responses. Anergy was uncommon as illustrated by infrequent invalid results due to weak positive control responses. Younger age was associated with borderline results but at clinically insignificant levels. The various draw sites had differential positivity rates, suggesting that targeted IGRA use should consider a population's pre-test probability of TBI. Our results support IGRA use in young children.

PRELIMINARY RESULTS OF NATIONAL SURVEILLANCE OF CHILDHOOD TUBERCULOSIS IN CANADA

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BACKGROUND: This study characterizes the epidemiologic, clinical, and treatment data for all cases of TB in children under age 15 in Canada through the Canadian Pediatric Surveillance Program (CPSP).

METHODS: TB cases were identified through a monthly form sent to approximately 2500 active pediatricians, and select non-pediatricians including TB program clinicians. For cases meeting inclusion criteria, a detailed questionnaire was sent followed by 6-month follow-up surveys.

RESULTS: Results presented include cases from September 2013 to May 2016. 126 reported cases both met inclusion criteria and returned a detailed questionnaire. Selected demographic data is shown in Table 1. Intrathoracic TB was reported in 116/126 (92%) of cases including 102 with pulmonary disease. Of 100 patients who underwent investigations for pulmonary disease (sputum in 54, brochoalveolar lavage in 6, and gastric aspirates in 55), one or more positive cultures TB were obtained in 41 (41%). Of these 41 patients, 3/10 (30%) were <12 months old, 14/34 (41%) 1-4 years old , 8/19 (42%) 5-9, years old and 16/28 (57%) 10 years or older. Extrathoracic TB was reported in 24% (n=30), including 13 (39%) patients >10+ years old. There was one MDR-TB case.

CONCLUSIONS: First Nations and Inuit Canadians accounted for almost half of reported cases. The majority of children with pulmonary disease had negative cultures. Culture positivity increased with age. Rates of extrathoracic TB in the older children and adolescents were higher than has been described in the global literature. Data retrieval for reported cases without a returned questionnaire is ongoing.

RETROSPECTIVE COHORT STUDY OF TRANSMISSION AMONG CHILD HOUSEHOLD CONTACTS OF PULMONARY TUBERCULOSIS CASES IN TORONTO, CANADA

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BACKGROUND: Interventions to interrupt tuberculosis (TB) transmission to household child contacts require a thoughtful balance between effective prevention and control, while striving to minimize family disruption. To better guide policy decisions and improve patient-centred care, this study sought to assess the transmission rate among child household contacts in a large urban jurisdiction in Canada.

METHODS: Public health paper charts were reviewed for all pulmonary TB cases with child household contacts diagnosed in Toronto from May 1, 2009 to April 30, 2012 and the respective child household contacts <18 years of age. Data were collected on demographics, clinical characteristics, and circumstances of exposure.

RESULTS: There were 191 pulmonary TB cases with 354 corresponding child household contacts identified during the study period. Prior to diagnosis, cases spent an average of 130 days (range 0 to 419 days) at home while infectious. At the time of public health follow-up, 39 (11.0%) household child contacts demonstrated conversion on tuberculin skin test. There were a total of 13 child secondary cases, representing a secondary transmission rate of 3.7%. No secondary cases were <1 year of age.

CONCLUSION: Despite long periods of exposure to infectious pulmonary TB cases prior to diagnosis and follow-up by public health, a low rate of transmission was observed among child household contacts in Toronto.

TUBERCULOSIS AMONG FOREIGN BORN CHILDREN AND ADOLESCENTS EMIGRATING TO ONTARIO, CANADA

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BACKGROUND: Requirements for tuberculosis (TB) screening among children and adolescents migrating to low-TB- burden immigrant-receiving countries vary widely. We assessed the effects of Canadian immigration medical surveillance (IMS) and examined these relationships by countries of origin.

METHODS: A retrospective population based cohort of migrants <18 years of age was established using linked reportable diseases and health admin data for those migrating to Ontario, Canada between January 2002 and December 2011. Cumulative rates were calculated as the number of TB cases developed within the study per 100,000 individuals.

RESULTS: Of 232,169 migrants there were 132 TB cases (rate: 57 [95%CI: 48, 67]); and of 845 IMS referrals there were 14 TB cases (rate: 1,657 [95%CI: 989, 2,762]). TB cases occurred in those emigrating from 34 countries, with India, Philippines, Nepal and Pakistan accounting for approximately 50% overall, and Philippines and Kenya alone accounting for 36% of TB cases <11 years of age. Prior treatment for TB correlated very closely with referral for IMS ($\kappa = 0.92$). A total of 406/17,901 (2.3%) of those migrants from the Philippines had a past history of TB treatment as compared with 35/31,120 (0.1%) from India, and 11/20,432 (0.05%) from Pakistan.

CONCLUSION: IMS referred children had higher rates of TB than other migrants, however the current process fails to predict a majority of cases; likely because IMS referring practice is not based on testing for TB infection. Referrals may reflect differential rates of empiric treatment between specific countries and world regions.

G. TECHNOLOGY AND mHEALTH SOLUTIONS TO TB CARE AND PREVENTION

EVALUATING THE USE OF AN ARTIFICIAL INTELLIGENCE (AI) PLATFORM ON MOBILE DEVICES TO MEASURE AND SUPPORT TUBERCULOSIS MEDICATION ADHERENCE

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BACKGROUND: Tuberculosis (TB) programs administer in-person Directly Observed Therapy (DOT) to measure and maximize adherence to treatment of TB disease and latent TB infection (LTBI). DOT is costly and logistically complex, hindering universal use. The Los Angeles County Department of Public Health (DPH) collaborated with AiCure to pilot using AI in lieu of in-person DOT for TB disease and LTBI patients in one public health TB clinic.

METHODS: Active TB patients in the continuation phase of treatment and new LTBI patients were eligible to participate. Patients were loaned smartphones with the AI application pre-installed and trained in its use. Unlike video-recorded DOT sessions that require 1:1 viewing, the AI platform relies on software algorithms to ensure correct dosing. Real-time data are transferred to centralized dashboards and missed or incorrectly administered doses are automatically flagged for follow-up.

RESULTS: The pilot has enrolled 25 patients to date, of which 16 (64%) have LTBI. Seven patients (28%) completed treatment; 3 (12%) discontinued due to medication toxicity, and 15 (60%) are still on treatment. Mean cumulative adherence based on visual confirmation of drug ingestion is 98%; 1,991 adherence parameters have been collected. 30 interventions were reported in response to adherence and side effect data.

CONCLUSION: Patients had high treatment adherence while using a mobile AI application and were able to easily use the technology. Real-time data and notifications allowed for immediate follow-up. Preliminary pilot data indicate that automated treatment monitoring using an AI platform is safe and feasible for active TB and LTBI patients.

DEVELOPING DATA VISUALIZATION TOOLS TO SUPPORT DECISION-MAKING FOR TUBERCULOSIS PREVENTION AND CONTROL

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BACKGROUND: Healthcare practitioners and policymakers are increasingly accessing health data through electronic interfaces such as databases and dashboards. Although research shows that how data is visualized affects patients' and health professionals' decision-making, there is little research in how to best visually present public health data. Using tuberculosis as a use case, we explored how best to design data visualization software to facilitate TB controllers' daily tasks, such as mapping a cluster of cases or identifying patients for follow-up.

METHODS: We conducted a series of qualitative studies with clinicians, nurses, epidemiologists, and researchers involved in tuberculosis management at the BC Centre for Disease Control to gather data on how participants interacted with the data in our Provincial TB Registry. Their answers helped us design a prototype visualization tool, which we refined through a series of user consultations.

RESULTS: We developed EpiCOGs – a tool that allows TB controllers to visually query and explore patient datasets in a way that facilitates their daily workload. Future development will expand EpiCOGs' functionality and support visualization of genomic and contact network data.

CONCLUSIONS: Using principles from qualitative research and software development, we were able to develop and assess the efficacy of a web-based data visualization tool for tuberculosis management.

ONLINE TUBERCULOSIS KNOWLEDGE BASE

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BACKGROUND: Practitioners are frequently aware of gaps in knowledge and face uncertainty in clinical decision-making. Point-of-care (POC) questions may result in referral to a specialist—especially when a condition is uncommon or has a broad differential diagnosis (e.g. tuberculosis), self-guided inquiry, or not finding replies to the question. Self-guided inquiries to online resources or primary sources can provide answers, but responses are often long, fail to address the clinical context, and are not adaptable to local practice. The Mayo Clinic Center for Tuberculosis developed a tool to guide clinicians managing tuberculosis.

METHODS: The Online Tuberculosis Knowledge Base is a comprehensive Internet POC application allowing practitioners to access various information sources in reply to queries that arise in clinical practice. (https://kb.centerfortuberculosis.mayo.edu/tb/home.aspx). The application gives POC direction and provides a central repository linking to existing tuberculosis resources, and promotes consultation with CDC Regional Training and Medical Consultation Centers.

RESULTS: Since the launch of the Tuberculosis Knowledge Base, the site has had over 17,000 page views, and 1,500 users. Users originated primarily from the US, but also from several countries in Europe, Asia and Canada.

CONCLUSION: The Tuberculosis Knowledge Base aligns to the specifications of clinical decision support systems developed by WHO. Currently, there are over 65 topics related to tuberculosis and more will be added to increase the value to clinicians worldwide. Future adaptations can include interactive features using patient-specific data. The tool can be adapted for use in conditions other than tuberculosis.

THE IMPACT OF DIGITAL HEALTH TECHNOLOGIES ON TB TREATMENT COMPLETION: A SYSTEMATIC LITERATURE REVIEW

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BACKGROUND: Tuberculosis programme managers are capitalizing on the diffusion of affordable mobile electronic devices to address critical challenges in tuberculosis care. We reviewed the literature for studies of effects on tuberculosis treatment outcome attributable to three digital technologies suitable for large-scale implementation: short message service (SMS), video directly-observed therapy (VDOT) and electronic medication monitors (e.g., digital pill dispensers).

METHODS: MEDLINE/PubMed, EMBASE, the Cochrane Library of trials, Web of Science, clinicaltrials.gov and Global Health were searched in July 2016 for the effect of digital health on cure or treatment completion of active tuberculosis. Given a dearth of published studies the search was extended to unpublished literature. Seven geographically-diverse studies that included control groups and provided summary effect estimates were eligible for full review.

RESULTS: Four randomized controlled SMS trials showed no statistically-significant effect on cure or treatment completion when compared with local standard TB care. Two observational studies of VDOT reported risk ratios for treatment completion of 1.02 and 1.47 (neither statistically- significant). For medication monitors, one observational study reported an effect on cure (risk ratio=2.3, 95%CI: 1.6-3.4) and one randomized controlled trial reported no statistically- significant effect.

CONCLUSIONS: Despite interest in applying digital technologies in tuberculosis care, effects have been variable and evidence from implementation studies remains sparse. However, evidence suggests that these technologies might be at least as effective as standard care. Data from ongoing and future research, including non-inferiority studies, need to promote practical approaches to optimizing interventions, such as using interactive SMS and blending technologies to achieve large-scale impact.

ESTIMATING THE BURDEN OF ACTIVE TUBERCULOSIS IN LONG-TERM CARE FACILITIES IN ONTARIO USING DATA COLLECTED FOR REPORTABLE DISEASE SURVEILLANCE, 2006 TO 2015

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BACKGROUND: Ontario long-term care facility (LTCF) residents must be screened for tuberculosis (TB) within 14 days of admission or have had a TB screen within the last 90 days. Screening all new LTCF admissions has considerable resource implications for health system partners. Estimating the burden of active TB within LTCFs will help assess whether this resource-intensive screening approach is ideal.

METHODS: Data from the integrated Public Health Information System (iPHIS), Ontario's reportable disease management and reporting database, were used to estimate the TB burden among LTCF residents between 2006 and 2015. TB case addresses were matched with addresses listed for all operating LTCFs in Ontario. Other data fields searched were: risk factors, where TB treatment was initiated, and various free-text comment boxes.

RESULTS: Between 2006 and 2015, 6495 TB cases were reported in Ontario. Among these, 77 cases were identified as potential LTCF residents, representing 1.2% of all Ontario TB cases diagnosed. Sixteen of 36 public health units had one or more TB cases in potential LTCF residents. Toronto had the majority of these cases (44/77; 57.1%).

CONCLUSION: This analysis demonstrated that a small proportion of active TB cases reported in iPHIS potentially occur in LTCF residents. Due to iPHIS data limitations, the true number of TB cases in LTCF residents may differ. Conducting chart reviews of these TB cases in potential LTCF residents could produce more accurate burden estimates. The low proportion of TB cases among LTCF residents suggests the current screening approach for LTCF admissions may not be ideal.

SIX YEARS OF MONITORING TB TREATMENT WITH VIDEO DIRECTLY OBSERVED THERAPY (VDOT) IN THE U.S. AND MEXICO: HOW DID IT WORK?

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BACKGROUND: Directly observed therapy (DOT) for tuberculosis (TB) treatment monitoring reduces mortality, disease transmission, and acquired drug resistance. However, resource limitations and patient burden create barriers to DOT limiting its use. Observing patients taking anti-TB medications using videos made and sent via smartphones, called "Video DOT" (VDOT), could overcome these barriers; however, rigorous evaluations of VDOT are needed.

METHODS: VDOT demonstration projects, including one comparing treatment observation rates by VDOT versus in-person DOT, were conducted through TB control programs in the U.S. and Mexico. The U.S. sites included four urban and two rural counties; one of two Tijuana, Mexico sites targeted HIV-positive TB patients. TB patients age >18 years-old who had >30 treatment days of anti-TB treatment remaining were invited to participate. Participants were interviewed before and after using VDOT to assess sociodemographics, behavioral risk factors, and perceptions of VDOT. All participants had some prior in-person DOT experience. Proportions of expected doses actually observed and patient treatment perceptions were assessed.

RESULTS: In 2010-2016, 365 U.S. and 24 Mexican participants were enrolled and used VDOT for 5.5 months on average (range: 1-13); age range was 18-87 years. The mean proportion of expected doses observed was >90% across sites; patient perceptions were mostly positive; and providers generally agreed that VDOT was feasible and cost less than in-person DOT. No differences were observed between urban and rural or U.S. and Mexico sites.

CONCLUSIONS: VDOT was effectively implemented in a range of TB control programs and could be a cost-saving complement to in-person DOT.

DEVELOPING A TOOLKIT FOR TB PROGRAMS TO IMPLEMENT EDOT

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BACKGROUND: Directly observed therapy (DOT) is the most effective strategy for ensuring that tuberculosis (TB) patients
adhere to treatment. However, because DOT can be time and resource intensive, there is interest in alternative, cost-efficient methods of delivering DOT for both TB disease and latent TB infection. The Communications, Education, and Behavioral Studies Branch at the CDC Division of Tuberculosis Elimination (DTBE) developed an eDOT toolkit to aid health departments in implementing this activity.

METHODS: The systematic health education process was used to develop the materials (i.e., needs assessment, development, pilot testing, implementation, and assessing effectiveness). During the needs assessment phase, a questionnaire was provided to participants attending the 2015 National TB Controllers Conference to assess interest in the project and to identify potential topics and format for the toolkit. To identify key information to include in the toolkit, site visits and telephone interviews were conducted with TB programs that currently have an eDOT program.

RESULTS: Using the results, a web-based toolkit was developed. Topics include an introduction to eDOT, steps for implementing an eDOT program, and sample forms, policies, and protocols. The toolkit will be available on the DTBE website and marketed to TB programs. The toolkit will be a living document on the website and updates to the toolkit will continue after implementation.

CONCLUSIONS: eDOT is an additional strategy to help TB patients adhere to treatment. Using the systematic health education process ensured the development of an effective educational tool to meet the needs of the target audience.

DIGITAL HEALTH TECHNOLOGIES FOR THE TREATMENT OF LATENT TB INFECTION: A COST- EFFECTIVENESS ANALYSIS

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BACKGROUND: Digital technologies, e.g. short message service (SMS), video observed therapy (VDOT) and electronic medication monitors (MM), are in early stages of application to TB treatment. Our objectives were to estimate cost, effectiveness and cost effectiveness relative to standard self- administered treatment, of 2-way SMS, VDOT, and MM to enhance adherence to isoniazid for latent TB infection (LTBI) in Brazil, a high-burden setting with widespread access to mobile technology.

METHODS: We developed a decision analysis model to simulate two cohorts with LTBI: 1) an unselected group, and 2) close contacts of persons with active TB. Model inputs including estimates of effectiveness for digital interventions were derived from published literature, using Brazilian reports and costing data whenever available. The analysis used a 20 year time frame, with 3% discounting. Costs (2016 US dollars) were estimated from the health system perspective.

RESULTS: Refer to Table 1.

CONCLUSION: For unselected persons with LTBI, all three technologies appear poorly cost-effective, despite potential gains in treatment completion. For close contacts, two-way SMS communication may be cost-effective. Until VDOT and electronic monitors become substantially cheaper, they will also be poorly cost-effective for contacts.

Table 1

	Treatment completion (%)	TB cases per 1000 persons	Cost per 1000 persons ($)	Cost per case prevented ($) relative to standard care
Unselected persons with LTBI				
Standard care	63%	1.66	$49,640	-
SMS	92%	0.37	$129,520	$61,784
VDOT	75%	1.15	$384,160	$646,865
MM	75%	1.15	$400,600	$678,657
Close contacts				
Standard care	63%	15.9	$55,600	-
SMS	92%	3.0	$130,550	$5,821
VDOT	75%	10.8	$388,140	$64,562
MM	75%	10.8	$404,580	$67,754

INNOVATING METHOD TO MONITORING HIV/TB CO-INFECTION TREATMENT IN A U.S.-MEXICO BORDER CITY: VIDEO- TAES PILOT STUDY

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BACKGROUND: Adherence and completion of TB and HIV treatment is critical to improve the survival of people with HIV co-infected with TB (PWHIV/TB). Several, factors such as treatment length and patient burden contribute to high rates of treatment abandonment in Mexico — the leading cause of Multi/Extensively Drug Resistant TB (M/XDR-TB). Thus, innovative strategies to improve prevention and completion of TB treatment and adherence to ARVs are needed to reduce morbidity and mortality among PWHIV/TB. This pilot study proposes to evaluate Video Direct Observed Therapy (VDOT) effectiveness to monitor TB treatment among PWHIV/TB.

METHODS: This study that has been conducted since April 2016 in Tijuana, Mexico. PWHIV/TB aged ≥18 years and with
oral TB medications prescribed were eligible to participate in this pilot study. Participants are using VDOT until they complete their TB treatment (> 6 months). Adherence rate is calculated as the proportion of observed doses to expected doses.

RESULTS: We have enrolled 15 participants, 14 are active using VDOT and one has successfully completed TB treatment. Overall, 12 are men and mean age is 32.4 (SD=6.84). Five participants have <1 year with HIV diagnosis, six between 1- 5 years and four >5 years; and 93% (n=14) are taking ART. Pulmonary TB is reported in 9 participants and one has DR-TB. Adherence rate is 87% and in general, participants have expressed the convenience of the VDOT system.

CONCLUSION: High adherence has been observed in these preliminary results and VDOT seems to be a good method to improve TB treatment adherence among PWHIV/TB.

A TALE OF TWO DISEASES: A DESCRIPTIVE STUDY COMPARING TWO HASHTAGS

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BACKGROUND: The advent of internet and social media (SM) has revolutionized communication. HIV advocacy and communication has quickly proven instrumental in increasing funding and raising awareness. SM provides infinite potential in promoting awareness. Our study aims to understand the potential relationship between funding allocation and SM advocacy.

DESIGN/METHODS: Our SM platform was Twitter, which allows users to post "tweets": 140 character long messages with hashtags (#) containing a topic next to it (e.g. #tuberculosis). Searches can be completed for specific hashtags to enumerate the number of related tweets and participants following. Utilizing Symplur, a website that collects information on healthcare based hashtags, we compared #tuberculosis and #HIV from 01/01/2015-06/31/2016. For these hashtags, we searched the number of tweets per month and the number of participants tweeting. SM usage and trends were compared using Excel and synthesized within the context of funding.

RESULTS: From Jan 2015-June 2016, we identified 1,178,861 #HIV tweets compared to 103,177 #tuberculosis tweets. Hence, twitter users were 11.4 times more likely to tweet about HIV than TB. In 2016, the Global Fund disbursed $4,768,197,743 for TB versus $16,431,420,966 in funding for HIV. Although up 6% for HIV and 7% for TB from 2015, 3.45 times more funding was allocated for HIV than TB.

CONCLUSION: We highlight a tremendous missed opportunity for TB advocacy that could improve TB funding allocation. SM has great advocacy potential and could dramatically strengthen the voice of TB. Data on message timing, ideal SM platform, and message quality should inform these efforts to maximize impact.

DIGITAL HEALTH TECHNOLOGIES FOR THE TREATMENT OF ACTIVE TB: A COST–EFFECTIVENESS ANALYSIS

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BACKGROUND: Ensuring adherence using directly observed therapy (DOT) – the gold standard for tuberculosis treatment monitoring – remains a major challenge. Video-observed therapy (VDOT) via smartphone video, and medication monitors (MM) which send text (SMS) reminders to patients and providers when pill bottles are not opened, could help support DOT. Objectives were to estimate the cost, effectiveness and cost effectiveness of VDOT and MM relative to DOT in treatment of active TB in Brazil – a high-burden setting with widespread access to mobile technology.

METHODS: Cohorts of drug-sensitive (DS) and multidrug-resistant (MDR) TB patients were simulated in decision analysis models that compared VDOT and MM with standard DOT. Estimates of effectiveness were obtained from published literature: MM may improve treatment success rates, while VDOT does not. Treatment outcomes and cost inputs were obtained from Brazilian data. The analysis was conducted from the health system perspective, and followed patients over three years from treatment initiation. Costs were expressed in 2016 US$.

RESULTS: VDOT led to cost savings of 39% ($348.26) per patient for DS-TB and 19% ($1302.55) per patient for MDR-TB relative to standard DOT, with similar treatment outcomes. MM was estimated to improve cure rates from 71% to 83% for DS-TB and from 59% to 75% for MDR-TB, with minimal cost savings: 2.5% ($23.05) for DS-TB and 1.1% ($71.99) for MDR-TB.

CONCLUSION: VDOT is likely cost saving, and can potentially replace some or all standard DOT visits for active TB. MM may also replace DOT visits; it could improve cure rates, but with minimal, if any, savings.

EVALUATION OF THE COMPLETENESS OF NONCOUNTABLE TUBERCULOSIS CASE REPORTING, NATIONAL TUBERCULOSIS SURVEILLANCE SYSTEM, UNITED STATES, 2010–2014

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BACKGROUND: To avoid duplicating tuberculosis (TB) case reports, CDC's National Tuberculosis Surveillance System (NTSS) instructs reporting areas to exclude from official case counts persons who received TB treatment initially in another country, who were counted by another NTSS reporting area, whose TB disease recurred <12 months after completing TB therapy, or who left the United States (U.S.) before completing 90 days of treatment. These noncountable TB cases present a substantial burden on health departments, but are not reflected in national TB funding allocations.

METHODS: To measure the noncountable TB burden, NTSS areas began voluntary reporting of noncountable TB cases in 2009. We analyzed noncountable TB cases reported during 2010–2014. We surveyed NTSS surveillance staff in 2015 to determine attitudes and practices toward reporting noncountable TB cases.

RESULTS: Of 54,067 TB cases reported to NTSS, 1,720 (3.2%) were noncountable; 47 (78%) areas reported at least one noncountable TB case. Of 34 (57%) survey respondents, 23 (68%) had additional noncountable TB cases in their surveillance system that were not reported to NTSS. Eleven (32%) respondents stated that completing the data collection form for noncountable cases was itself burdensome and not worthwhile because these cases are not considered for TB funding.

CONCLUSION: To better capture the true burden of caring for all U.S. TB cases and to appropriately allocate TB resources, reporting areas should report all noncountable TB cases to NTSS. A streamlined reporting system to facilitate submission of noncountable TB cases might encourage more reporting areas to submit these data.

ETHICAL CHALLENGES IN THE IMPLEMENTATION OF NEW TB TECHNOLOGIES: AN EMPIRICAL STUDY OF TB STAKEHOLDER PERSPECTIVES

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BACKGROUND: The introduction of new tuberculosis drugs (e.g., bedaquiline) and diagnostics (e.g., Xpert MDR/RIF) into existing TB programs raises a host of ethics challenges that have not been examined empirically. We present the main results from a qualitative study that examined stakeholder perspectives concerning key ethics challenges associated with emerging TB technologies and how they should be addressed.

METHODS: We conducted semi-structured interviews with an international group of healthcare workers, advocates, funders, and policy makers working in TB. Interviews lasted approximately one hour, were audio recorded, transcribed, and coded using NVivo 11. Using Braun and Clarke's thematic analysis method, we developed a shared codebook, coded the interviews, and met regularly to develop themes and discuss analytic discrepancies.

RESULTS: We identified five themes: (1) inequity in access, e.g., challenges national TB programs face when implementing new technologies; (2) underlying power dynamics, e.g., the role of philanthropy in shaping the adoption of new technologies; (3) balancing the risks and benefits of new technologies, e.g., navigating the limited availability of safety data for bedaquiline with the need for new drugs in treating M/XDR-TB; (4) challenges to solidarity amongst TB stakeholders, e.g., global TB community not listening to the expressed needs of those in high-burden countries; and (5) stakeholders' perceived responsibilities, e.g., who is responsible for growing the R&D pipeline.

CONCLUSION: Respondents agreed that the development of new diagnostics and drugs is long overdue but that the successful implementation of technologies requires addressing the complex background ethics challenges, as identified above, faced by high-burden countries and vulnerable populations.