

END TB

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Abstracts for Oral Presentation

Cost-Effectiveness of Triage of Persons with Tuberculosis Symptoms by Artificial Intelligence-Based Chest X-Ray Interpretation in Karachi, Pakistan

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Association of Test Results and Other Characteristics with LTBI Treatment Outcomes

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Assessing Catastrophic Cost in MDR-TB Patients in Guyana

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Time to Development of Secondary Tuberculosis: A Retrospective Cohort Study Using Whole Genome Sequencing in British Columbia, Canada

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Use of Syndromic Surveillance Data to Locate Lost Tuberculosis Patients and Facilitate Return to Care in New York City

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Civil Surgeon Latent TB Infection Reporting in California

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A. MDR-TB

A1. THE EPIDEMIOLOGY OF DRUG-RESISTANCE TUBERCULOSIS IN MASSACHUSETTS, 2009-2018

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BACKGROUND

Drug-resistant tuberculosis (TB) has been increasing across the world and in some parts of the United States where a significant proportion of the population is foreign-born. We sought to clarify the number of cases of drug-resistant TB in Massachusetts in the past decade, any trend in drug resistance over this period, and epidemiologic predictors of drug resistance.

DESIGN/METHODS

In collaboration with the Massachusetts Department of Public Health (MDPH) we used TB surveillance data from 2009 to 2018 to create a data set of all culture-confirmed cases of TB in this period with available drug-resistance testing for isoniazid and rifampin (N = 1,507). Potential epidemiologic predictors of drug resistance that differed between drug-susceptible and drug-resistant individuals at a significance level of $p \leq 0.2$ were assessed in multivariate logistic regression models.

RESULTS

From 2009 to 2018 we found evidence for 32 cases of multi-drug resistance and 158 cases of isoniazid resistance without rifampin resistance. In the multivariate model only four variables were associated with drug resistance (or lack thereof): increasing age (by decade) at TB diagnosis (OR 0.80, CI 0.73-0.88, $p < 0.001$), prior TB treatment (OR 3.04, CI 1.64-5.61, $p < 0.001$), White race (OR 0.60, CI 0.41-0.89, $p = 0.01$), and year of TB diagnosis in order of most distant to most recent (OR 1.06, CI 1.00-1.12, $p = 0.04$).

A2. PREVALENCE OF DRUG RESISTANCE AMONG PATIENTS WITH SMEAR-POSITIVE PULMONARY TUBERCULOSIS IN TANZANIA, 2017-2018

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BACKGROUND

Anti-tuberculosis (TB) drug resistance (DR) is a major public health concern worldwide. A nationally-representative drug resistance survey was conducted in Tanzania to determine the prevalence of DR-TB and associated risk factors among patients with sputum-smear positive pulmonary TB.

METHODS

All individuals with sputum-smear positive TB, including previously treated, were eligible for enrolment during June 2017 – July 2018 at 45 selected facilities. Additional sputa were collected and tested using the GeneXpert MDR/RIF[®] assay, culture, and drug susceptibility testing on Loweinsten-Jensen media. We used multiple imputation model to estimate DR-TB prevalence and multivariate logistic regression to assess factors associated with DR-TB.

RESULTS

Out of 1,557 enrolled individuals, 1,270 (82%) had M. tuberculosis positive sputum, including 1,151 (91%) new and 119 (9%) previously treated; 307 (24%) were HIV positive. The prevalence of rifampin-resistant TB was 1.5% (95% confidence interval (CI): 0.7-2.2), including 0.9% (95%CI: 0.3-1.5) among new and 7.0% (95%CI: 2.0-11.9) among previously treated persons. Previous history of TB treatment (odds ratio=8.2 (95%CI: 3.2-21.2)) was significantly associated with rifampin resistance. The prevalence of multidrug-resistant (MDR)-TB (TB with resistance to at least isoniazid and rifampin) was 1.2% (95%CI: 0.6-2.0); 0.8% (95%CI: 0.4-1.6) among new and 4.6% (95%CI: 1.5-10.5) among retreatment patients. No cases with extensively drug-resistant (XDR)-TB, or pre-XDR-TB were identified.

CONCLUSION

The estimated prevalence of drug resistance in Tanzania is low compared to other sub-Saharan countries. The prevalence of MDR-TB among new TB cases (0.8%) was slightly lower compared to the results of a previous survey (1.1%) conducted in Tanzania in 2007.

A3. IMPACT ASSESSMENT OF THE GXALERT ON LINKAGE OF DRUG-RESISTANT TUBERCULOSIS PATIENTS' SPECIMEN TO FURTHER TESTING AT THE NATIONAL TUBERCULOSIS REFERENCE LABORATORY UGANDA

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BACKGROUND

According to the Global Tuberculosis Report (2018), Uganda is listed among the 30 highest Tuberculosis (TB)/human immunodeficiency virus (HIV) infection-burdened countries. Despite increases in the notification of TB, progress in closing detection and treatment gaps is slow. The findings by the World Health Organization indicate that only 2.0 million of the 6.7 million individuals diagnosed and notified with TB were tested for Rifampicin resistance (RR), an indicator that other anti-TB agents were most likely not tested for at all.

METHODS

The study was conducted between January and March, 2019, at the National Tuberculosis Reference Laboratory (NTRL). Data concerning the notified RR patients within the period between January 2014 and December 2015 were imported from the GxAlert database. Data on details of referral were then imported from the NTRL-Laboratory Information System database and entered into a record book.

RESULTS

The health facilities were grouped into regions, basing on the latest map of Uganda describing the regional distribution by district. Only 240 (73.39%) of the notified RR patients had had their samples sent to the laboratory setting for baseline culture and had undergone subsequent drug susceptibility testing. The average time taken to refer the samples from the RR patients to the NTRL was found to be 19 days.

CONCLUSION

There was more than 55% rise in notified Rifampicin resistant patients in 2015 probably due to the procurement of more GeneXpert machines and installation of the GxAlert software on these machines. This resulted into capturing of more patients with Rifampicin resistance among the diagnosed patients.

A4. **ASSESSING CATASTROPHIC COST IN MDR-TB PATIENTS IN GUYANA**

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BACKGROUND

One of the three main targets of the End TB strategy, 2016-2035, states that no patient or household should experience catastrophic cost due to TB. In 2019, the World Health Organization reported unknown number of patients facing catastrophic cost for TB in Guyana. However, other evidences suggest that in low and middle income countries approximately US\$55 to US\$8198 is spent on diagnosis and treatment of TB, which leads to impoverished households.

METHODS

A cohort retrospective study was done using all MDR-TB patients registered in 2018 by data extraction from medical charts and short interviews, mainly to estimate the proportion and value of patients who experienced catastrophic cost. Catastrophic cost was defined as total TB care costs exceeding 20% of annual household income. Values for $\alpha=0.05$.

RESULTS

Of 17 MDR-TB patients, mean age was 39.9 years with standard deviation of 12.101 years; 71% were males. With other variables reported as 58.9% of MDR-TB cases being new patients, 76.5 % as non urban residence, 11.8% homeless, 41.2% substance user, 58.8% employed, 5.8% HIV positive and 23.5% hospitalized. Average household earnings per annum of US\$2,364.00 and average direct cost (excluding food) due to TB of US\$204.00 were reported. Overall, 47% of the household faced catastrophic cost with significant results ($p=0.019$) in patients who faced hospitalization during treatment for MDR-TB.

CONCLUSION AND RECOMMENDATIONS

Despite free TB services in Guyana, almost half of the household with MDR-TB faced catastrophic costs. Similar study should be conducted in general TB patient group and further ascertain social consequences, coping strategies and expected remedy from patients' perspectives.

A5. **INJECTABLE AGENT-ASSOCIATED ADVERSE EVENTS AMONG PATIENTS WITH MULTIDRUG-RESISTANT TUBERCULOSIS IN NEW YORK CITY TUBERCULOSIS CLINICS**

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BACKGROUND

Although the World Health Organization no longer recommends injectable agents (IA) as first-line treatment for multidrug-resistant tuberculosis (MDR-TB), IAs may remain important options for patients who cannot tolerate other agents. We aim to describe the frequency of IA-related ototoxicity and nephrotoxicity among patients treated for MDR-TB at New York City (NYC) Health Department TB Clinics.

DESIGN/METHODS

We retrospectively studied patients treated for MDR-TB with regimens that included IAs during January 1, 2016-December 31, 2018. Data were extracted from clinic medical records and the NYC TB registry. Adverse reactions studied were clinical signs of ototoxicity, defined as a 20-decibel decrease at one frequency or a 10-decibel decrease at two frequencies, and nephrotoxicity, defined as a creatinine increase ≥ 1.5 times the pre-treatment baseline.

RESULTS

Of 31 patients on an IA, 17 (55%) received capreomycin, 7 (23%) received amikacin, and 7 (23%) received both. Mean duration of IA treatment was 196 days (SD ± 78.7). The mean age was 40.5 (SD ± 16), 19 (61%) were female, 17 (55%) were Asian race, and one (3%) was HIV positive. Of the 31 patients, 28 (90%) received ≥ 1 audiogram screening and 18 (58%) developed ototoxicity. Ototoxicity was more common among patients who received amikacin alone (6/7, 86%) than among those who received capreomycin alone (6/17, 35%). Nine (29%) patients developed nephrotoxicity; all had received capreomycin during treatment.

CONCLUSION

A high proportion of patients developed ototoxicity or nephrotoxicity. If IAs are used to treat MDR-TB, close monitoring to detect adverse events early is essential.

A6. MOLECULAR CHARACTERISATION OF SECOND LINE DRUG RESISTANCE CONFERRING MUTATIONS AMONG DRUG RESISTANT TUBERCULOSIS SAMPLES REFERRED TO THE NATIONAL/SUPRANATIONAL TUBERCULOSIS REFERENCE LABORATORY FOR THE SECOND LINE PROBE ASSAY; JUNE 2017-JULY 2019 UGANDA

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BACKGROUND

In East Africa, there are no nationwide screening studies published so far to establish aminoglycoside and fluoroquinolone resistance among drug-resistant Tuberculosis (DR-TB) isolates. The purpose of this study was to evaluate the second line drug mutation characteristics of drug resistant Mycobacterium tuberculosis (M. Tuberculosis) isolates referred to the National TB Reference Laboratory (NTRL) since the inception of the second line probe assay in Uganda.

METHODS

In a retrospective study performed at the NTRL in Kampala, extraction and review of data of the DR-TB patients qualifying for Second Line LPA between the periods of June 2017 to July 2019 was performed and results analyzed.

RESULTS

570 clinical M. tuberculosis strains were identified as drug-resistant using first line DST, including 18% (100) single drug-resistant (SDR) and 82% (470) multidrug-resistant (MDR) strains. The predominant mutations conferring resistance to fluoroquinolones were found in the gyrA A90V locus. The highest frequency of resistance to aminoglycosides was observed in both rrs gene A1401G mutation and eis gene C14T mutation. The number of patients diagnosed with resistance to any arm of drugs was found to increase steadily by $\geq 50\%$ since June 2017. The isolates with second-line drug resistance defined as extensively drug-resistant TB (XDR-TB) by the Line Probe Assay were 1.58% (09/570), with 44.44% (4/9) attributed to isolates referred from Uganda over the course of the study period.

CONCLUSION

The study findings generally predict the emergence of XDR-TB in the near future given the gradual rise of Pre-XDR TB if precise screening and patient centered treatment is not embraced.

A7. TIME TO SPUTUM CULTURE CONVERSION AMONG MULTI-DRUG-RESISTANT CASES REFERRED TO THE UGANDA NATIONAL/SUPRANATIONAL TUBERCULOSIS REFERENCE LABORATORY BETWEEN JUNE 2017 AND DECEMBER 2018

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BACKGROUND

Drug-resistant tuberculosis (DR-TB), especially multi-drug-resistant Tuberculosis (MDR-TB), is a serious medical problem in Sub-Saharan Africa due to the co-epidemic of human immunodeficiency virus infection. In Uganda, no nationwide studies have been conducted yet to demonstrate the time to sputum culture conversion among MDR-TB patients.

METHODS

A retrospective review was conducted on DR-TB patient data profiles contained in the Laboratory Information Systems for patients referred to the NTRL between June 2017 and December 2018; The data was cleaned and organized in Microsoft Excel before importation into STATA v14 for analysis. The analysis included Kaplan–Meier survival analysis across different patients’ variables and use of the chi square (Fisher’s exact test) and log-rank tests.

RESULTS

554 cultures were identified as MDR-TB upon retrieval from the database. Of these, 506 (91.3%) tested positive at baseline (month0), but only 504 met the eligibility criteria. 398 of the 504 (71.8%) were registered in archived entries, with the majority of cultures traceable to men (70.4%) compared to women (29.6%). The median age of the patients was 70 years with an interquartile range of 34 years. The sputum cultures of patients aged <20, 20–35, and >65 years took 1 month to convert from positive to negative compared to those from patients aged 36–65 years who took 2 months.

CONCLUSION

The time to sputum culture conversion among MDR-TB cases referred to the Uganda NTRL was found to be within 2 months for most cases and is in agreement with similar studies conducted elsewhere, with a few outliers.

A8. ETHIONAMIDE POPULATION PHARMACOKINETIC MODEL AND MONTE CARLO SIMULATION IN PATIENTS WITH MULTIDRUG-RESISTANT TUBERCULOSIS

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BACKGROUND

Published data on ethionamide (ETA) are limited. We present ETA pharmacokinetic (PK) data combined from several countries.

MATERIALS AND METHODS

Healthy volunteers and MDR-TB patients from 3 continents were included. Monolix 2019R1 (Lixoft), and the mlxR 4.0.6 package in R software were used. We simulated 10,000 patients receiving total doses of 750, 1000, 1250, 1500, and 1750 mg/day. Target attainment (TA) analyses were done for free area under the concentration-time curve from 0 to 24 hr to minimum inhibitory concentration ratio ($fAUC/MIC$). The breakpoint was set at 90% for the highest MIC. We assumed ETA unbound fraction of 70%.

RESULTS

15 healthy volunteers and 159 patients were included, with 1,106 plasma samples. Median (range) age was 40 years (17-80) and 119 (68%) were men. A one-compartment model with first order absorption and lag time (T_{lag}) was used. The final mean parameter estimates (omega) were T_{lag} 0.52 hr (0.51), k_a 0.38 hr⁻¹ (0.08), V/F 54.0 L (0.72), and CL/F 47 L/hr (0.52). No covariates were significant. For $fAUC/MIC$ target of 10, the breakpoint was 0.5 mg/L for 750-1250 mg dosing regimen and 1 mg/L for 1500-1750 mg dosing regimen. For $fAUC/MIC$ of 56, none of the dosing regimens achieved 90% target attainment.

CONCLUSION

MCS showed that at least 1500 mg/day is needed to achieve 90% of TA at MIC of 1 mg/L for 1.0-log kill target, while the $fAUC/MIC$ target of 56 was not achievable even for doses up to 1750 mg/day.

A9. POPULATION PHARMACOKINETICS OF LINEZOLID IN TB PATIENTS: DOSING REGIMENS SIMULATION AND TARGET ATTAINMENT ANALYSIS

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BACKGROUND

We simulated several dosage regimens to determine the most effective linezolid dosing regimen with the lowest risk of toxicity.

METHODS

PK data were from 3 continents. Monolix (2019R1) and mlxR package (v4.0.0) in R software were used. We simulated 1000 TB patients: 300 mg QD, 450 mg QD, 300 mg BID, and 600 mg QD. We used $fAUC/MIC > 119$ as the PKPD target for optimal kill (EC_{80}). Protein binding was 31%. Probability of target attainment (PTA) was defined as 90% for the highest MIC. Trough concentration of ≥ 7 mg/L was the threshold for toxicity.

RESULTS

508 linezolid plasma concentrations were included from 104 patients with TB. The average age was 40 years. A one-compartment model with first-order absorption and elimination was used. The PK parameter estimates (omegas) were k_a 1.1 h^{-1} (0.54), V/F 37.9 L (0.08), and CL/F 6.02 L/h (0.36). Weight and CrCL were included in the model. The PKPD breakpoint was 0.125 mg/L for 300 mg QD regimen. The remaining regimens (450 mg QD, 300 mg BID, and 600 mg QD) had a breakpoint of 0.25 mg/L. The 300 mg BID regimen had the highest risk of toxicity; probability of achieving $C_{min} > 7$ mg/L was 41% compared to 10% in the 600 mg QD regimen.

CONCLUSION

At least 450 mg QD or 300 mg BID regimen is needed for MIC 0.25 mg/L. None of the simulated regimens achieved PKPD breakpoint of 0.5 mg/L or higher.

A10. OUTCOMES OF LATENT TUBERCULOSIS INFECTION (LTBI) FOR CONTACTS TO MULTIDRUG-RESISTANT TUBERCULOSIS (MDR TB), MINNESOTA, 2016–2019

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BACKGROUND

During 2016–2018, Ramsey County, Minnesota reported an outbreak of 13 cases of multidrug-resistant tuberculosis (MDR TB). Contact investigations (CIs) for 11 pulmonary cases identified 629 contacts in households, worksites, a nursing home, and an adult day center. CI goals were to evaluate all contacts and treat cases of active TB disease and latent TB infection (LTBI).

INTERVENTION/RESPONSE

We defined MDR LTBI as documented exposure to an infectious MDR TB patient and positive TB testing with no evidence of active TB. We recommended MDR LTBI treatment (i.e., nine months of daily fluoroquinolone) for contacts with new LTBI, previously untreated or inadequately treated LTBI, previous TB or LTBI adequately treated >10 years prior, and immunocompromised contacts regardless of TB testing results. We recommended two years of medical monitoring for contacts who refused or stopped taking MDR LTBI treatment or who completed treatment for active TB or LTBI within the previous 10 years.

RESULTS

We fully evaluated 396 (63%) contacts; 48 had previous positive tests, 67 had new positive tests, 16 were immunocompromised. Four contacts were diagnosed with active TB disease. We recommended MDR LTBI treatment for 122 contacts; 62 initiated treatment, 40 completed, 2 continue, and 20 did not complete due to side effects (13), non-adherence (5), or provider decision (2). No patients who completed MDR LTBI treatment developed active TB disease. Two patients who discontinued MDR LTBI treatment developed active MDR TB.

CONCLUSION

MDR LTBI treatment was effective at preventing progression to TB disease.

A11. SPATIAL HETEROGENEITY BETWEEN RIFAMPICIN-RESISTANT AND EXTENSIVELY DRUG RESISTANT-TUBERCULOSIS IN WESTERN CAPE, SOUTH AFRICA

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BACKGROUND

Methods to identify high burden areas of extensively drug-resistant tuberculosis (XDR-TB; resistance to rifampicin plus second-line drugs) are needed to limit emergence and spread. Whether XDR-TB is spatially different from rifampicin-resistant (either second-line drug susceptible or resistant) TB (RR-TB) has not been documented. We aimed to characterize the spatial heterogeneity of XDR-TB adjusting for RR-TB in the Western Cape (WC) Province in South Africa.

DESIGN/METHODS

TB patients were identified from routinely collected laboratory data from the WC National Health Laboratory Services between January 2012 and July 2015. We mapped the percentage of RR-TB cases with XDR-TB ("XDR-TB proportion") by subdistrict. We created inverse distance weighting heatmaps and did hotspot analysis of XDR-TB proportions in Cape Town at the clinic-level using Getis-Ord G_i^* .

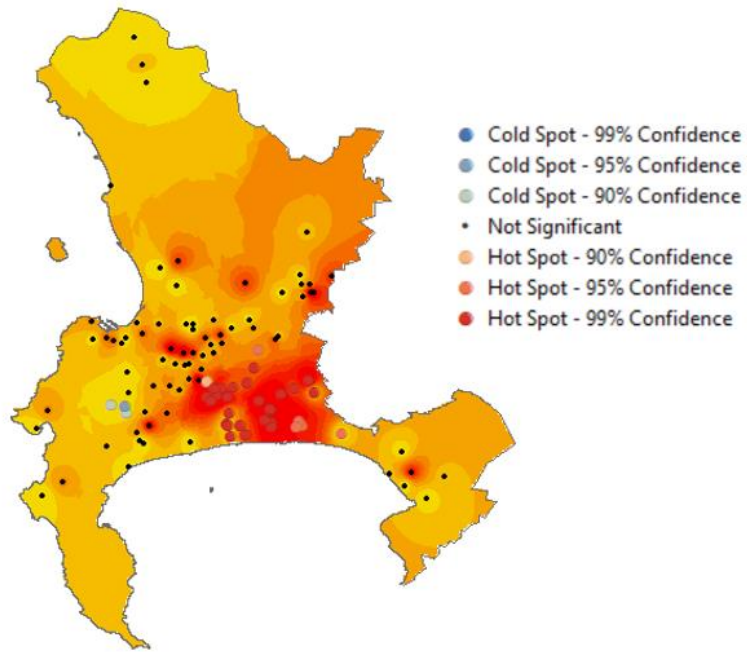
RESULTS

Of 93,619 TB patients, 6,986 (7.4%) were RR-TB, of which 6,301 (90.2%) were mappable to a clinic. Amongst those, 340 (5.4%) patients were XDR-TB. The XDR-TB proportion ranged from 0 to 10.5% across subdistricts, and from 0% to 42.9% within Cape Town clinics. Cape Town had 76.8% of all XDR-TB in the WC, which is greater than the 64.4% of all WC RR-TB patients and 64.2% of the total WC population in CPT. We detected significant heterogeneity across Cape Town (Figure 1). No biases were caused by small clinic sizes or proportion of RR-TB patients with second-line testing.

CONCLUSION/RECOMMENDATIONS

Our findings demonstrate spatial heterogeneity of XDR-TB proportions across subdistricts and within Cape Town. XDR-TB patients were also more concentrated in Cape Town relative to RR-TB patients and the general population.

Figure 1. Inverse Distance Weighting map and hotspot analysis of XDR-TB proportions in the city of Cape Town between 2012 and 2015 (dots indicate clinics)



B. CLINICAL

B1. **DIABETES AS A RISK FACTOR FOR TUBERCULOSIS IN HOSPITALIZED PATIENTS IN NEW JERSEY 2008-2017**

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BACKGROUND

Diabetes is a known risk factor for tuberculosis. Understanding the epidemiology of this association in New Jersey (NJ) can help identify approaches to tuberculosis control.

METHODS

A case-control study was carried out using discharge data from NJ's hospitals for the years 2008-2017. There were 4362 tuberculosis cases and 160,721 controls with primary discharge diagnosis of either deep venous thrombosis, pulmonary embolism, or appendicitis. Diabetes co-morbidity was extracted for all subjects. We explored the association between diabetes and tuberculosis, considering age-groups, gender, race, ethnicity, and time trends.

RESULTS

20.93% cases and 15.21% controls had diabetes. In subjects under 25 years, diabetes increased the tuberculosis risk nearly four times (OR=3.85; 95% CI= 1.94 7.66). From ages 35-64 years, diabetes almost doubled the risk. In older subjects (65+), the impact was relatively smaller (OR=1.35; 95% CI 1.20 1.52). No association was identified among those aged 25-34 years. Diabetic Asians had a greater risk of tuberculosis than diabetic Whites: OR=3.30 vs. 1.34; $p<0.05$. Association of diabetes and tuberculosis was higher among Hispanics than non-Hispanics: OR=1.89 vs. 1.43; $p<0.05$. In Blacks, diabetes was inversely associated with tuberculosis (OR=0.66; 95%CI 0.56, 0.78). The unadjusted odds ratio increased from 1.13 in 2012 to 1.92 in 2017 ($p=0.03$ for trend).

CONCLUSION

The increasing association of diabetes with TB may reflect secular changes in NJ demographics, management of control conditions, among other factors. Our findings suggest that efforts need to be directed at integrating diabetes and tuberculosis prevention and control strategies in NJ, especially in Hispanics, Asians, and subjects under 25 years.

**B2. DISSEMINATED BCG-DERIVED *MYCOBACTERIUM BOVIS*, ARKANSAS 2009-2019;
CANCER OF BLADDER CONNECTION**

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BACKGROUND

The Bacillus Calmette-Guérin (BCG) vaccine has commonly been used in intravesical immunotherapy for treating early-stage bladder cancer, since 1976. This therapy has the potential of leading to disseminated tuberculosis disease. In this study, we sought to describe this phenomenon in Arkansas over a ten-year period.

METHODS

Reviewed genotyping data from 2009-2019 to identify BCG derived strains. Genotyping and surveillance data were then linked to enable the description of the characteristics of the cases.

RESULTS

From 2009-2019, 12 cases, genotype G03731 (BCG strain), were reported in Arkansas. All the cases were males, age 59-88 years and all strains were PZA resistant. About 92% (11) of the study were white of non-Hispanic ethnicity. Approximately 42% (5) of the cases have died. The major sites of disease were pulmonary (5), abdominal aorta (2), bone marrow, and hip. Three of five pulmonary cases grew *M.bovis* from sputum. The interval between the last BCG instillation appointment and development of disease ranged from 3 weeks to 8 months. Two cases had no known connections with bladder cancer.

CONCLUSION

Disseminated disease due to BCG derived *M. Bovis* have severe consequences in our cases. CDC has advised against counting these cases based solely on reporting a BCG related strain in the National Genotyping database. This is clearly beyond colonization. Airborne transmission of this strain needs further study.

BCG immunotherapy protocol needs to be reviewed.

Engage oncologists and urologists about BCG derived *M. Bovis* in their patients.

Discuss counting of these cases with Division of Tuberculosis Elimination at CDC.

B3. INCIDENCE, TREATMENT, AND OUTCOMES OF ISONIAZID RESISTANT *MYCOBACTERIUM TUBERCULOSIS* (TB) INFECTIONS IN ALBERTA, CANADA FROM 2007-2017

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BACKGROUND

Isoniazid resistant TB (Hr-TB) is the most frequently encountered resistance phenotype in North America but limited data exists on the effectiveness of current therapeutic regimens. Ineffective treatment of Hr-TB increases patient relapse and anti-mycobacterial resistance.

DESIGN/METHODS

We undertook a multi-centre, retrospective review of culture-positive Hr-TB patients in Alberta, Canada (2007-2017). We assessed incidence and treatment outcomes, with a focus on fluoroquinolone (FQ)-containing regimens, to understand the risk of unsuccessful outcomes. Rates of Hr-TB were determined using the mid-year provincial population and odds of unsuccessful treatment was calculated using a Fisher's Exact test.

RESULTS

One hundred eight patients of median age 37 years (IQR: 26-50) were identified with Hr-TB (6.3%). Seven percent reported prior treatment. Rate of foreign birth (94%) was high, but continent of origin did not predict Hr-TB ($p=0.47$). Mean compliance was 95.3% with no difference between FQ and non-FQ regimens (94.7% vs 96.8%, $p=0.26$). Treatment success was high (91.8%). FQ-containing regimens were frequently used (72%), with a trend to higher rates of on-treatment death and treatment non-completion compared to the non-FQ group, though not reaching statistical significance (9.6% vs. 3.8%, OR 2.7, 95% CI 0.3-126.1, $p=0.35$). Notably, all unsuccessful FQ-based regimens were used less than 9 months ($p<0.01$).

CONCLUSION

Treatment success was high, with a trend towards unsuccessful outcome in patients receiving FQ-containing regimens for less than 9 months. Regimens excluding FQs remain a viable option considering the growing literature demonstrating adverse effects of FQs. Prospective, multi-centre studies are needed to further validate this and determine the optimal treatment for Hr-TB.

B4. **MEASURING HEALTHCARE DELAYS AMONG PRIVATELY INSURED TUBERCULOSIS PATIENTS IN THE UNITED STATES**

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BACKGROUND

TB diagnosis can be challenging due to its protean symptoms. A high index of suspicion is needed to initiate appropriate testing, yet US healthcare providers are becoming less familiar with the disease as rates decline.

METHODS

We conducted a retrospective observational cohort study among privately insured members between 2007-2016. Among patients with active TB based on diagnosis codes and receipt of anti-tuberculosis treatment, healthcare delays were measured as the time difference between the first healthcare visit for a symptom related to TB and the initiation of anti-tuberculosis treatment. We assessed if delays varied across time, different US states, and by patient and system variables.

RESULTS

Among 18,962,414 members, we confirmed 738 active TB cases. The median healthcare delay was 24 days (IQR 10-45). In multivariate regression, longer delays were associated with older age and immunosuppression, 8.4% per 10 years increase in age (95% CI 4%-13.1%, P<.01) and 23.8% increase with immunosuppression (95% CI 3%-55%, P=.04). Presenting with 3 or more symptoms at the first encounter was associated with shorter delays, -22.4% relative to presenting with one symptom (95% CI -2.0%--39.1%, P=.04). The use of chest imaging, a TB microbiological test, or care by a TB specialist was associated with shorter delays. Longer delays in care were associated with a higher rate of respiratory complications even after controlling for patient characteristics.

CONCLUSION

In the US, the median healthcare delay for privately insured patients with TB exceeds WHO recommended levels. Provider engagement and a more granular understanding of system contributors to delay are needed.

B5. TB OUTCOMES AMONG CONTACTS OF TUBERCULOSIS PATIENTS WITH DIABETES MELLITUS

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BACKGROUND

Diabetic tuberculosis patients are more likely to have severe symptoms, poor treatment outcomes, and an increased likelihood for post-recovery reactivation. Mathematical modelling suggests that reduction of diabetes incidence could have a significant impact on the tuberculosis epidemic trajectory. The relative transmissibility between diabetic and non-diabetic tuberculosis patients has not been quantified yet. Here, we evaluated the risk of tuberculosis outcomes among household contacts exposed to a diabetic tuberculosis patient using a cohort study conducted in Lima, Peru.

DESIGN/METHODS

Between 2009 and 2012, we enrolled 3,109 microbiologically-confirmed pulmonary index tuberculosis patients and their 12,767 household contacts. We evaluated the tuberculosis infection status of contacts at enrollment and measured TST conversion and incident tuberculosis disease over a one-year follow-up. We evaluated the associations between self-reported index diabetes and the tuberculosis outcomes of their contacts.

RESULTS

Among the 12,767 contacts, 676 (5.3%) were exposed to a diabetic tuberculosis patient. We found no evidence to support that index diabetes altered the risk of TB infection in contacts (aRR [95% CI] at baseline=1.07 [0.96-1.19], $p=0.21$; aHR for TST conversion=1.05 [0.77-1.45], $p=0.75$). Contacts exposed to a diabetic case were less likely to develop tuberculosis disease compared to those exposed to a non-diabetic case (aHR=0.33 [0.13-0.86], $p=0.027$).

CONCLUSION

We found that diabetes did not significantly impact the infectiousness of a tuberculosis patient. However, contacts exposed to a diabetic tuberculosis patient had reduced incidence of tuberculosis disease. Our results suggest that the potential impact of diabetes on the tuberculosis epidemic trajectory may be more complicated than what researchers had proposed.

B6. COUNSELING TO TUBERCULOSIS PATIENTS BY HEALTH WORKERS IN A TUBERCULOSIS HOSPITAL AND A GENERAL HOSPITAL

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BACKGROUND

A proper counseling is a must and a right of a patient. It helps the patients to understand the disease, how it spreads and the challenges during the treatment. Eventually, a proper counseling keeps the patient adhered to the treatment and stops the transmission.

METHODS

We interviewed 100 TB patients in the Out-Patient Department (OPD) of Regional Tuberculosis Center (RTC) and 9 TB patients Matrishu Miteri Hospital in Pokhara, Nepal in 2018 on the counseling they had received.

RESULTS

Out of 100 patients interviewed in RTC, 96 of them (96%) said that they were explained clearly about the signs and symptoms, side-effects of the drugs, follow-ups, nutritional needs and the consequences of not following the treatment protocol. Out of the 9 patients interviewed in Matrishu Miteri Hospital, 8 patients (88%) said that the information was not enough.

CONCLUSION

Due to various reasons, the health workers in general hospitals could not satisfy the needs of TB patients unlike the health workers in Tuberculosis hospital of Nepal. This describes the need of TB departments with skilled health workers in general hospitals for the patients deserve a minimum package of holistic TB care services.

B7. KNOWLEDGE AND ATTITUDE OF FAMILIES AND FRIENDS OF TB PATIENTS IN NEPAL ON TUBERCULOSIS

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BACKGROUND

The knowledge of Tuberculosis and the timely identification of positive cases can permit interruption of transmission. It is also essential that the contacts are aware of positive cases since the infectious period of this disease usually last about 12 weeks before the positive TB diagnosis or onset of symptoms. Likewise, strong support from relatives and friends is essential for adherence to the treatment.

METHODS

We interviewed 100 patients' relatives and friends who came with them in the Out-Patient Department (OPD) of Regional Tuberculosis Hospital, Pokhara, Nepal in 2017 before the start of treatment.

RESULTS

Out of 100 people interviewed, 22 (22%) had some knowledge about the disease, how it spreads and how the patient could have been infected. 79 of them (79%) were worried about the stigma that they must face in society. 15 of them (15%) knew about some adverse effects. All of them (100%) were concerned about the outcome of the treatment and relapse and hadn't realized that the TB patients will need their support during the treatment.

CONCLUSION

Nepalese society still holds the stigma against TB patients. There is a need to counsel the TB patients as well as their relatives and friends for the proper adherence to the treatment and positive outcomes. The TB campaign should be continued stronger than ever as we are committed in the fight to end TB as a public health problem by 2035.

B8. TUBERCULOSIS TREATMENT OUTCOMES AND ADVERSE DRUG EVENTS IN OLDER PATIENTS AT WEST PARK HEALTHCARE CENTRE, TORONTO, CANADA

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BACKGROUND

Life expectancy has increased globally, leading to an increase in TB incidence in older persons. However, data on TB treatment outcomes in this population is limited.

METHODS

Retrospective review of older (≥ 65 years) patients treated for TB at our institution from 2010-2018, with MDR-TB patients excluded. Patients were divided into 3 groups based on age at treatment initiation; (1) 65-69 years, (2) 70-79 years, and (3) ≥ 80 years. Demographic, clinical, and treatment characteristics were compared using chi-square and Kruskal-Wallis tests.

RESULTS

194 patients were included; 42, 72, and 80 in groups 1, 2, and 3, respectively. Overall, 108 (56%) were female, and 184 (95%) foreign-born, without difference between groups. 162 (84%) patients were hospitalized; 71%, 85%, and 89% in groups 1, 2, and 3, respectively ($p=0.047$). Most patients (55%) were treated for <12 months and achieved sputum culture conversion in ≤ 1 month (54/93, 58%), without difference between groups. Among patients receiving a particular drug, discontinuation for an adverse event occurred in 14% with INH, 19% with a rifamycin, 45% with pyrazinamide, and 15% with ethambutol; a difference was only seen with ethambutol, with discontinuation more common in group 1 ($p=0.036$). Treatment outcomes differed between groups ($p=0.020$); success was lower in group 3 (59%, versus 81% in groups 1 and 2), and death higher in group 3 (16%, versus 7% and 4% in groups 1 and 2).

CONCLUSION

Drug discontinuation due to an adverse event was common among older patients. Hospitalization and poor treatment outcomes were most frequent in the oldest patients.

B9. BREAST TUBERCULOSIS. DESCRIPTION OF 31 CASES WITH ETIOLOGICAL CONFIRMATION OF INFECTION WITH MYCOBACTERIUM TUBERCULOSIS COMPLEX.

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BACKGROUND

Breast tuberculosis is a rare manifestation of extrapulmonary tuberculosis. Diagnosis of this condition is usually challenging.

METHODS

From February to September 2019, 34 women who sought the outpatient clinic with mastitis for longer than 1 month and that did not respond to antimicrobial treatment were submitted to the following diagnostic protocol: 1) breast core needle biopsy and/or 2) microbiological investigation of secretions obtained by fine needle abscess aspiration, papillary discharge or breast fistula, using the MGIT and Myco/F lytic system (BD®), and if positive is submit to MPT64 protein by immunochromatography and/or 3) Real time DNA polymerase chain reaction for Mycobacterium tuberculosis complex (RT PCR-MTB) by Abbott®

RESULTS

22(65%) patients were white; Their median age was 38 years (IQR 34-42), and they reported median of 12 years of schooling (IQR 10-12). Median time interval between onset of symptoms and diagnosis was 8 months (IQR 5-18). Clinical presentations included fistulized breast abscesses (n=30) and papillary discharge (n=3) (One patient presented both symptoms). The Tuberculin skin test was negative for 17/25(68%) patients. Histopathological exams revealed granuloma in 12/20 cases and histiocytic/plasmocytic (8/20) cells. A acid fast bacilli were detected for 3 patients. RT PCR-MTB were negative in all 23 patients tested. MGIT cultures are negative so far. In contrast, 31/34 (91%) patients yielded Myco/F culture system isolation of M. tuberculosis complex within 15 days.

CONCLUSION

Collection of breast secretion and inoculation in the Myco/F lytic culture system are helpful diagnostic tools for breast tuberculosis and provide timely diagnosis within 15 days.

B10. COST-EFFECTIVENESS OF TRIAGE OF PERSONS WITH TUBERCULOSIS SYMPTOMS BY ARTIFICIAL INTELLIGENCE-BASED CHEST X-RAY INTERPRETATION IN KARACHI, PAKISTAN

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BACKGROUND

Artificial-intelligence (AI) based chest X-ray (CXR) analysis could assist the triage of persons presenting with possible TB symptoms, in settings without access to radiologists. However, there is limited evidence of the cost-effectiveness of triage using this technology.

METHODS

We developed a decision analysis model to evaluate the cost-effectiveness of AI-based triage strategies for patients presenting with symptoms suggestive of pulmonary TB in Karachi, Pakistan. These strategies were compared to the current standard of care using microbiological testing with a) smear microscopy or b) GeneXpert, without prior triage. Software diagnostic accuracy was based on a prospective study in Karachi. Other inputs were obtained from a Karachi hospital's TB clinic. The analysis was conducted from the health care payer perspective and costs were expressed in 2019 US\$.

RESULTS

Compared to diagnosis based on up-front smear microscopy, all triage strategies were projected to: 1) lower costs by 67% (from \$57,441 per 1,000 persons), and 2) lower false-positive empiric diagnoses by 93%-97% (from 365 per 1,000). With smear-based testing, empiric treatment is a key determinant of cost. Compared to diagnosis based on GeneXpert without triage, AI triage strategies 1) lowered costs by 5%-19% (from \$31,049 per 1,000), 2) averted approximately 7% additional disability-adjusted life years (DALYS) (from 407 per 1,000), 3) reduced missed diagnoses by 2%, and 4) reduced microbiologic tests by about 50%.

CONCLUSION

The addition of AI-based CXR triage before microbiologic testing for persons with possible TB symptoms can reduce costs and empiric treatment, and in some situations avert additional DALYs.

B11. LIFE AFTER TUBERCULOSIS: NOT ALWAYS BACK TO NORMAL.

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BACKGROUND

Left untreated tuberculosis may cause significant morbidity and mortality. In many instances adequate antimycobacterial therapy does not prevent chronic respiratory complications. Bronchostenosis is an under recognized complication with potentially grievous complications.

METHODS

Patients with evidence of bronchial stenosis and lung volume loss who were previously treated with pulmonary tuberculosis were included in our retrospective review. Patients were all found to be IGRA or TST positive with no microbiologic evidence of active infection.

RESULTS

4 patients qualified for our case series. This included 2 male and 2 females. Ages ranged from 24 to 75. All reported completing treatment for pulmonary tuberculosis. None exhibited evidence of active pulmonary tuberculosis. 3 patients noted chronic respiratory symptoms without any other identifiable etiology. 2 patients demonstrated bronchoscopic evidence of stenosis. 4 patients had radiologic evidence lung volume loss with hyperinflation of contralateral lung. One patient's symptoms improved after bronchoscopic dilation. One patient developed multiple recurrent infections distal to the stenosis. One patient developed pulmonary hypertension with evidence of cor pulmonale.

CONCLUSION

Bronchostenosis is a recognized complication of tuberculosis, which occurs despite appropriate therapy. Bronchostenosis is a frequent consequence of endobronchial tuberculosis which is observed in greater than a third of pulmonary tuberculosis cases. Clinicians should monitor for residual ventilatory impairment after treatment of pulmonary tuberculosis. If clinical scenario warrants, bronchoscopic evaluation may be required for identification and management of fibrotic changes. Further study is needed to ascertain the benefit of corticosteroids and extended RIPE therapy. Asymptomatic patients may be followed clinically.

B12. EVALUATION OF COMMUNITY PHARMACIES DISPENSING PATTERN AND PRACTICE OF ANTITUBERCULOSIS DRUGS IN NORTH KARNATAKA REGION

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BACKGROUND

Tuberculosis is a major global public health challenge. Over a quarter of recorded deaths were reported from India, which carries the largest burden of the disease, with increasingly high rates of MDR-TB. Infected individuals to seek care from a variety of local primary care providers.

DESIGN/METHODS

A cross sectional, prospective study was conducted at Belagavi, Karnataka, India. based on survey of pharmaceutical outlets in the locality. A structured interview form was used to assess availability and non-availability of Anti-TB drugs, dispensing Anti-TB drugs, Community pharmacist dispensing pattern of Anti-TB drugs in weekly and monthly basis.

RESULTS

A total of 228 community pharmacists participated in the Survey. Of these, 204 community pharmacists (90.35%) were male and 22 community pharmacists (9.65%) were female. The majority of 198 community pharmacists (86.84%) Diploma in Pharmacy (D.Pharm). 86 community pharmacies (37.72%) were dispensing Anti-TB drugs. The majority (37.04%) of the community pharmacies were expecting to dispense Anti-TB drugs for 2 to 3 tuberculosis patients monthly. Community pharmacies located near Government civil hospital, 108 to 137 tuberculosis patients seeking Anti-TB drugs monthly. 53 community pharmacies (61.62%) dispensing Anti-TB drugs through Private Physicians prescriptions.

CONCLUSION

Tuberculosis patients are neglecting where Revised National Tuberculosis Control Programme (RNTCP) facility for free treatment are available. Violation of the guidelines and regulations of dispensing Anti-TB potentially contribute to emergence of drug-resistant Mycobacterium tuberculosis. The community pharmacist should be encouraged to participate Directly observed treatment, short course (DOTS) program through RNTCP training.

B13. RISK OF TUBERCULOSIS IN PATIENTS PRESCRIBED MEDICAL IMMUNOSUPPRESSIVE THERAPIES IN BRITISH COLUMBIA, CANADA: RETROSPECTIVE COHORT STUDY

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BACKGROUND

Immunosuppressive (IS) therapies to treat medical conditions may diminish the body's defense against new and emerging infections, and are potential risk factors for relapse and reinfection of Mycobacterium tuberculosis (TB). We examined the relationship between IS therapies and TB in a large cohort of people who immigrated to British Columbia, Canada.

DESIGN/METHODS

We identified all foreign-born individuals who landed in Canada from 1996-2012, and became residents of BC up to 2013. We linked multiple administrative databases and provincial disease registries, and extracted data on demographics, immigration history, TB outcomes and comorbidities. We used multivariable extended Cox regression to determine the association of IS therapies (i.e. TNF- α inhibitors, high-risk DMARDs and high-dose steroids) and active TB.

RESULTS

Of 730,363 individuals, 3.8% were dispensed IS therapies, including: TNF-alpha inhibitors (n=1142 people); high-dose steroids (n=23822), and high-risk DMARDs (n=2775). The hazard ratio (HR) for TB was highest for people prescribed TNF-alpha inhibitors (adjHR=23.4, 95%CI:9.7,56.5), followed by DMARDs (adjHR=7.6, 95%CI:4.5,12.6) and steroids (adjHR=2.9, 95%CI:2.3,3.6), after adjustment for age at time of immigration, gender, TB incidence in birth country, immigration type, contact status, HIV, chronic kidney disease, and diabetes.

CONCLUSION

Active TB risk was increased following treatment with TNF-alpha inhibitors, high-risk DMARDs and steroids. This data supports the use of LTBI screening in patients starting therapy with TNF- α inhibitors and high-risk DMARDs. Given the high prevalence of steroid use in the population, and the low rate of TB, further study is needed to refine thresholds and populations at risk of TB before initiating mass screening.

B14. **FOOD INSECURITY IS ASSOCIATED WITH MENTAL DISORDERS AMONG TUBERCULOSIS PATIENTS IN BOTSWANA**

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BACKGROUND

Tuberculosis (TB) patients may experience food insecurity that reduces dietary quality and quantity and causes psychosocial stress, which may lead to mental illness. The aim of this study was to explore the role of food insecurity on depression and anxiety among newly diagnosed TB patients in Botswana.

DESIGN/METHODS

Our cross-sectional study assessed depression, anxiety, and food insecurity with Patient Health Questionnaire (PHQ9), Zung Anxiety Self-Assessment Scale (ZUNG), and Household Food Insecurity Access Scale, respectively, among participants at the time of TB diagnosis. Food insecurity was dichotomized as experiencing “food security or mild insecurity”, or “moderate to severe food insecurity”. Poisson regression models with robust variance were used to examine correlates of depressive symptoms (DS; PHQ9 ≥ 10) and anxiety symptoms (AS; ZUNG ≥ 45).

RESULTS

Between January and November 2019, 170 TB participants were enrolled from primary health clinics, of whom 92 were HIV-positive. Overall, 46 (27.1%) and 83 (49.1%) participants reported DS and AS, respectively, and 67 (39.4%) experienced moderate to severe food insecurity. After adjusting for age, HIV status, and gender, we found moderate to severe food insecurity was associated with a higher prevalence of DS (adjusted prevalence ratio [aPR] = 2.15; 95% confidence interval [CI] = 1.31, 3.53) and AS (aPR = 1.31; 95% CI = 0.97, 1.77). Similar findings were observed when restricting the analysis to HIV co-infected participants only.

CONCLUSIONS

Mental disorders are common among newly diagnosed TB patients, which may be affected by food insecurity and should be addressed in TB care interventions.

C. EPIDEMIOLOGY

C1. INVESTIGATION OF REACTIVATION OF LATENT TUBERCULOSIS AMONG PERMANENT RESIDENTS IN ALBERTA

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BACKGROUND

We hypothesize that latent tuberculosis reactivation risk remains constant and that high rates of TB early after immigration are explained by diagnosis of prevalent active disease or identification of subclinical disease via active surveillance.

METHODS

All TB cases diagnosed from 2000 to 2017 were identified in the Alberta registry. Using aggregate national data, we determined the number of permanent residents who arrived in Alberta during the same time period. We calculated incidence rates per 100,000 persons according to years since arrival, with and without exclusion of prevalent TB cases diagnosed within 6-months of arrival and cases diagnosed via post-immigration surveillance. We fitted Poisson regression models to investigate effects of age, sex, and county of origin on annual TB incidence.

RESULTS

There were 484,555 arrivals and 984 TB cases. The incidence in the first year of arrival was 76.6 per 100,000 and between 20-30 per 100,000 for subsequent years. When excluding prevalent and actively identified disease, the incidence rate in the first year decreased to 21.4 per 100,000 but remained unchanged in subsequent years. When examining the whole cohort, there was a statistically significant difference in the annual TB incidence, $p < 0.001$. This difference was absent after exclusion of prevalent and actively identified disease. Country of origin had the greatest effect on TB incidence post arrival with an IRR of 3.83 ($p < 0.01$) from the highest to lowest TB incidence in home country.

CONCLUSION

After accounting for cases not representing true latent TB reactivation, the incidence of tuberculosis among immigrants to Alberta is stable over time and mostly impacted by TB incidence in home country.

C2. **THE INCIDENCE AND RELATIVE INFECTIOUSNESS OF ASYMPTOMATIC (SUBCLINICAL) VS SYMPTOMATIC (ACTIVE) SMEAR-NEGATIVE PULMONARY TUBERCULOSIS: A POPULATION-BASED COHORT STUDY IN CANADA**

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BACKGROUND

Subclinical tuberculosis is a state where *M. tuberculosis* is viable and detectable but not associated with classical TB-related symptoms. Because little is understood about this state, we sought to compare the epidemiology, clinical characteristics, and transmissibility of subclinical vs active TB.

METHODS

Using public health and laboratory databases over a 12-year period beginning January 1, 2004, we identified all cases of smear-negative, culture-positive pulmonary TB (PTB) in Alberta. Subclinical cases were asymptomatic. Active cases had respiratory or constitutional symptoms. We identified transmissions using RFLP or MIRU-VNTR sequencing combined with conventional epidemiology and supplemented with whole genome sequencing. We used Poisson regression to compare the incidence of secondary cases in each group.

RESULTS

There were 464 smear-negative, culture-positive PTB cases, 136 (29%) were subclinical and 328 (71%) were active. Of active cases, 72% had cough. Of asymptomatic patients, 92 (68%) were diagnosed via immigration referral and 18 (13%) were diagnosed via contact tracing. Time to culture positivity did not differ (~18 days in both groups). Subclinical patients were younger (45 vs 49 years old) but there was no difference in sex, population group, HIV status, radiographic presentation, or number or age of contacts. There was one secondary case arising from a subclinical case vs eight arising from active cases. This difference was not statistically significant.

CONCLUSION

Based on our findings, subclinical disease has a similar bacillary burden and transmissibility capabilities as active disease. However, larger studies are required to establish whether subclinical cases require the same infection control and treatment regimens as active disease.

C3. **ECONOMIC BURDEN AND INCIDENCE OF CATASTROPHIC HEALTH EXPENDITURE OF HIV AND TB CARE IN ETHIOPIA.**

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BACKGROUND

Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) are major global health threats. The global effort increased access to care and saved more lives. Though many countries, including Ethiopia, offer “free” and “decentralized” HIV and TB services, such policies do not adequately provide realistic financial risk protection. Hence, we aim to estimate the household economic burden and incidence of catastrophic health expenditure (CHE) incurred by HIV and TB care across income quintile in Ethiopia.

METHODS

A cross-sectional study was employed in 27 health facilities of Afar and Oromia regions for TB, and data from nationwide household survey were used for HIV. Both direct and indirect patient costs were analysed from 1,006 HIV and 787 TB patient samples. Data analysis was done using STATA version 16. The incidence and intensity of CHE were calculated.

RESULTS

The mean age of HIV and TB was 39 (SD: 10), and 30 (SD: 14) years, respectively. Among HIV, 36% had illness, while 7% of TB cases were co-infected with HIV. The mean (SD) annual patient cost of HIV was \$ 91 (199) and \$ 115(118) for TB. The direct cost of HIV and TB constituted 68% and 46% of the total cost, respectively. The mean (SD) indirect cost was \$ 28(77) per year for HIV and \$ 63(83) per TB episode. The incidence of CHE for HIV was 22%; with 46% of the poorest and 6% of the richest income-quintile experienced CHE (Chi-square for trend -3.62, P <0.001). Similarly, for TB, the incidence was 40%; with 58% and 20% of the poorest and richest income-quintile experienced CHE, respectively (Chi-square for trend -6.79, P <0.001). This figure was higher for drug resistant TB (62%).

CONCLUSION

HIV and TB are causes of substantial economic burden and CHE for vulnerable individuals and households, mainly affecting those in the poorest income quintile. Broadening government benefit package to include strategies that reduce the substantial direct and indirect costs associated with HIV and TB care is urgently needed.

Keywords: TB, DR-TB, HIV, cost, economic burden, equity, catastrophic health expenditure, Ethiopia

C4. **MORTALITY RISK IN MIGRANTS COMPLETING TREATMENT FOR TUBERCULOSIS IN BRITISH COLUMBIA, CANADA, 1985-2015.**

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BACKGROUND

People diagnosed with tuberculosis (TB) have higher prevalence of risk factors that may increase this population's risk of mortality. In Canada, 75% of TB occurs among immigrants. Within the immigrant population of British Columbia (BC), we compared mortality risk among persons completing treatment for TB with non-TB controls.

METHODS

This retrospective cohort study used Canadian immigration data linked to BC health administrative data. All people immigrating to BC during 1985-2015 (N=1,082,234) were included with n=2,487 completing TB treatment in BC. People with TB diagnosed but incomplete treatment were excluded. Outcomes were time-to-mortality for the following causes of death: (1) all non-TB causes, (2) respiratory, (3) cardiovascular, (4) cancer, and (5) injury/poisoning. Age/sex-adjusted and covariate-adjusted Cox regressions were used, with a time-varying exposure variable for TB diagnosis. Individuals contributed both exposed and unexposed person-time. Exposed time means person-time after TB diagnosis date up to event or censoring date.

RESULTS

All non-TB-caused mortality: age/sex-adjusted HR=1.93 (95%CI: 1.72-2.17); covariate-adjusted HR=1.74 (95%CI: 1.55-1.96). Respiratory mortality: age/sex-adjusted HR=3.24 (95%CI: 2.41-4.36); covariate-adjusted HR=2.85 (95%CI: 2.11-3.86). Cardiovascular mortality: age/sex-adjusted HR=1.72 (95%CI: 1.39-2.12); covariate-adjusted HR=1.61 (95%CI: 1.30-1.99). Cancer mortality: age/sex-adjusted HR=1.74 (95%CI: 1.40-2.16); covariate-adjusted HR=1.50 (95%CI: 1.21-1.87). Injury/poisoning mortality: age/sex-adjusted HR=2.33 (95%CI: 1.59-3.40); covariate-adjusted HR=2.09 (95%CI: 1.42-3.08).

CONCLUSION

In any given year, if an individual was diagnosed with TB, their adjusted risk of non-TB mortality was 74% higher than if they were not diagnosed with TB. Post-TB-treatment chronic disease prevention and management are warranted. Prospective cohort studies of people diagnosed with TB are needed to understand morbidity and mortality within this population.

C5. **DIABETES MELLITUS AMONG TUBERCULOSIS PATIENTS IN NEW YORK CITY**

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BACKGROUND

Management of patients with tuberculosis (TB) is complicated by comorbidity with diabetes mellitus (DM).

DESIGN/METHODS

We conducted a retrospective analysis of patients diagnosed with TB in NYC to examine the prevalence of DM comorbidity and compare TB treatment outcomes of patients with and without DM. Cochran-Armitage was used to test for trend. DM was self-reported or obtained from medical chart reviews during routine TB case management efforts.

RESULTS

From 2013-2017, 18% (545/2,970) of TB patients in NYC had DM; 15% (66/453) among U.S.-born and 19% (479/2,514) among non-U.S.-born. The non-U.S.-born TB sub-populations with highest DM prevalence were Filipinos (37%, 56/150), Bangladeshi (33%, 45/137), Mexicans (25%, 44/178), and Chinese (14%, 78/574). DM prevalence increased only among Filipinos, from 21% in 2013 to 44% in 2017 ($p=0.05$). For patients eligible to complete TB treatment in <366 days, median days-to-completion was 272 [range:119-756] for patients with DM compared to 251 [range:113-740] for patients without DM ($p<0.01$). Of those with positive sputum culture, 58% (220/377) converted to negative within 60 days in patients with DM compared to 69% (968/1405) in patients without DM ($p<0.01$). When looking at country of birth as an independent factor for DM comorbidity, patients with DM were more likely to be Filipinos [adjusted odds ratio (aOR):2.46;95%CI:1.61-3.77], Mexicans [aOR:3.94;95%CI:2.44-6.38], or Bangladeshi [aOR:3.25;95%CI:2.02-5.22] and less likely to be Chinese [aOR:0.52;95%CI:0.38-0.71] compared to all other non-U.S.-born patients.

CONCLUSION

Prevalence of DM among TB patients varies between populations. Additional analysis is needed to determine how DM (or factors associated with DM) impacts TB treatment in specific populations.

C6. EPIDEMIOLOGIC FACTORS ASSOCIATED WITH CLUSTERING OF *M. TUBERCULOSIS* STRAINS IN THE UNITED STATES

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BACKGROUND

Disparities exist in the distribution of tuberculosis (TB) disease in the United States (US). Examining factors associated with *M. tuberculosis* strain clustering can provide insights that enhance TB prevention and control efforts.

METHODS

Data was obtained from National Study of Determinants, Diagnosis, Prevention, and Treatment of TB of the Tuberculosis Epidemiological Studies Consortium Task 23, a prospective cohort study using a sample of US-born individuals with TB, diagnosed in nine US states and the District of Columbia. Molecular typing of *M. tuberculosis* strains using spoligotyping, MIRU1 and MIRU2 were used to identify clustered strains within the reporting jurisdictions. Epidemiologic and clinical risk factors were obtained from interviews and health department records. Generalized estimating equations were used for multivariable logistic regression modeling of *M. tuberculosis* strain clustering.

RESULTS

437 subjects, of whom 335 (76.66%) were non-Hispanic blacks, had genotyping results. Adjusting for age and race/ethnicity at TB diagnosis, diabetes (OR: 1.56, 95% CI: 1.02, 2.40) was significantly associated with *M. tuberculosis* strain clustering. Birth state outside the state reporting the case was inversely associated with clustering (OR: 0.73, 95% CI: 0.55, 0.96).

CONCLUSION

TB patients with diabetes were more likely to develop TB disease due to recent transmission. TB controllers should prioritize TB prevention in populations with a high prevalence of diabetes. Lack of clustering among persons who had specimens genotyped outside their state of birth echoes the lack of clustering among foreign-born TB cases in the US. Data sharing among TB controllers across state jurisdictions should be encouraged.

C7. **EPIDEMIOLOGICAL STUDY OF TUBERCULOSIS IN THE STATE OF MEXICO, MEXICO, DURING THE PERIOD FROM 2015 TO 2018**

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BACKGROUND

The 2030 Agenda for a Sustainable Development Transformed Our World", established the objective of eliminating pandemic diseases, including HIV and TB. In Mexico, TB is a public health problem and is among the 20 causes of mortality in the country. The Diabetes Mellitus (DM) is main chronic degenerative disease that is affected to the Mexican population with 9.21% (6.4 million people), caused serious economic losses in health services by treatment. The objective: To know the variants of *Mycobacterium* spp. in the México State.

METHODS

4903 samples were obtained from patients, during the period 2015 to 2018. The samples were processed in Laboratory of the State Health Institute of Mexico (LESP-ISEM). The diagnostic method for *Mycobacterium* is routine. Statistical analysis was performed using, χ^2 , CHAID using to categorize independent variables, and $P \leq 0.05$ is significant.

RESULTS

The prevalence was 25.4% (1185/4660) positive for *Mycobacterium* spp, while 1089/1146 (93.9%), and only 6.1% (37) detected other NTM species. Comorbidity with the highest number of positive cases was DM 28.3% (1386/4903) $p = 0.015$, while HIV only 7.6% (374/4903) were positive for *Mycobacterium*. In the 0.6% (15/2408) treatment was not successful and only 0.2% (9/4903) if the microorganism was resistant to any antibiotic. Patients with treatment / diabetes 19.8% (818/4903) were MTB positive.

CONCLUSION

DM is considered in this study as an important factor in the increase of positive TB cases. And it would be an aspect to consider in the success or failure of TB treatment.

C8. PREDICTIVE VALUE OF ENGLISH LANGUAGE INTERPRETER USE AS A PROXY FOR BIRTH OUTSIDE THE UNITED STATES

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BACKGROUND

Persons born in high tuberculosis (TB) incidence countries are a priority to test for latent TB infection (LTBI). However, country of birth is often missing in medical record data. We evaluated the performance characteristics of English-language interpreter use as a proxy for foreign birth among persons screened for TB.

DESIGN/METHODS

During 2012-2017, 11 states in the United States (U.S.) enrolled study participants at high TB risk, including persons from countries whose populations in the United States have high TB rates, and performed three tests—tuberculin skin test (TST) and two interferon gamma release assays (IGRAs). Self-reported country of birth was used as the gold standard for non-U.S.-birth. We calculated sensitivity and specificity of interpreter use during the study interview. LTBI was defined as having a positive TST and at least one positive IGRA.

RESULTS

Of 21,808 participants, 13,781 (63%) had lived in United States <2 years and 9,753 (45%) were refugees. Of 17,987 non-U.S.-born, 13,015 (72%) used an interpreter. Sensitivity, specificity, and positive predictive value of interpreter usage for birth outside the United States were 72%, 97%, and 99%, respectively. Among the non-U.S.-born, LTBI prevalence was similar between those using and not using an interpreter (23% vs 23%, p=0.46).

CONCLUSIONS

The high specificity suggests that persons who need an interpreter would be appropriate to test. However, the moderate sensitivity indicates that 28% of non-U.S.-born individuals would not be identified if testing were based on using an interpreter. Our study was among high-risk persons and the sensitivity might be much lower in other settings.

C9. **ASSESSMENT OF SECONDARY TUBERCULOSIS AMONG CONTACTS EXPOSED TO INFECTIOUS TUBERCULOSIS PATIENTS IN HAITI**

Richard M, Pierre RKA. National Tuberculosis Program, Haiti.

BACKGROUND

The NTP targeted evaluation of 95% of contacts to smear positive TB patients as a strategy to increase detection in Haiti. 88 % of the contacts completed evaluation. The purpose of this study was to determine the contribution of the community contact tracing to the detection.

METHOD

A cohort analysis of the cases detected and contacts identified in the country from January to December 2018 using SPSS package was performed. Variables of interest included: demographics, Department of residence, relationship with the index case, HIV and sensitivity to Rifampin; descriptive statistics and Chi-Square test were used.

RESULTS

Contacts were traced for 7906 in 10021 confirmed cases, among them 1399 under five asymptomatic children received INH for latent TB and 622 community cases detected and put on sensitive treatment, however, only 5 detected and treated for RR. 35% of the cases were in metropolitan area; the highest rate of secondary cases detection (11%) was observed in the South-east where notification rate is the lowest (106/100000); 48% of those cases were 24-35 years and 48% were male; 13% were HIV positive; Secondary cases represented 4,4% of the total cases. Significant association was observed only with location of residence.

CONCLUSION

Living in slums of the metropolitan area and being HIV were two factors associated with conversion to disease among the contacts; despite these findings, other studies are needed to modify policy.

C10. **SURVIVAL ANALYSIS OF TIME TO TUBERCULOSIS DIAGNOSIS FROM DATE OF U.S. ENTRY — UNITED STATES, 2011–2018**

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BACKGROUND

Approximately 90% of U.S. TB cases among non–U.S.-born persons are attributable to progression of latent TB infection (LTBI) to TB disease. Identifying characteristics that affect time to TB disease might help target interventions to prevent TB disease through early LTBI identification and treatment. Using survival analysis, we investigated if birth place is associated with time to TB disease based on diagnosis date among non–U.S.-born persons.

DESIGN/METHODS

We examined 40,725 TB cases among non–U.S.-born persons reported to CDC during 2011–2018. We grouped the >200 reported birth countries and territories into 19 geographical regions. We determined median time from initial U.S. entry to TB diagnosis. We derived a Cox regression model comparing differences in time to TB diagnosis between regions by using adjusted hazard ratios (aHRs) that accounted for sex, birth year, and age at diagnosis.

RESULTS

The median time from U.S. entry to TB diagnosis was 11.9 years (range: 4.3–24.0 years). Compared with persons from Western Europe, the hazard rate of developing TB was significantly higher ($P \leq .05$) for persons from all other regions, except Northern America and Northern Europe, and highest among persons from Middle Africa (aHR = 7.0; 95% CI: 6.5–7.4).

CONCLUSION

Time to TB diagnosis among non–U.S.-born persons varied by birth region, which might represent an important prognostic indicator for progression to TB disease. Targeted LTBI testing and treatment for persons from regions with comparatively higher hazard rates of developing TB might advance progress toward TB elimination in the United States.

C11. USING EHR DATA TO DESCRIBE TUBERCULOSIS IN COMMUNITY HEALTH SETTINGS: A COHORT ANALYSIS IN A LARGE SAFETY NET POPULATION

Todd J, Zlot A, Schmidt T, Oakley J, Puro J. OCHIN, Portland, OR, USA.

BACKGROUND

Eliminating tuberculosis (TB) in the United States requires strategies to help identify, test, and treat persons at risk for latent tuberculosis infection (LTBI). Appropriate interventions require robust surveillance systems capable of measuring risk factors, screening, and treatment.

DESIGN/METHODS

Patients seen in safety net clinics between January 2012 and December 2016 were extracted from a large US-based EHR network with clinics in 18 states. We defined TB testing based on the availability of test codes and tuberculin skin test (TST) that were extracted from either testing, immunization data, or in provider notes. We defined diagnosis based on ICD codes. Treatment data was extracted based on prescription data of ordering clinicians.

RESULTS

Among the 2,190,686 patient records extracted, 151,195 (6.9%) patients had a TB diagnostic test; 8% of those were positive by any test. TSTs were the most frequently documented diagnostic test (139,561, 75.1%). Among patients with any positive test, <1% had an ICD code for TB only and 73% had an ICD code for LTBI only. Among those with an ICD code for only TB (and not LTBI), 10% were prescribed a TB treatment regimen. Among those with only an LTBI (and not TB) ICD code, 15% were prescribed LTBI treatment; 11% were prescribed INH, and 4% were prescribed RIF or 3HP.

CONCLUSIONS

This study demonstrates that EHR data is a valuable source to describe LTBI in community health clinics. However, more awareness and systematic use of ICD codes are needed to accurately capture TB disease.

C12. OCCUPATIONAL HEALTH PROGRAMS FOR ARTISANAL AND SMALL-SCALE GOLD MINING: A SYSTEMATIC REVIEW FOR THE WHO GLOBAL PLAN OF ACTION FOR WORKERS' HEALTH

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BACKGROUND

Workers in the informal economy often incur exposure to well-documented occupational health hazards. Insufficient attention has been afforded to rigorously evaluating intervention programs to reduce the risks, especially in artisanal and small-scale gold mining (ASGM).

OBJECTIVES

This systematic review, conducted as part of the World Health Organization's Global Plan of Action for Workers' Health, sought to assess the state of knowledge on occupational health programs and interventions for the informal artisanal and small-scale gold mining (ASGM) sector, an occupation which directly employs at least 50 million people.

METHODS

We used a comprehensive search strategy for four well-known databases relevant to health outcomes: PubMed, Engineering Village, OVID Medline, and Web of Science, and employed the PRISMA framework for our analysis.

FINDINGS

Ten studies met the inclusion criteria of a primary study focused on assessing the impact of interventions addressing occupational health concerns in ASGM. There were no studies evaluating or even identifying comprehensive occupational health and safety programs for this sector although target interventions addressing specific hazards exist. Major areas of intervention – education and introduction of mercury-reducing/eliminating technology were identified, and the challenges and limitations of each intervention taken into assessment. Even for these, however, there was a lack of standardization for measuring outcome or impact let alone long-term health outcomes for miners and mining communities.

CONCLUSION

There is an urgent need for research on comprehensive occupational health programs addressing the array of hazards faced by artisanal and small-scale miners.

Keywords: informal economy; artisanal and small-scale gold mining; occupational health; health and safety; workplace safety

D. PEDIATRICS

D1. GUMMY DRUGS: NOVEL ANTI-TUBERCULOSIS PEDIATRIC FIXED-DOSE COMBINATION ORAL FORMULATIONS

Virgilio K, Braun N, Stagnaro V, Tison C. Luna Innovations, Charlottesville, VA, USA.

BACKGROUND

In 2017 an estimated 1 million children aged 0-14 fell ill and 230,000 died from Tuberculosis (TB). TB is treatable and curable with a standard 6-month course of antimicrobial drugs. Unfortunately, there are few pediatric formulations of anti-TB drugs available, making treatment adherence in younger patients challenging. To meet the needs for pediatric-friendly anti-TB drugs, Luna Innovations and industry partners are working to finalize development of a fixed-dose combination (FDC) gummy formulation that is palatable to children.

DESIGN/METHODS

Luna has created chewable gels containing WHO-recommended anti-TB drugs: Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide (PZA). Drug loading and stability of the gummies were evaluated with High Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS), and texture was analyzed with an Instron Universal Testing Machine.

RESULTS

Luna is currently optimizing the drug-loading to meet the WHO-recommended dosing (50/75/150 mg for INH, RIF, PZA, respectively) based on the gummy's loading efficiency. To test stability, Luna performed 3-month stability testing on FDC gummies and HPLC analysis showed no degradation following storage. Additionally, the texture of the gummy was optimized such that the peak compression force is comparable to commercially available pediatric gummies.

CONCLUSION

Luna's anti-TB gummies have shown to maintain drug stability for up to 3 months and the gummy texture has been shown to be comparable to pediatric applications. Work is ongoing to complete accelerated stability testing and eliminate API degradation in the presence of reducing sugars.

D2. **PEDIATRIC TUBERCULOSIS IN THE GREATER TORONTO AREA (GTA): RELATIONSHIP TO BIRTHPLACE AND TRAVEL HISTORY**

El Hafid M, Morris S, Kourdi H, Lam R, Kitai I. University of Toronto; The Hospital for Sick Children, Toronto, ON, Canada.

BACKGROUND

There are limited data about the relationship of birthplace, parents' birthplace, and travel history to pediatric tuberculosis (TB) disease in Canada. Travel history is not routinely collected by public health authorities for cases of TB in Canada.

DESIGN/METHODS

We reviewed prospectively collected TB clinic data (which include travel histories) and records of patients aged 0-17 years managed for TB disease at the SickKids TB clinic between January 1, 2002 and December 31, 2018.

RESULTS

Ninety-four of 185 patients were foreign-born. Of the Canadian-born patients, only one case had both parents who were Canadian-born. In comparison to foreign-born patients, Canadian-born patients were more likely to have a history of travel to a TB-endemic country (50/91 [55%] versus 19/94 [20%], odds ratio [OR] 5; 95% confidence interval [CI] 3.3-9.8 $p < 0.001$), and to have a known index case in Canada (61 [76%] versus 19 [24%], OR 8.1; 95% CI 4.1-15.8, $p < 0.001$). As compared to Canadian-born patients, foreign-born patients had more isolated extrapulmonary disease (24 [26%] versus 8 (9%), OR 3.6; 95% CI 1.5-8.4, $p < 0.004$).

CONCLUSION

Canadian-born children often acquired TB through contact with an infectious source case in Canada; however, travel was likely important in a significant minority of cases. Post-immigration travel may also have been important in TB acquisition in some foreign-born individuals. This may reduce the estimated effectiveness of screening children for TB infection and disease upon immigration. Strategies to prevent and detect travel related TB are needed to reduce pediatric TB in the GTA.

D3. **TUMOR-NECROSIS FACTOR A INHIBITOR THERAPY FOR LIFE-THREATENING TUBERCULOMA AND VASCULITIS IN A PEDIATRIC PATIENT**

Mijovic H, Roberts A. British Columbia Children's Hospital and University of British Columbia, Vancouver, BC, Canada.

BACKGROUND

Children are disproportionately affected by tuberculous meningitis (TBM) compared to adults. Central nervous system (CNS) tuberculoma and vasculitis are potentially life threatening inflammatory complications of TBM and may be refractory to steroid therapy.

Tumor-necrosis factor α (TNF- α) inhibitors impede granuloma formation and may mitigate inflammatory response in TBM. The role of monoclonal antibody (MAB)-based TNF- α inhibitors in treating CNS tuberculoma and vasculitis is not well established.

DESIGN/METHODS

We describe preliminary treatment outcomes in a 13-year-old, human immunodeficiency virus (HIV) negative girl with TBM complicated by progressive, steroid refractory CNS tuberculoma and vasculitis. She is currently undergoing salvage therapy with infliximab (MAB TNF- α inhibitor). Literature search (Embase, Medline, Web of Science) was conducted to identify other reports of CNS tuberculoma or vasculitis treated with MAB-based TNF- α inhibitors in adults or children.

RESULTS

Our patient's serial MRIs (month 2, 4, 6, 8) show ongoing decrease in tuberculoma size and enhancement. Cerebrovascular compromise remains unchanged. She has not experienced any adverse effects from infliximab.

We identified 8 publications reporting on 11 adult patients (3 HIV positive) with steroid refractory tuberculoma (10) or vasculitis (1), all of whom responded favorably to MAB-based TNF- α inhibitor (infliximab or adalimumab).

CONCLUSION

To our best knowledge, this is the first report of MAB-based TNF- α inhibitor treatment for inflammatory complications of TBM in a pediatric patient. TNF- α inhibitors may provide an effective treatment option for TBM associated CNS tuberculoma. Further studies are needed to confirm efficacy and safety of this innovative treatment.

D4. DIAGNOSTIC PERFORMANCE OF QUANTIFERON-TB GOLD-PLUS ASSAY IN CHILDREN WITH EXCLUSIVE EXTRA-PULMONARY TUBERCULOSIS DISEASE

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BACKGROUND

Although QuantiFERON-TB Gold Plus (QFT-Plus), the 4th generation QuantiFERON-TB assay, has shown good performance in adults, little data is available on its performance in children with extra-pulmonary TB (EPTB).

DESIGN/METHODS

De-identified data from TB-suspected patients age <18 years with QFT-Plus results, who were admitted or screened for TB at the National Lung Hospital in Ha Noi, Vietnam in 2017, were assessed. EPTB was confirmed by a TB pathologic result on biopsy or culture. The diagnostic performance of QFT-Plus for EPTB was evaluated.

RESULTS

From 4/2017-12/2017, 222 children were screened for TB with the QFT-Plus (19 pulmonary TB [PTB], 7 EPTB and 7 PTB+EPTB). Of 20 children screened and having confirmed extra-pulmonary involvement with available biopsy or culture results, 13 were ruled out for TB and 7 were confirmed with exclusive EPTB. The proportion of QFT-Plus (+) results in the exclusive EPTB and no TB groups was 14.3% (1/7) and 7.7% (1/13), respectively. Patients had a mean age of 10 years with one-third <5 years. EPTB patients had lower BMI z-scores with nearly two-thirds having failure to thrive or at least one sign/symptom suggestive of TB. QFT-Plus had a sensitivity of 14.3% in exclusive EPTB patients compared with 84.2% in children with PTB. The assay specificity in all children with EPTB, children <5 years and 5-17 years was 92.3%, 66.7% and 100%, respectively.

CONCLUSION

QFT-Plus had poor sensitivity in diagnosing pediatric EPTB. Although the assay had good specificity in older children (≥5 years), the specificity in children <5 years was poor.

D5. REVIEW OF TUBERCULOSIS EXPOSURES IN NEONATAL HOSPITAL SETTINGS: HOW OFTEN IS TB TRANSMITTED?

Palmer V, Wendorf K. Tuberculosis Control Branch, California Department of Public Health, Richmond, CA, USA.

BACKGROUND

Tuberculosis (TB) exposures in neonatal hospital settings result in large contact investigations (CIs) and concern because of the potential severity of TB in infants. Literature guiding investigations is limited. We reviewed published literature and California records on neonatal hospital CIs to help guide future CIs.

DESIGN/METHODS

We conducted a retrospective review of the international literature since 1974 and available California state and local health department records between 2008-2018 on CIs resulting from infectious healthcare workers or patients exposing neonates to TB. We identified rates of TB infection (TBI) and TB disease among exposed individuals.

RESULTS

During 8 CIs in California, no TB cases or TBI diagnoses were made among 1,327 infants, 681 healthcare workers, or 601 visitors; however, 5 infant mothers (0.4%) of 1251 exposed mothers were diagnosed with TBI. In the literature, among 3,582 infants evaluated across fifteen CIs, 10 (0.3%) had TBI and 6 (0.2%) had active TB; 18 (1.6%) of 1,108 healthcare workers, 27 (4%) of 672 visitors, and 20 (6.2%) of 324 infant mothers had TBI.

CONCLUSION

TB transmission in California neonatal settings appears low, with no transmission identified among exposed infants. TB cases are rare among exposed infants in the literature. Protective factors might include CI procedures, hospital environmental controls, and neonatal environment including use of enclosed infant beds. Hospital CIs are limited by lack of baseline TB testing results, complicating interpretation of positive tests following an exposure. TB transmission to newborn, hospitalized infants is rare; transmission is more common to adult contacts.

E. LABORATORY

E1. **ANTIMICROBIAL POTENTIAL OF METABOLITES FROM MANGROVE ACTINOBACTERIA AGAINST TUBERCULOSIS (TB) SURROGATE MYCOBACTERIA**

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BACKGROUND

Majority of antibiotics derive from Actinobacteria, including the discovery of the first tuberculosis cure, Streptomycin from *Streptomyces* sp.. Harsh environments such as mangroves may harbor new Actinobacteria with antimicrobial potential. Thus, this study aims to evaluate the antimicrobial potential of actinobacteria isolated from Malaysian mangrove ecosystem against slow growing *Mycobacterium tuberculosis* (MTB) surrogate mycobacteria (*M.smegmatis*, MTB H37Ra) and fast growing Methicillin-resistant *Staphylococcus aureus* (MRSA).

METHODS

Sediment and water from crab holes, rhizosphere roots, undisturbed and disturbed areas were collected and pretreated using the dry heat at 100°C method. Actinobacteria isolated from sediment were cultured on selective starch casein agar supplemented with 80 µg/mL cycloheximide while water samples were cultured without pretreatment.

RESULTS

31 isolates were successfully cultured, with most isolates from sediment samples (n=25) and majority from rhizosphere roots (n=12). The antimicrobial activity of isolates were evaluated using the cross-streak method after an initial incubation period of 5 days followed by further incubation periods of 2 days, 10 days, and 1 day for *M.smegmatis*, MTB H37Ra, and MRSA respectively. The zone of inhibition (ZI) was measured after incubation. Controls used surrogate TB organisms, where the positive control was prepared without inoculating the actinobacteria and the negative control was grown in the presence of commercial antibiotics Vancomycin, Streptomycin and Rifampicin. In total, 17 isolates were active against at least one of the test organisms. Among them, four isolates showed activity against only one test organisms, 12 isolates showed activity against two test organisms and only one isolate from a water sample of Site B (Rhizosphere roots), WB b, exhibited antimicrobial activity against all three test microorganisms and showed the strongest inhibition effect against *M.smegmatis* (ZI≥25mm), MRSA (ZI=18.5mm), and MTB H37Ra (ZI=18mm) compared to standard antibiotics used as controls which showed ZI ≤ 25 respectively.

CONCLUSION

Mangrove Actinobacteria may be a significant source of new antibiotics against tuberculosis warranting further investigation.




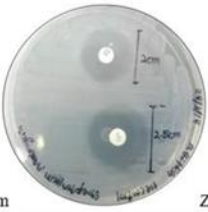
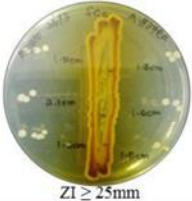
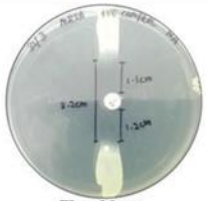

| | Vancomycin (30) | Streptomycin (10) | Clindamycin (2) | Actinobacteria Isolates |
|---------------------|---|--|---|--|
| <i>M. Smegmatis</i> |  ZI = 23 mm |  ZI = 10mm | NA |  ZI ≥ 25mm |
| MTB H37Ra |  ZI = 20 mm ZI = 25 mm | | NA |  ZI ≥ 25mm |
| MRSA | NA | NA |  ZI = 25mm |  ZI ≥ 25mm |

Figure 1

E2. NETWORK MEDICINE APPROACH TO TREAT TUBERCULOSIS AND ITS ASSOCIATED DISEASE

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BACKGROUND

Network analysis is playing the crucial role at the cellular level, since most of the cellular components are linked to each other via complex regulatory and metabolic mechanisms as well as protein–protein interactions. As we know that many genes are associated with more than one disease, and the pharmacology of drug-disease interactions unveils complex links between heterogeneous classes of therapies.

METHODS

In this way, we have visualized the possible interconnection among tuberculosis is to build a disease-network of which five major diseases (Diabetes mellitus, Rheumatoid arthritis, Cardiovascular diseases, Parkinson's disease and lung cancer) are connected and multiple genes shared by often quite distinct disorders indicates that these diseases may have common genetic origins. Next, we obtained the disease associated genes and products (target proteins) and their target drugs. This was followed by the union of the drug-target interaction, drug-drug interaction and target-protein interaction in the network.

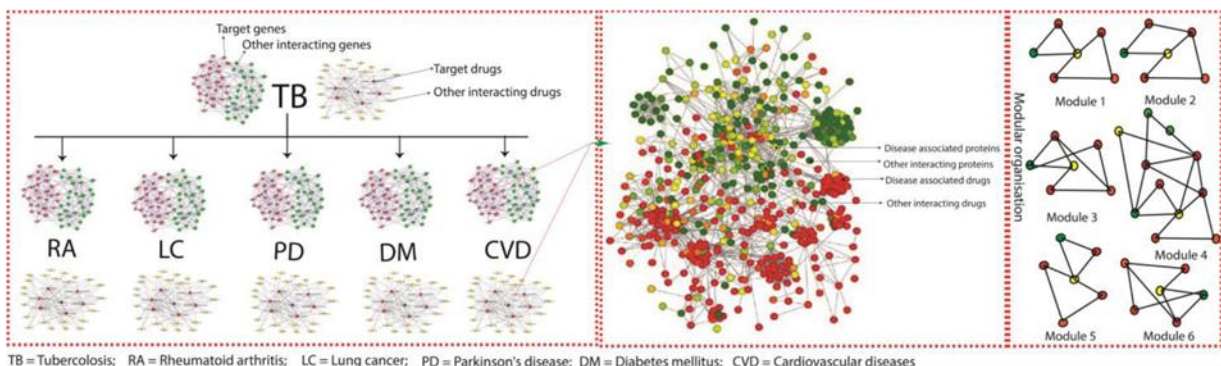
RESULTS

In our study, the modularity organization suggests that well-known drugs are not only important for specific disease targets but also can trigger other disease targets. Similarly, we identified few genes that are TB associated but they also involved in Diabetes mellitus, Rheumatoid arthritis, Cardiovascular diseases, Parkinson's disease and lung cancer.

CONCLUSION

The system-based approaches to illuminating drugs and targets interaction in the Tuberculosis and its associated disease and lay the base for a unique approach to explore new targets and multidrug treatment in tuberculosis.

Keywords: System biology, Network medicine, topological properties, Modularity, Key regulator



E3. PUTATIVE RARE VARIANTS IN *WHIB7* PROMOTER FOUND IN SEVEN UNEXPLAINED KANAMYCIN RESISTANT CLINICAL MYCOBACTERIUM TUBERCULOSIS ISOLATES

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BACKGROUND

Identifying genetic markers of antibiotic resistance is essential for developing rapid molecular diagnostics to guide patient treatment. However not all resistant isolates carry known markers. These unexplained resistant isolates may be the result of alternative resistance markers too rare to be discovered by conventional genome wide association studies.

METHODS

We downloaded published genome sequences and accompanying DST results for 851 clinical *M. tuberculosis* isolates, and called variants against reference strain H37Rv. An additional 323 clinical isolates were collected by our collaborators in India, Moldova, the Philippines, South Africa, Sweden, and Belgium. DNA from these additional strains was SMRT sequenced, assembled, and aligned to H37Rv to call variants. DST for the SMRT sequenced isolates was performed on the MGIT 960 platform.

RESULTS

DST reported resistance to kanamycin in 270 isolates, 21 of which carried no known kanamycin resistance markers. Seven of these unexplained resistant isolates carried variants in the *whiB7* promoter that no kanamycin susceptible isolate carried. None of these variants were present in more than one isolate. Similarly, known rare marker *rrs*:A1484T was present in only four isolates.

CONCLUSION

The *whiB7* gene has previously been implicated in kanamycin resistance, and regulates *eis*, whose role in kanamycin resistance is established. Distinct variants in the *whiB7* promoter could potentially cause the same phenotype, resulting in diverse rare variants each causing resistance, none of them prevalent enough to be detected by a genome wide association study. Rare variants like these challenge research on antibiotic resistance, and may threaten the sensitivity of molecular diagnostics.

E4. **OVERCOMING THE CHALLENGE OF CYTOKINE/CHEMOKINES ANALYSIS - NORMAL DISTRIBUTION OR NEEDING TRANSFORMATION?**

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BACKGROUND

The objective was to determine immune parameters (IP) associated with LTBI, compared to active TB and healthy individuals using previously published literature.

DESIGN/METHODS

We conducted a systematic search using Google Scholar and PubMed databases, combining the MesH terms: latent tuberculosis, *Mycobacterium tuberculosis*, cytokines, and biological markers; with the free terms, biomarkers and cytokines. Spanish, English and Portuguese articles comparing the concentration of IP associated with LTBI, either in plasma/serum or in vitro, in adults, non-immunocompromised, versus individuals with TB or without *M. tuberculosis* infection between 2006-july/2018-july were included. Two blinded reviewers carried out the searches, read the abstracts and selected the articles for analysis. Participant's information, diagnostic criteria, IP, detection methods, and biases were collected.

RESULTS

We analyzed 37 articles (of 637 abstracts), which reported on 87 IP. 22, 5, and 2 IP were increased in active TB, LTBI, and healthy individuals, respectively. We found high heterogeneity between studies including failure to account for the time/illness of the individuals studied; varied samples and protocols; different clinical classification of TB; different laboratory methods for IP detection, which in turn leads to variable units of measurement and assay sensitivities; selection bias regarding TST and booster effect. None of the studies adjusted the analysis for the effect of ethnicity on the association between IP and the different stages of TB.

CONCLUSIONS

Studying IP in LTBI is important in order to prioritize preventive treatment. Heterogeneous study populations, samples and experimental conditions, and pooling of LTBI at various times, prevented identification of biomarkers associated with recent infection. PROSPERO-CRD42017073289.

E5. **ROLE OF CYTOKINES/CHEMOKINES IN PEOPLE WITH RECENT INFECTION BY *MYCOBACTERIUM TUBERCULOSIS***

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BACKGROUND

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

DESIGN/METHODS

We evaluate sociodemographic variables and 18 cytokine/chemokine in plasma samples from 50 patients with pulmonary TB, 24 new tuberculin skin test convertors (negative LTBI that became positive during follow up), and 47 people without infection after two-years of follow-up, from two Colombian prisons. We performed partial least squares-discriminant analysis, and a multinomial regression to evaluate the immune parameters associated with each group.

RESULTS

The cytokine/chemokines concentrations changes between the groups and a combination of CCL20, sCD14, IL-18, IP-10, MCP-1, and TNF- α allows classifying people with active TB, recent LTBI and non-infected by *M. tuberculosis*. There are differences in the cytokines/chemokines concentration in people getting MTB infection after two years of incarceration compared to those who recently entered the prison.

CONCLUSIONS

Recent infection with *M. tuberculosis* is associated with an identifiable cytokine pattern that can be used to prioritize LTBI treatment to those at greatest risk for developing active TB.

E6. **BLOOD-BASED DETECTION OF TUBERCULOSIS BIOMARKERS ASSOCIATED WITH EXTRACELLULAR VESICLES IN SUBJECTS WITH HIV NEGATIVE STATUS**

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BACKGROUND

In 2018, 9 million global TB cases occurred in HIV negative individuals. Due to low sensitivity for TB in HIV- subjects by existing point of care (POC) tests, affordable early TB detection in HIV- subjects presents a critical challenge to the End TB strategy.

We have developed a novel lab-on-a-chip that isolates extracellular vesicles (EVs) in unprocessed blood matrices using AC Electrokinetics (ACE). A feasibility study using an ACE-based method to co-detect two EV-associated TB biomarkers in HIV- subjects was conducted.

METHODS

Frozen serum samples from 20 TB positive (TB+) and 20 TB negative (TB-) subjects with confirmed HIV negative status were procured from a biobank. 25 µL of serum was flowed into the chip and an electrical signal was applied to capture EVs. Antibodies against lipoarabinomannan (LAM) and Antigen 85 (Ag85) were incubated for 1 hour, followed by fluorescent dye-conjugated secondary antibodies for detection. Relative biomarker abundance was determined using image analysis software. Results were evaluated using the Receiver Operating Characteristic curve method.

RESULTS

Exo-LAM and exo-Ag85 levels were elevated in TB+ serum. The area under the curve (AUC) for differentiating between TB+ and TB- cohorts was 0.9975 and 1.00 for the markers, respectively.

CONCLUSION

The results demonstrate early feasibility using ACE method for on-chip detection of EV-associated TB biomarkers in HIV- subject serum and the potential to differentiate between TB positive and negative cohorts. Future feasibility work will focus on expanding the study scope and optimizing the test workflow toward meeting WHO target profiles for TB biomarkers.

E7. SIMPLE INACTIVATION OF MYCOBACTERIA SAMPLES FOR SAFE TRANSPORT AND LABORATORY PREPARATION USING COBAS MICROBIAL INACTIVATION SOLUTION

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BACKGROUND

As NAATs are increasingly used to diagnose tuberculosis, inactivation of mycobacterium for safe laboratory handling is essential. This study was conducted to determine the mycobacterial inactivation efficacy of the **cobas**[®] Microbial Inactivation Solution (MIS).

DESIGN/METHODS

To verify inactivation of *Mycobacterium tuberculosis* (MTB) complex organisms, culture panels of two MTB strains (MTB-H37rv; MTB-CDC268) were prepared at microBIOMix GmbH, UKR. Cultures were grown to ~1E+08 CFU/mL then diluted to test concentrations (5E+07 CFU/mL; 2E+06 CFU/mL) in sterile PBS and shipped to three sites: Institute of Clinical Microbiology and Hygiene (IMHR), Roche Diagnostics (RDI) and Lucerne Cantonal Hospital (LUKS).

At each site, 0.4 mL of sample was inactivated according to manufacturer's instructions and then centrifuged. The bacterial pellet was resuspended in 0.5mL PBS and inoculated into liquid or solid culture and followed for up to 8 weeks post inactivation and inoculation. Negative (PBS buffer) and positive (treated with PBS only) controls were included. Five replicates of samples treated with MIS and two replicates each of the positive and negative controls were included. Liquid cultures were performed at IMHR and RDI. Solid cultures were performed at LUKS. Liquid culture was done using the (MGIT) BACTECTM MGITTM-320 Mycobacterial Detection System (Becton Dickinson) and solid culture was done using Lowenstein-Jensen slants.

RESULTS

All replicates of MTB cultures of both strains and both concentrations were fully inactivated and showed no culture growth eight weeks post inoculation (Table 1). One culture was not interpretable due to contamination by rapid growing nontuberculosis-mycobacteria.

CONCLUSION

Pre-analytic treatment by MIS is effective in reducing MTB infectivity.

Table 1:

| Culture Isolate | Bacterial Load | Testing Site | Culture type | Duration of culture (weeks) | Postive Results (%) |
|---|----------------|--------------|--------------|-----------------------------|---------------------|
| MTB (CDC 268) | 5E+07 CFU/ml | RDI | Liquid | 8 | 0/15 (0%) |
| | | LUKS | Solid | 8 | 0/15 (0%) |
| | | IMHR | Liquid | 8 | 0/15 (0%) |
| | 2E+06 CFU/ml | RDI | Liquid | 8 | 0/15 (0%) |
| | | LUKS | Solid | 8 | 0/15 (0%) |
| | | IMHR | Liquid | 8 | 0/15 (0%) |
| MTB (H37rv) | 5E+07 CFU/ml | RDI | Liquid | 8 | 0/15 (0%) |
| | | LUKS | Solid | 8 | 0/15 (0%) |
| | | IMHR | Liquid | 8 | 0/15 (0%) |
| | 2E+06 CFU/ml | RDI | Liquid | 8 | 0/15 (0%) |
| | | LUKS | Solid | 8 | 0/15 (0%) |
| | | IMHR | Liquid | 8 | n/a* |
| *Invalidated due to contamination by non-mycobacteria | | | | | |

E8. SYNTHESIS AND CHARACTERIZATION OF BIOMIMETIC NANOPARTICLES FOR MACROPHAGE ACTIVATION: A STRATEGY TOWARDS INTRACELLULAR *MTB* ERADICATION

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BACKGROUND

Macrophages are the primary host cells for *Mycobacterium tuberculosis* (*Mtb*) and are inactivated in the latent and active form of Tuberculosis. Due to increasing cases of multi-drug resistant TB, novel strategies to eradicate *Mtb* are urgently required. A conjugate between curdlan and poly (D, L-lactide- co-glycolide) (PLGA) was recently used to synthesize nanoparticles (NPs) that can activate macrophages. We now aim to understand the interaction of these NPs with macrophages and to determine the capacity of these NPs to stimulate intracellular eradication of *Mtb*.

METHODS

PLGA NPs functionalized with up to 8% (w/w) curdlan were synthesized using the emulsion solvent evaporation method. The physicochemical properties of the NPs were determined using DLS, HR-TEM, NMR, and X-ray photoelectron spectroscopy. 1D SDS-PAGE gel electrophoresis and the Bradford assay were used to study the protein corona formation in supplemented DMEM media. Cytotoxicity was evaluated in RAW264.4 macrophages Using MTT assay.

RESULTS

Monodispersed PLGA NPs curdlan were successfully synthesized. The NPs were shown to have a spherical shape and an average size of approximately (~) 400 nm, and were also found to maintain their physicochemical properties in DMEM media; no statistical difference between the opsonisation of the NPs was observed. The presence and of curdlan on the NP was confirmed and no cytotoxicity was observed after 72 hours of treatment.

CONCLUSION

Stable biomimetic PLGA NPs were successfully synthesized and characterized. The NPs were found to be non-toxic against macrophages, and the NPs will be subsequently assessed for the capacity to stimulate eradication of intracellular *Mtb*.

F. TRAINING AND EDUCATION/SPECIAL POPULATIONS

F1. **NO MORE ANNUAL TB TESTING FOR MOST HEALTH CARE PERSONNEL: COMMUNICATING CDC AND NTCA'S 2019 UPDATED TB SCREENING, TESTING, AND TREATMENT RECOMMENDATIONS**

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BACKGROUND

In May 2019, the U.S. Centers for Disease Control and Prevention (CDC) and the National TB Controllers Association (NTCA) released updated screening, testing, and treatment recommendations for health care personnel (HCP) in the United States. CDC's communications objectives were to raise awareness of the recommendations among clinicians and public health professionals, develop new patient and clinician resources, and update existing content and materials.

INTERVENTION OR RESPONSE

CDC created a communication plan that used a broad dissemination strategy to promote the recommendations using internal and external communications channels, partner outreach with professional associations, and social and traditional media. CDC developed materials including videos, FAQs, and infographics for health care organizations and HCPs. CDC also updated and re-launched existing web content and materials to ensure consistent guidance and messages.

RESULTS

In the two months following publication of the recommendations and supporting materials, visits to the HCP testing page increased by 23%. The FAQ webpage was viewed approximately 8,500 times. Engaging content on Twitter, Facebook, and YouTube also helped drive traffic to CDC resources. Proactive outreach strategies to partners and media outlets amplified the CDC messaging and created additional promotional opportunities.

CONCLUSION

Through comprehensive communication planning and promotion, CDC raised awareness of the updated recommendations among clinicians, occupational health, and public health professionals. Developing and disseminating materials in multiple formats through a variety of channels allowed CDC to reach target audiences, and engaging partners helped amplify communications efforts.

F2. **IMPACT OF INTER-COMMUNITY AND INTER-JURISDICTIONAL (PROVINCIAL) MOBILITY OF FIRST NATIONS PATIENTS WITH TUBERCULOSIS ON TUBERCULOSIS PREVENTION AND CARE PROGRAMMING**

Heendeniya A, Hackett P. University of Saskatchewan, Saskatoon, SK, Canada.

BACKGROUND

This research explored the potential impact of inter-jurisdictional mobility of First Nations (FN) on existing Tuberculosis (TB) prevention and care programs. Objectives included: (1) identify mobility patterns, (2) assess current policies covering FN TB care and prevention programming, and (3) evaluate the potential impact of inter-jurisdictional mobility on TB and TB programming.

DESIGN/METHODS

The study community is a remote FN community in northern Saskatchewan (SK) located near the Alberta (AB) border. Semi-structured interviews were conducted with community participants around mobility patterns. A multi-level document review of TB prevention and care policies and interviews with healthcare providers in both provinces were also conducted.

RESULTS

Due to the community's remote location external mobility is frequent. Motivations include healthcare, work, family, entertainment, shopping, and traditions. Frequency and destinations of travel vary by season with inter-provincial mobility to Alberta being most common in the winter via temporary winter roads. Currently, there are no federal or provincial policies or procedures in place for mobile TB patients. However, informally health care workers follow a standard treatment procedure for mobile patients. Lines of communication between provinces and communities are clear but direct communication between communities is not.

RECOMMENDATIONS/CONCLUSION

Without clear policies, the possibility of treatment non-completion and failure may be increased, as patients may slip through the "cracks." Specific policies across jurisdictions are needed to address this. One solution may be to abandon current TB programming based on multiple jurisdictions (on-reserve, off-reserve, and provincial) in favour of interventions centred on a regional (and interprovincial) approach.

F3. **BRITISH COLUMBIA'S (BC) TUBERCULOSIS (TB) SCREENING COMPETENCIES:
ADVANCING HEALTH EQUITY IN NURSING PRACTICE**

MacDougall M, Jiwa S. BC Centre for Disease Control, Vancouver, BC, Canada.

BACKGROUND

The BC's Provincial TB Screening Competencies outline the knowledge, skills, attitudes and behaviours needed for nurses to competently perform TB screening. They also support TB educational and program initiatives that aim to improve client and population health outcomes. In 2018, a review of the 2014 TB Screening Competencies was initiated with the goal of conducting an evidence-based, health equity analysis to ensure the resource was accurate and reflective of best practice.

INTERVENTION/RESPONSE

A provincial working group (PWG) of nursing professionals representing regional and First Nations health authorities as well as frontline and professional practice, was formed to facilitate a robust review. An evaluation tool, including questions on addressing health equity in practice, was distributed to the PWG to guide their individual analysis. Responses were collated and identified themes validated by the PWG. A literature review focusing on health equity and populations disproportionately affected by TB in BC was conducted. This evidence summary, along with the results of the group analysis, was discussed over four teleconferences in a five month period to guide the review.

RESULTS/LESSONS LEARNED

An updated and evidence-based provincial TB Screening Competencies document which is a one-page, accessible and user friendly resource supported by a diverse network of nursing professionals in BC. The approach used to update these competencies was a collaborative and successful process.

CONCLUSION

The BC Provincial TB Screening Competencies reflect an evidence-based, equity-oriented resource for nurses involved in TB screening in BC. The review process and the resource itself may be useful for other TB programs interested in competency-based professional development.

F4. THEMES OF COMMUNITY ENGAGEMENT AND TUBERCULOSIS IN INDIGENOUS RESEARCH

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BACKGROUND

Recurrent TB can arise either endogenously (relapse) or exogenously (reinfection). The individual, clinical, programmatic and policy implications of these two potential mechanisms are distinctive. The current Canadian TB standards conclude that most cases of recurrent TB in Canada are relapses and does not provide specific guidance for differentiating and managing these distinct entities.

We are undertaking a project to quantify the relative contribution of relapse and reinfection to recurrent TB in four jurisdictions (Alberta, Nunavut, Ontario and Saskatchewan) in Canada. Using a reciprocal learning and integrated knowledge translation approach we will be developing an inclusive public health policy for recurrent TB in Canada.

DESIGN/METHODS OR INTERVENTION/RESPONSE

On May 2019 the team gathered to explore the themes of TB knowledge that surface in Sharing Circles with specific reference to its significance for Indigenous communities. The gathering was held in the Treaty Six territory of the Cree and homeland of the Metis (Prince Albert, Saskatchewan) and was open to the public. Indigenous Elders, Community Stakeholders, an Indigenous community engagement coordinator and TB doctors shared their experiences, concerns and questions about TB.

RESULTS

The participants experienced TB disease from a cascade of lived experience to prevention to diagnosis, management and appropriate policy development. Sanatoria were perceived extensions of residential schools where multigenerational TB physically and culturally dislocated Indigenous patients from their communities.

CONCLUSION

TB elimination requires effective and ethically sound public health practice which depends upon respectful partnerships. We present a model for initiating conversation and establishing relationships upon which policies can be built.

F5. **CONNAISSANCE, ATTITUDE, ET PRATIQUE DES PERSONNES VIVANT AVEC LE VIH VIS A VIS DE TUBERCULOSE À JACMEL**

Valesco ML. DSSE, Haiti.

Haiti a le taux d'incidence estimée le plus élevée de la région des Amériques (176/100000), une prévalence élevée de VIH dans la population générale et 15% des tuberculeux sont coinfectés TB/VIH; si la tuberculose est la principale cause de décès chez les PVVIH en Haiti, très peu est connu sur leur connaissance, attitude et pratique face à cette maladie d'où la raison de notre enquête à Jacmel.

METHODE

Un questionnaire de 25 questions déjà approuvé et utilisé, porté sur leur connaissance, attitude et pratique face à la maladie et les patients TB a été employé auprès de 271 PVVIH résidant à Jacmel et aux environs après avoir été choisis au hasard dans la liste des patients VIH lors de leur rendez-vous de suivi.

RESULTATS

60% des répondants étaient des femmes, 70% âgés de 24-45 ans; 63% vivent en milieu rural, 20% sont illettrés, 49% ont fait la primaire, 28% la secondaire et 2% l'université; 25% ont déjà fait la TB; 89% ont déjà entendu parler de TB; et ils ont entre 1 à 17 ans depuis qu'ils vivent avec le VIH; 82% pensent qu'il y a un lien entre le VIH et la TB; 33% aurait un accès limité aux services TB par la géographie et 15% par crainte de discrimination; 71% ont une connaissance sur la TB; 62% n'utiliserait pas un ustensile d'un patient TB et 33% ne partagerait pas son lieu de travail avec lui; cependant, 69% accepterait de prendre soin d'un parent tuberculeux; 78% iraient à l'hôpital quand ils sont malades et 13% chez le guérisseur. Une association significative a été notée entre le niveau d'éducation, le lieu de résidence et une bonne connaissance sur la TB.

CONCLUSION

en regard du taux de décès élevé, de la discrimination et une connaissance limitée sur la TB des PVVIH de Jacmel, des efforts sont obligatoires pour améliorer, cependant, vue les limites de cette enquête d'autres sont nécessaires pour mieux comprendre la situation et prendre des décisions spécifiques.

F6. **COMMON GROUND, COMMON PURPOSE: EVALUATING PUBLIC HEALTH AND PRIVATE SECTOR HEALTHCARE PROFESSIONALS' COMMITMENT TO CONTINUED ENGAGEMENT FOLLOWING A TUBERCULOSIS ELIMINATION-FOCUSED SYSTEMS THINKING SYMPOSIUM**

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BACKGROUND

Because reactivation of latent tuberculosis infection (LTBI) accounts for over 80% of active tuberculosis (TB) cases in the US, domestic elimination strategy includes targeted screening and treatment of at-risk persons. To prompt interdisciplinary thought around opportunities to increase appropriate private sector LTBI-related care, the University of North Texas Health Science Center hosted a Systems Thinking Symposium. Professionals representing a diverse range of fields within private healthcare and public health participated in facilitated, structured discussions intended to identify barriers to LTBI-related care and opportunities for health system change. We sought to understand participants' perceptions of the event and interest in future involvement.

DESIGN/METHODS

Attendees were emailed a link to an online survey one-month post-symposium. Participants were asked to identify their professions, strengths/weaknesses of the symposium, whether they made valuable professional connections, and their interest in continued involvement.

RESULTS

The survey was completed by 73.3% (22/30) of participants representing 10 health-related professions. Of these, 95.5% (21/22) recommended a similar symposium be repeated in the future and 100% (22/22) reported making valuable professional connections. Additionally, 81.8% (18/22) of survey participants were interested in continued involvement.

CONCLUSION

The Systems Thinking Symposium effectively involved individuals from a broad spectrum of health-related fields. Effective collaboration between public health and private sector healthcare is critical to domestic TB elimination, and positive interdisciplinary experiences such as those reported by symposium participants may contribute to such collaboration. Events involving facilitator-led structured discussions amongst interdisciplinary groups show promise in engaging persons from a variety of health-related professions in public health initiatives.

G. MOLECULAR EPIDEMIOLOGY AND OUTBREAKS

G1. **USE OF SYNDROMIC SURVEILLANCE DATA TO LOCATE LOST TUBERCULOSIS PATIENTS AND FACILITATE RETURN TO CARE IN NEW YORK CITY**

Ahuja S, Burzynski J, Chuck C, Cummins D, Daskalakis D, Knorr J, Mathes R, Parton H, Simmons C, Sullivan Meissner J, Trieu L.

BACKGROUND

Tuberculosis (TB) patients who are lost to care prior to treatment completion are at risk for poor disease outcomes, development of drug resistance, and community transmission.

INTERVENTIONS

The New York City Health Department receives chief complaint information daily from emergency departments and other healthcare facilities (HCF). A matching algorithm was developed to query syndromic data to help locate TB patients lost to medical follow-up. Patient date of birth (DOB), residential ZIP code, and gender were matched to incoming syndromic data. Patients without an address were matched on gender and DOB. Auto-generated match alerts included HCF, chief complaint, encounter date/time, and disposition. Alerts were verified through regional health information exchange (RHIO) databases and directly with the HCF. Verified matches were referred for chart review, HCF notification, and field visits.

RESULTS

Between July 1, 2018 and September 30, 2019, 40 patients were included in the match process, resulting in 395 alerts for 21 patients. Of these, 16 (4%) alerts for 9 patients were verified as true matches; 5 patients were returned to TB care.

CONCLUSION

This novel use of routinely-collected syndromic surveillance data helped the Health Department locate 5 TB patients who were lost to care, leading to prompt initiation of infection control protocols and resumption of TB treatment. Automated matching and alerting processes, prompt review of alerts, and timely follow-up with HCF facilitated successful patient re-engagement. Access to RHIO data facilitated match verification using minimal resources. Further evaluation is needed to identify variations in data timeliness and completeness and opportunities to improve patient outcomes.

G2. RE-EXAMINING TRANSMISSION OF TUBERCULOSIS FROM SMEAR NEGATIVE PATIENTS: A COMPARISON OF MOLECULAR, CONVENTIONAL EPIDEMIOLOGY, AND GENOMIC TECHNIQUES

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BACKGROUND

Sputum smear microscopy is the most common surrogate for tuberculosis infectiousness, with programs relying on it for triaging contact tracing and infection control. Studies comparing transmissions from smear-negative vs smear-positive cases have used DNA fingerprint clustering and estimate that smear-negative cases contribute to 13-20% of transmissions. We re-examined these findings using higher resolution techniques.

METHODS

All TB patients in Alberta from 2003-2017 were included. We replicated previous studies by clustering identical DNA fingerprints as determined by RFLP genotyping. Next, using RFLP or MIRU-VNTR combined with conventional epidemiology, we identified transmissions among named contacts. Finally, to investigate transmissions among unnamed contacts, we did whole genome sequencing (WGS) on temporally and geographically linked DNA fingerprint clusters. The primary outcome was the proportion of transmissions attributable to smear-negative cases and the relative transmission rate.

RESULTS

There were 1767 TB cases, including 1176 culture-positive, pulmonary TB patients with 23,131 named contacts. 564 were smear-negative and 614 smear-positive. Using DNA fingerprint clustering, 16% of transmissions were attributable to smear-negative cases and the relative transmission rate was 0.19. When DNA fingerprinting was combined with conventional epidemiology, 8% of transmissions (8/101) were attributable to smear-negative sources and the relative transmission rate was 0.09. Then, using WGS, we identified 13 more transmissions (3/13 from smear-negatives). Thus, our best estimate of the true proportion of transmissions arising from smear-negative patients was 10% (11/114), with a relative transmission rate of 0.12.

CONCLUSION

When replicating DNA clustering techniques, our findings match previous results. After enhancing molecular data with epidemiologic and genomic data, we conclude that smear-negative cases are less infectious than previously thought.

G3. **WHOLE GENOME SEQUENCING FOR EPIDEMIOLOGICAL STUDIES OF TUBERCULOSIS: A SYSTEMATIC REVIEW OF APPLICATIONS AND REPORTING PRACTICES**

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BACKGROUND

Genomics promise to transform our understanding of tuberculosis epidemiology. In 2014, guidelines called STROME-ID were published to provide recommendations for reporting and to reduce bias in genomic epidemiology studies. We compare quality and completeness of reporting practices before and after STROME-ID publication.

DESIGN/METHODS

This study is registered on PROSPERO (CRD42017064395). MEDLINE, Embase Classic and Embase were searched on May 3, 2017 (updated April 23, 2019). 651 titles and abstracts were screened, with 114 full-texts eligible for inclusion. The proportion of STROME-ID criteria reported was tabulated for each article, and means were compared before and after STROME-ID's publication date. A 6-month lag period after STROME-ID was included to account for articles in press; sensitivity analyses were also performed. Differences in mean proportions of criteria were compared pre/post publication using a t-test.

RESULTS

The proportion of applicable criteria met in included articles ranged from 24.39-83.33% (mean 50.78%), with no difference between mean proportions of criteria comparing before and after guideline publication (Table 1). The least and most reported criteria were assessed qualitatively, to explore differences between periods. Prepublication, the criteria requiring definitions for molecular terminology was least fulfilled, while epidemiological objectives of using molecular typing and data sources were most reported. Post publication, how multiple-strain infections were detected was least reported, while study objectives were most reported.

CONCLUSION

Reporting quality in genomic epidemiology studies of tuberculosis is poor, despite publication of STROME-ID guidelines. Future studies should investigate factors affecting adherence to these guidelines to improve the value and utility of evidence.

Table 1. Comparison of the mean proportion of STROME-ID criteria met preceding and following its publication

| Analysis | Pre-STROME | Standard Deviation | Post-STROME | Standard Deviation | p-value |
|---------------------------------|------------|--------------------|-------------|--------------------|---------|
| 6 Month Lag | 0.49 | 0.11 | 0.51 | 0.12 | 0.80 |
| 12 Month Lag ^a | 0.49 | 0.11 | 0.51 | 0.11 | 0.66 |
| 6 Months Excluded ^b | 0.48 | 0.11 | 0.51 | 0.12 | 0.42 |
| 12 Months Excluded ^b | 0.50 | 0.10 | 0.50 | 0.11 | 0.94 |

^aPapers published within 12 months following STROME-ID were classified as ‘unexposed’, i.e., we considered that authors may not have seen the guidelines or had the opportunity to incorporate them. ^bPapers published in this time period following the STROME-ID publication date were excluded from the analysis altogether.

G4. **CONTRIBUTION OF WHOLE GENOME SEQUENCING TO IDENTIFYING AND UNDERSTANDING TUBERCULOSIS TRANSMISSION IN A REMOTE SETTING**

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BACKGROUND

Few studies have used genomic epidemiology to understand tuberculosis (TB) transmission in rural and remote settings, such as northern Canada's Yukon Territory (YT). It is unclear how useful whole genome sequencing (WGS) is in such settings, where detailed contact tracing and interview data are often available. To improve our understanding of TB transmission dynamics and utility of WGS, we conducted a retrospective analysis using a mixed methods approach.

METHODS

Using 24-locus MIRU-VNTR genotyping, WGS, and contact investigation data for all YT *Mycobacteria tuberculosis* culture-positive TB cases (2005–2014), we compared two approaches – field-based (which included MIRU-VNTR) and genomic-based – to identify the most likely TB sources. Following independent investigations using these approaches, an in-person meeting established consensus on transmission events. Additionally, knowledge, attitudes, and practices around genotyping and WGS were assessed using online surveys and a group interview.

RESULTS

Three sustained transmission networks were identified, each with at least one likely super-spreader. There was independent agreement on 26 of 32 (81%) cases for likely location of TB acquisition, with less agreement in identifying specific source cases (13/22 or 59% of cases). Single-locus MIRU-VNTR variants and limited genetic diversity complicated the analysis – revealed during an in-person meeting between the genomic- and field-based teams.

CONCLUSIONS

WGS revealed that TB transmission dynamics in YT are distinct and that the combination of WGS and epidemiological data can provide actionable information to local public health teams.

G5. **PARTNERSHIP FOR COMMUNITY-BASED TUBERCULOSIS SCREENING IN MONTREAL**

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Since 2003, there has been an ongoing outbreak of pulmonary tuberculosis in the Montréal resulting in 38 cases caused by a same strain. 33 have one or several risk factors in common: alcoholism, drug addiction, frequenting crack houses, prostitution, homelessness, criminal activity, incarceration, HIV and/or HCV infection.

Using a mobile x-ray unit, the program aimed to identify active TB cases among people at high risk.

The target clientele presented many risk factors and had frequented crack houses where cases of active tuberculosis had been reported.

In June and September 2017, the Direction régionale de santé publique (DRSP) coordinated an active case finding program that involved taking chest X-rays in a mobile unit. The program included provision of health and social services in the community. The DRSP worked on planning and implementation in partnership with local community groups and clinical teams, and with the INSPQ mobile radiology unit.

60 people participated. All had at least one targeted risk factor and several had frequented the same crack houses as known TB cases.

This project shows it is possible to develop care that is acceptable for hard-to-reach population usually not reached through conventional approaches used by the health system. The program also contributed to establishing service agreements and developing collaborations and trust between DRSP de Montréal, community groups and target populations.

Partnership between the community groups concerned and various organizations such as INSPQ and the health network make it possible to plan and implement the program.

G6. **EVALUATION OF MOLECULAR TYPING OF MYCOBACTERIUM TUBERCULOSIS STRAINS CULTURED FROM THE UGANDA NATIONAL TUBERCULOSIS REFERENCE LABORATORY**

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BACKGROUND

Molecular epidemiological data plays a central role in assessing Tuberculosis (TB)-management policy outcomes. IS6110 restriction fragment-length polymorphism (IS6110-RFLP), mycobacterial interspersed repetitive unit–variable-number tandem repeat (MIRU–VNTR) analyses and whole genome sequencing (WGS) are major molecular epidemiological tools for investigating the transmission or reactivation of active TB.

METHODS

A total of 72 strains of *Mycobacterium tuberculosis* initially set on M-kit (Multiplexing MTB DST kit) at the Uganda NTRL were subcultured at the Korean Institute of Tuberculosis (KIT). 64 culture strains had confluent growth fit for use for the IS6110 RFLP technique. Ten (10) strains representative of the susceptibility status of the 64 were run on the Miseq platform for WGS analysis and from this, *In silico* spoligotyping and MIRU-VNTR data was obtained.

RESULTS

Generally, the IS6110-RFLP technique demonstrated 8 clusters revealing possible dominant strains among the affected populations; WGS showed the ability to reveal more information on the Drug resistance status of patients which was otherwise concealed on M-kit phenotypic DST.

CONCLUSION

The molecular typing techniques evaluated on 64 *Mycobacterium tuberculosis* strains cultured from the Uganda NTRL are very purposeful for us as NTRL/SRL to not only establish the prevalence of *Mycobacterium tuberculosis* strains with identical genotype patterns of active TB and their related differences but also the dominant ones. Urgent priority ought to be given to areas with high risks of transmissions to achieve the priority areas of ENDTB Strategy and thereby provide a basis for a more patient centered approach to increase the likelihood of the desired treatment outcome.

G7. CONTACT TRACING OF TUBERCULOSIS AT THE GEORGETOWN CHEST CLINIC, GUYANA IN 2018

Phillips M, Mohanlall J, Khan D, Nero N. National Tuberculosis Programme, Ministry of Public Health, Guyana.

BACKGROUND

Implementing of the DOTS in Guyana was crucial to the decrease in incidence of Tuberculosis ,however to END TB it means we must effectively screen all close contacts for latent TB infection and active TB disease as recommended by WHO and be placed on respective treatment. Georgetown chest clinic is located in region 4 and is the site with the highest burden accounting for over 60 % of the TB cases nationally.

METHODS

Monthly cohorts for contact tracing were given to DOTS workers. Form included: Name, chart number, age, sex, TB site, contacts identified, contacts evaluated, number placed on IPT and on TB treatment. Data was reviewed and analyzed from January to December 2018.

RESULTS

188 patients were admitted to the programme. 172(91%) persons were diagnosed with Pulmonary TB and 16 (9%) with extra-pulmonary TB. 528 household contacts were identified out of which total of 353 (66%) were screened for latent TB .58 persons (16%) were placed on preventative therapy and 3(0.8%) persons were placed on active TB disease treatment.

CONCLUSION

Although there are numerous challenges encountered in carrying out contact tracing, this study shows that there is need for intensifying and boosting of efforts to improve our active case detection numbers in our goal to END TB, and can be used as a marker for improvement for further studies.

G8. TIME TO DEVELOPMENT OF SECONDARY TUBERCULOSIS: A RETROSPECTIVE COHORT STUDY USING WHOLE GENOME SEQUENCING IN BRITISH COLUMBIA, CANADA

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BACKGROUND

When combined with detailed epidemiological data, whole genome sequencing (WGS) can help confirm individual tuberculosis (TB) transmission events to a degree not possible with traditional genotyping. The objective of this study was to combine WGS data with patient-level clinical and epidemiological data to calculate the timing of confirmed secondary TB transmission amongst contacts of people with active TB in British Columbia, Canada between 2005 and 2014.

METHODS

A confirmed TB transmission event was defined as a culture-positive case whose *Mycobacterium tuberculosis* WGS varied by ≤ 5 Single Nucleotide Polymorphisms (SNPs) from another isolate with a history of contact. The time to development of secondary TB was calculated by subtracting the source case diagnosis date from the active TB diagnosis date of the contact. Secondary transmissions that were diagnosed within 30 days of index diagnosis were removed to account for an unknown source case. Clusters of ≥ 5 people were removed to account for dynamic outbreak transmission patterns.

RESULTS

We identified 30 confirmed secondary TB transmission events, attributed to 28 unique index cases with pulmonary TB, of which 28 (93.3 %) were smear positive. Of the 30 people with confirmed secondary TB, 23 (76.7%) were household contacts. The median time to development of secondary TB was 11.0 (Q1, Q3: 4.5, 24.3) months.

CONCLUSION

Results from this study suggest that the opportunity to prevent secondary TB among contacts is more time-limited than previously recognized. These findings emphasize the importance of timely contact investigations and initiation of preventative therapy.

G9. **AN EXPLORATION OF THE GENETIC DIVERSITY OF MYCOBACTERIUM TUBERCULOSIS (MTB) IN A CANADIAN CONTEXT**

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BACKGROUND

Tuberculosis (TB) is the largest global infectious disease killer. In Canada, some groups suffer from high incidence rates that often exceed those of low income countries. Today whole genome sequencing (WGS) is improving our understanding of TB dynamics, due to its increased discriminatory power over traditional methodologies. This is useful when investigating recurrent TB in remote areas, where classification is difficult due to limited diversity.

DESIGN/METHODS

Raw WGS data was obtained from the National Center for Biotechnology Information (NCBI) Sequence Read Archive. Thirty isolates were randomly selected to investigate the intra- and inter-group genetic diversity of one urban (>400 people/km²) and two remote (<400 people/km²) regions. Alignment, using NCBI's Basic Local Alignment Search Tool and a H37Rv reference stain, was performed to gain insight on single nucleotide polymorphisms (SNPs) and hypervariable regions.

RESULTS

We observed that each location had significant differences in the mean total number of SNPs and intragroup variances ($p < 0.05$). Surprisingly, the urban region was most closely related to the reference strain and had the lowest intragroup genetic variance, compared to the remote region.

CONCLUSION

The urban region was observed to be least genetically diverse, refuting our hypothesis. This lack of genetic diversity may have been observed due to biases in reporting, as the available isolates were likely outbreaks in nature. In addition, geographical isolation, temporal variation, or inconsistencies between study methodologies could have contributed to the observed results. This demonstrates value in improving the standardization of open access data for future molecular epidemiological investigations.

G10. INTENSIFIED CONTACT TRACING LEADS TO IMPROVED PEDIATRIC CASE FINDING IN SURINAME

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BACKGROUND

The World Health Organization recognizes contact investigation as a good tool for identifying childhood tuberculosis. For years the NTP followed a passive approach towards contacts of TB patients, i.e. contacts were expected to contact the TB program for follow up after they were identified. This led to a very low follow up rate among the children identified as contacts of TB in Suriname.

INTERVENTION/RESPONSE

In 2017 the nurses of the TB Program implemented an active approach regarding the follow up of contacts aged younger than 15 years. Parents of child contacts were called to remind them to come for testing and those who tested positive for TST were monitored if follow up by the pediatrician were done to rule out active TB. This process was monitored to make sure that as much as possible contacts identified were screened and followed up.

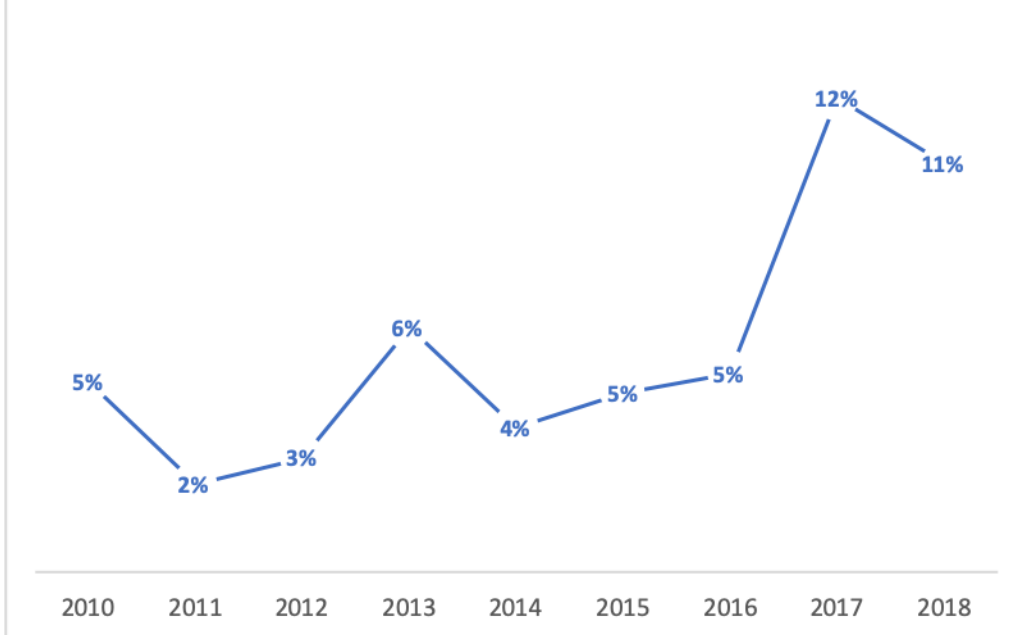
RESULTS

The screenings ratio among TB contacts went from 49% (n=280) in 2016 to 81% (n=403) in 2018. Also, the positive ratio of TST tests went from 40% to 59%. This resulted in an increase in the number of cases notified in 2018, namely 116 to 179 cases in 2018. Of the cases notified 7.4% (n=6), 21.0% (n=17) and 25.9% (n=21) were <15 years in 2016, 2017 and 2018 respectively.

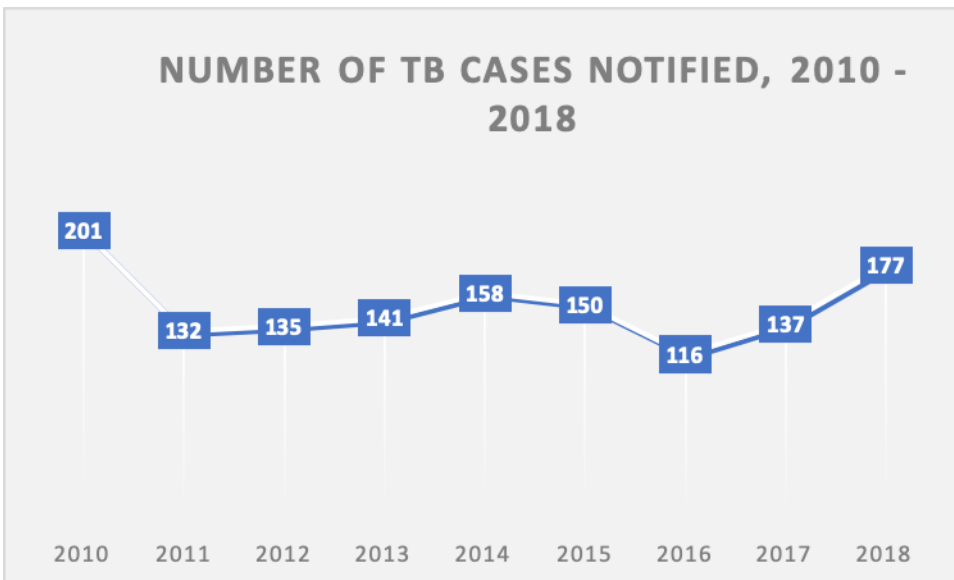
CONCLUSION

The approach of the nurses to actively follow up TB contacts increased case findings, especially among children. It is important that this intensified monitoring continues and is expanded to adults. This will further increase case detection rate.

PERCENTAGE CHILDREN (<15YEAR) AMONG NOTIFIED CASES, 2010 -2018



NUMBER OF TB CASES NOTIFIED, 2010 - 2018



H. PROGRAM EVALUATION

H1. THE PUBLIC – PRIVATE MIX STRATEGY FOR TB CONTROL: CONTEXTUAL FACTORS AFFECTING IMPLEMENTATION IN GHANA

Agbogbately M, Akweongo P. University of Ghana School of Public Health, Department of Health Policy, Planning and Management, Accra, Ghana.

BACKGROUND

The World Health Organization introduced the Public-Private Mix (PPM) initiative in the late 1990s to achieve TB control targets by strategically *engaging all health providers*. Ghana, one of the 30 high-burden TB countries implemented PPM in 2003 in some urban areas of the country. TB case notification, one outcome measure of PPM, has however been declining steadily in Ghana; the evidence from several studies in different locales, suggests that the performance of PPM is inevitably influenced by the context within implementing areas. This implementation research therefore explored contextual factors affecting the PPM initiative in Ghana.

METHODS

In-depth interviews with 23 purposively-selected TB focal persons in Accra and Kumasi Metropolitan areas of Ghana were held between April 2019 and June 2019. Thematic content analysis was used to use identify relevant themes.

RESULTS

Prominent amongst health system factors affecting PPM included, funding constraints - particularly the suspension of the enablers' package; monitoring and supervision challenges; and high attrition rates among TB staff in the private sector. A key enabling factor identified was the involvement of a new private implementing partner institution which was facilitating PPM activities.

CONCLUSION

Contextual factors are important barriers to PPM implementation; measures are needed to strengthen the initiative through addressing these.

H2. **HOW WELL DO HEALTHCARE WORKERS ESTIMATE TIME SPENT ON TUBERCULOSIS PATIENT CARE ACTIVITIES? A VALIDATION STUDY**

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BACKGROUND

Healthcare workers (HCW) perform numerous tasks throughout each work day. Quantifying HCW time allocation is important for planning and staffing. Continuous time and motion studies (TAMs) are considered the reference standard for quantifying workers' time spent on different activities, but are resource intensive and costly to perform. Our study aimed to validate the use of an interviewer-administered time-estimation questionnaire (TEQ) compared to a TAM study of HCW in five countries: Benin, Canada, Ghana, Indonesia and Vietnam.

METHODS

We developed and validated the TEQ to capture HCWs' time allocation across seven main categories of work activities. The TEQ was validated against the reference standard TAM, at the end of the same day, using correlation and equivalence testing. A linear mixed model was fit to estimate how well the TEQ measurements predicted the TAM time.

RESULTS

A total of 125 HCW participated in the TEQ study. The mean difference between the TAM and TEQ was less than 30 minutes (per day) for all categories of direct patient care activities. Correlation of the interviewer-administered TEQ with the TAM was above the criterion validity threshold of 0.70 in all categories of work activities. TEQ self-reports were equivalent to the TAM for total hours worked and LTBI patient care activities, but were not equivalent for active TB.

CONCLUSION

Our findings suggest that the TEQ performed well and achieved the threshold for criterion validity, as compared to the TAM. Self-reported time estimates may be useful in future research measuring health care resource needs.

Table 1: Comparison of Time* (hours) on the Same Day – TAM vs. TEQ for 125 HCW

| | TAM: Mean time, in hours, observed per HCW (range) | TEQ: Mean time, in hours, reported per HCW (range) | Mean Difference in time (hours) ¹ TAM – TEQ (95% CI) | Correlation coefficient ^{2,3} |
|---|--|--|---|--|
| Time Worked ⁴ | 5.8 (1-11) | 6.3 (3-11) | -0.7 (-1.0, -0.4) | 0.82 |
| Direct Patient Care | 2.2 (0-7) | 3.0 (0-9) | -1.0 (-1.3, -0.6) | 0.74 |
| Other Clinical Activity | 1.4 (0-7) | 1.4 (0-7) | 0.1 (-0.2, 0.2) | 0.80 |
| Training/Administrative Tasks | 2.1 (0-7) | 2.0 (0-7) | 0.3 (0.1, 0.6) | 0.92 |
| Direct Patient Care Activities ⁵ | | | | |
| Active TB | 0.8 (0-5) | 1.1 (0-5) | -0.4 (-0.6, -0.1) | 0.75 |
| LTBI | 0.6 (0-4) | 0.7 (0-6) | -0.1 (-0.3, 0.0) | 0.81 |
| Non-TB | 0.8 (0-4) | 1.1 (0-5) | -0.5 (-0.7, -0.2) | 0.84 |

¹Mean difference in time (and 95% CIs) in each category from a linear mixed model which accounts for clustering at the health facility level;

²Correlation was adjusted for the partial variance due to clustering at the health facility (site) level but did not change the coefficients;

³Note: All correlation coefficients were statistically significant at p-value <0.01;

⁴Total time worked = Direct Patient Care + Other Clinical Activity + Training/Administrative tasks;

⁵Direct Patient Care = time spent in direct contact with patients with Active TB + LTBI + Non-TB; *Note: Total time worked recorded on the TAM day included time on breaks but that time was removed from the analyses; HCWs were told not to include their break time for the interviewer-administered TEQ

H3. **LIGHTING THE SPARK - A PROCESS TO DETERMINE COORDINATED TB PROGRAM PERFORMANCE INDICATORS (PI) ACROSS PROGRAMS AND POPULATIONS IN CANADA**

Balakumar S, Haworth-Brockman M, Keynan Y. National Collaborating Centre for Infectious Diseases, Winnipeg, MB, Canada.

BACKGROUND

Coordinated TB program performance measurement across jurisdictions has been considered in Canada for several years. A federated system of surveillance with varying legislation, protocols, and public health capacity, necessitates cross-jurisdictional collaboration for any new monitoring initiatives. Varying circumstances and priorities across different TB-affected populations and communities requires additional consideration. The National Collaborating Centre for Infectious Diseases (NCCCID) has undertaken a suite of activities to support coordinated TB program PI development in Canada.

INTERVENTION/RESPONSE

NCCID conducted a needs assessment and environmental scan of Canadian TB programs and organizations representing TB-affected populations. This was followed by a review of Canadian and international TB programs and guidance documents to compile a large PI compendium as a resource for PI prioritization. In November 2018, NCCID convened a meeting to a) facilitate knowledge exchange on PI initiatives across regions, and b) undertake a PI prioritization exercise to assess the feasibility of implementing coordinated indicators across programs and populations.

RESULTS

First Nations, Inuit and urban and foreign born population-specific indicator discussions allowed for the creation of a proposed list of eight shared indicators across populations, as well as three larger population-specific indicator lists requiring further discussion and development. Work is ongoing to establish indicator definitions, mechanisms for data collection, governance and sharing, and a response plan for areas of underperformance.

CONCLUSION

NCCID's activities rely on flexible, formative and iterative consultation with an array of TB elimination stakeholders that builds on a shared understanding of the need for consistent and comparable TB program performance indicators to guide public health action.

H4. **TRAINING FOR THE NEW REPORT OF VERIFIED CASE OF TUBERCULOSIS (RVCT)**

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BACKGROUND

The Report of Verified Case of Tuberculosis (RVCT) was revised in 2019 to collect data on TB cases including risk factors, drug treatments, and diagnostic tests. CDC staff developed training to teach state and local TB surveillance staff how to accurately enter surveillance data on the new RVCT.

INTERVENTION OR RESPONSE

Trainings were conducted for state and local TB surveillance staff on how to accurately complete the new RVCT. Participants learned about the new RVCT variables by reviewing detailed case studies, completing mock data entry forms, and participating in group discussions. The interactive case study exercises were added after initial course evaluations indicated this would be an effective way to learn about the new variables.

RESULTS

Over 90% of the participants at several in-person trainings agreed that the training addressed gaps in their understanding of how to complete the RVCT. Following the addition of case studies to the course, participants reported that the interactive process of reviewing case studies and completing mock data entry forms was a highly effective method of learning.

CONCLUSIONS

Training that incorporates diverse and interactive learning methods such as case study exercises and mock data entry exercises can appeal to different learning styles and help learners build the skills necessary to accurately complete the new RVCT. Feedback from course evaluations will continue to inform future RVCT trainings. Accurate RVCT data gives TB program managers the information they need to improve TB programs.

H5. **MAKING SPACE FOR HEALTH EQUITY AND CULTURAL SAFETY WITHIN BC'S PROVINCIAL TUBERCULOSIS (TB) CLINICS**

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BACKGROUND

The Making Space for Cultural Safety and Health Equity Project aims to improve accessibility and appropriateness for Indigenous populations accessing the two provincial tuberculosis (TB) clinics at the BC Centre for Disease Control (BCCDC).

The need for this project was identified through baseline data indicating extremely low levels of Indigenous clients accessing our services, limited opportunities for cultural safety training for staff; clinical policies and procedures that are not equity enabling; and an overall lack of patient engagement.

INTERVENTION

In an effort to reduce barriers to care and improve cultural safety for Indigenous populations, we conducted an assessment of the provincial TB services' practices, and procedures, including a walk-through of our clinical spaces with Indigenous community members which yielded rich qualitative data.

Data collection from the walkthroughs and analysis occurred in July-August, 2019 with implementation of change ideas planned for October 2019.

RESULTS

Initial learnings include:

- The importance of family-friendly spaces that include basic childcare amenities.
- Ethnicity questions on intake forms should be thoughtfully and intentionally approached and rationale should be provided to clients explaining why questions are being asked.

CONCLUSION

Through this project we have learned some ways in which to improve the cultural safety within BCCDC's TB clinics. We plan to implement some of these changes in the fall, while continuing to work with our community partners, frontline staff, and leadership. We recognize that this project is a small, first step in making our clinical services more culturally safe and integrating reconciliation into practice.

H6. **VIRTUAL HEALTH FOR TUBERCULOSIS (TB) TREATMENT: AN EFFECTIVE WAY TO PROVIDE CARE?**

Jiwa S, Haag D, Cook V, Fenn K, Giffin C. British Columbia Centre for Disease Control, Vancouver, BC, Canada.

BACKGROUND

The Office of Virtual Health (OVH) in British Columbia (BC) is a Provincial Health Services Authority (PHSA) initiative mandated by the BC Ministry of Health to enhance virtual care as part of the care continuum for patients. In January 2019, the OVH and BC Centre for Disease Control's (BCCDC) Provincial TB Services Program (TBS) partnered to pilot a Virtual Health platform with patients to enhance access to care.

INTERVENTION/RESPONSE

In collaboration with the OVH, TBS developed workflows and recruitment criteria, trained staff and piloted the chosen Virtual Health solution. Recruitment started in April 2019 and included patients starting on Rifampin as their latent TB infection (LTB) treatment regimen. The process for the virtual care visit followed the same clinical guidelines as the clinic visit.

RESULTS

TBS began delivering Virtual Health patient-provider consultations in May 2019 to clients selected based on English proficiency and comfort with technology. From May to August 2019, 11 patients were recruited and 34 virtual visits were completed by two health care providers. Early feedback indicates positive patient and provider experiences.

CONCLUSION

The demonstration project is still in progress, but valuable lessons have been learned: selecting the appropriate patient audience for the technology is important, as is the need for dedicated clinical and operational resources to support successful implementation. Additionally, feedback indicates that patients on LTBI treatment value the time, cost and effort saved through Virtual Health consultations, but further evaluation of clinical outcomes is needed to ensure that the same quality of patient care is provided through Virtual Health.

H7. EVALUATION OF A HEALTH IMPROVEMENT STRATEGY BY CREATING A MOBILE HIV CARE TEAM (MHIVCT) IN COLLABORATION WITH COMMUNITY ACTORS (CAS) EXCLUDING MEDIATORS IN THE GOUDOMP HEALTH DISTRICT (GHD) – SEDHIOU/SENEGAL, 2017

Keita IM, Gomis VA, Diaw C, Anne M, Ndiaye S. GHD, Sedhiou Medical Regional Area, Ministry of Health and Social Action, Senegal.

BACKGROUND

Border Guinea Bissau, GHD is in southern Senegal and covered 270 villages/neighbourhoods with more than 550 staff. GHD created a MHIVCT which objective was to strengthen HIV&TB care in collaboration with CAs in GHD by 2017.

METHODS

The MHIVCT (Physician, Social Worker, HIV-Data Manager, TB treatment Manager, Laboratory Technician...) moved to disadvantaged and hard-to-reach areas to provide equitable HIV&TB care services. An retrospective cross-sectional study respecting ethical considerations was conducted in GHD, 2017. The data were collected by document reviews and DHIS2 exploitation. Data entry, analysis and interpretation required Excel and DHIS2 software. The results presentation forms are tables and graphs.

RESULTS

HIV testing increased by 10%, thus the number of newly recruited PLWHIV¹ increased by 27.2% including 15.2% of HIV2 and 4.5% HIV1&2. The share of VSC² increased from 42.7% (2016) to 79.5% (2017) including vulnerable groups (210MSM³ and 60SW⁴ were screened in 2017 compared to only 110MSM and 485 PLWD⁵ in 2016). The proportion of PLWHIV (newly screened) on ART⁶ has increased from 73% (2016) to 94% (2017) and the number of PLWHIV on ART lost to follow-up (excluding non-zones) decreased by 62.5%. And the proportion who received viral load increased from 37% (2016) to 46% (2017). The proportion of children, born to HIV-Positive mothers, who received definitive serology increased by 62.5%. Screening for TB-HIV co-infection was boosted by 46.2%. The proportion of PLWHIV on ART who died decreased from 31% (2016) to 18% (2017).

CONCLUSION

Created in 2017 by GHD, the multidisciplinary MHIVCT was a great success.

Keywords: Mobile team, HIV care, Community Actors, Goudomp, Sénégal

Abbreviations: ¹Person Living With HIV (PLWHIV); ²Voluntary Screening Campaign (VSC); ³Men Having Sex with Men (MSM); ⁴SW; ⁵Person Living With Disability (PLWD); ⁶Antiretroviral Treatment (ART)

H8. **MODERNIZING U.S. TUBERCULOSIS SURVEILLANCE: THE 2020 REPORT OF VERIFIED CASE OF TUBERCULOSIS**

Langer A, Magee E. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

Current U.S. tuberculosis surveillance is based on the 2009 version of the Report of Verified Case of Tuberculosis (RVCT). By 2015, quality assurance issues with some of the 2009 RVCT questions, the release of the 2015 National Action Plan for Multidrug-Resistant Tuberculosis (including 5-year goals related to surveillance), adoption of several Council of State and Territorial Epidemiologists position statements, and the National Notifiable Diseases Surveillance System Modernization Initiative demonstrated that RVCT revisions were necessary.

INTERVENTION OR RESPONSE

In 2016, CDC established a goal to implement a revised RVCT by 2020 and formed a workgroup of internal and external stakeholders to create a new RVCT. Following completion of the workgroup process, CDC invited extensive stakeholder review of the proposed 2020 RVCT. Concurrently, CDC modernized 2020 RVCT data transmission standards. CDC has periodically updated stakeholders through presentations and written communications and is developing reference documentation and training materials.

RESULTS

The collaborative process resulted in a restructured and more flexible RVCT with substantial support from stakeholders. CDC finalized the content and format of the 2020 RVCT in September 2019. The 2020 RVCT also establishes a framework for future latent tuberculosis infection surveillance initiatives. A new reference manual is nearly complete, and CDC has conducted two 2020 RVCT training courses, with additional courses and online training materials planned.

CONCLUSION

The methodical, collaborative process used for the 2020 RVCT has provided many lessons to inform future efforts to improve national tuberculosis surveillance. The initial years of 2020 RVCT use might provide additional insights to continually improve surveillance activities.

H9. COLLABORATION ACROSS NATIONS FOR IMPROVED TB TREATMENT AND PREVENTION

Ringsdorf L, Ledezma E, Lopez G. Department of State Health Services Public Health Region 8, San Antonio, TX, USA.

BACKGROUND

TB is a concern for both Mexico and the United States, with states on both sides of the border reporting higher incidence rates than their respective national rates. The fluidity of travel for border residents creates favorable opportunities for treatment lapses and TB transmission.

INTERVENTION/RESPONSE

A CDC funded binational tuberculosis prevention program, *Esperanza y Amistad* is combining clinical practice with prevention. A team of skilled clinicians collaborates with a multi-sector public health workgroup which includes the Kickapoo Traditional Tribe of Texas, the Texas Department of State Health Services and the Mexican Secretariat of Health, in an effort to reduce TB disease. In treating a recent patient with TB disease from Texas, 121 contacts in Texas and 26 contacts in Mexico were identified, with an infection rate of 21% and potential linkages in transmission, with three persons identified with the same genotype. An additional active case of TB was also identified through the contact investigation process in Mexico.

RESULTS

This collaboration allows for enhanced communication, development of reporting protocols and agreements across nations for patient management. This includes agreements in treatment of multi-drug resistant cases, collaboration in identifying and testing contacts, and conformity in the use of Rifampin for treatment of latent TB infection as well as the use of IGRA across countries.

CONCLUSION

A multi-sector and binational approach is necessary in treatment of tuberculosis especially in border areas with large population movement, increased potential for disease transmission, limited public health infrastructure and poor environmental conditions.

H10. **DEVELOPING A PROVINCIAL TUBERCULOSIS CONTACT TRACING CASCADE OF CARE FRAMEWORK AND INDICATORS IN BRITISH COLUMBIA, CANADA**

Leung JW^{1,2}, Johnston JC^{1,3}, Newhouse E⁴, Hayden A⁵, Zamanpour A¹, Bharmal A⁴, Fung C⁴, Romanowski K^{1,3}, Roth D¹, Gabler K⁵, Wolf I², Thompson C⁶, Swinkels H², Loughheed N⁷, Hoyano D⁸, Cook VJ^{1,3}, Wong J^{1,3} on behalf of the British Columbia Tuberculosis Surveillance Working Group. ¹British Columbia Centre for Disease Control; ²First Nations Health Authority; ³Faculty of Medicine, University of British Columbia, Vancouver; ⁴Fraser Health Authority, Surrey; ⁵Vancouver Coastal Health Authority, Vancouver; ⁶Ministry of Health, Victoria; ⁷Interior Health Authority, Kelowna; ⁸Island Health, Victoria, BC, Canada.

BACKGROUND

Strengthening contact tracing is a key component of the strategy to eliminate tuberculosis (TB) in the province of British Columbia (BC), Canada. Using a cascade of care approach, we developed indicators to monitor and identify opportunities for improvement in TB prevention among contacts.

INTERVENTION OR RESPONSE

Indicators were developed related to TB screening, latent TB infection (LTBI) diagnosis and treatment, and secondary cases of active TB among the total number of contacts reported. Indicators were stratified by completion at 12, 26, and 52 weeks after source case diagnosis. The indicators were reported from the provincial TB database that was implemented in March 2016.

RESULTS

There were 1,555 and 2,451 contacts reported in 2016 and 2017, respectively. Between the two years, 89%-93% of contacts completed initial TB screening, with the majority (72%-81%) completing screening within 12 weeks of source case diagnosis. A positive screen (i.e., reactive Interferon Gamma Release Assay (IGRA), or positive Tuberculin Skin Test without subsequent non-reactive IGRA) was identified among 18%-21% of contacts, of whom only 23% completed LTBI treatment (both years). Active TB was diagnosed in less than 1% of contacts.

CONCLUSION

These indicators are a valuable tool to assess outcomes of contact tracing and highlight opportunities for improvement to support TB elimination in BC. Time stratification of indicators is essential to understanding cascade dynamics and ensuring timely follow-up. Future work includes setting provincial targets and improving data quality to enable addition of indicators and stratifications.

H11. **EVALUATION OF TARGETED PEDIATRIC TUBERCULIN SCREENING IN SOUTH AND CENTRAL SASKATCHEWAN FIRST NATIONS COMMUNITIES, 2017 – 2018**

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BACKGROUND

Bacille Calmette-Guérin vaccination was discontinued in South and Central Saskatchewan First Nations communities (South Central) in 2011, leading to the implementation of targeted pediatric tuberculin skin test screening (TPTS). The changes to TPTS policy and procedures were evaluated to inform decisions for the subsequent screening year.

METHODS

The evaluation covered the period between September – December in 2017 and 2018, respectively. Data sources were standardized tuberculin skin test (TST) screening data, surveys, program data, and literature and document reviews. Tuberculosis healthcare professionals (TBHP) were surveyed on the benefits, barriers and relevance of the TPTS program to South Central. Screening took place in schools located in South Central. The population of South Central in 2018 was approximately 41,000.

RESULTS

During the screening period, 593 of 1,131 eligible children (six year old birth cohort) were screened for TB. There was one positive result in 2018, later diagnosed with latent TB infection (LTBI). An associate contact investigation of the LTBI case resulted in identification of five associates exposed to the case. Of the sixteen TBHP surveyed, the majority stated that the program did not adequately meet the TB screening needs of communities.

CONCLUSION AND RECOMMENDATIONS

Although yield of the screening program was low, the evaluation showed the importance of TB screening in high risk population groups. The evaluation highlighted the need to develop a data collection plan, revisit the high risk population targeted for screening, and develop a contingency plan for communities experiencing challenges in collecting TST data due to staff turnovers.

H12. **THOUGH THE EYES OF CIVIL SOCIETY ORGANIZATIONS, GAPS IN TB HEALTH SERVICES IN HINTERLAND POPULATION**

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BACKGROUND

To achieve some of the targets set by the National TB programme (NTP), collaboration is necessary with civil society organizations through community levels interventions with an aim of decreasing the incidence and prevalence of TB among key populations.

METHODS

The gap analysis for TB intervention was done by a Civil Society Organization engaged in the recently concluded grant. Report from activities implemented for the period August 2018 to March, 2019 was analyzed, since it was necessary for the continuation of the CSO engagement by the NTP. The gap analysis was informed by a survey utilizing questionnaires in 4 hinterland regions, focusing mainly on level 1 health care facilities, health workers and community members.

RESULTS

A total of 12 health facilities were assessed and 275 health workers and community members were interviewed. The majority of the respondents stated DOT as the means of curing TB with an 83% of systems in place for TB medication distribution. Over 92% of the interviewees indicated that a healthcare provider explained treatment benefits and consequences of non-adherence. Of the 12 facilities assessed 7 indicated TB screening was not done with a mere 25% of resources available for laboratory work. Majority (60%) of the health facilities have a system in place for the requisition of medicines, specifically anti-TB medication.

CONCLUSION

The collaborative efforts in TB implementation at the community level are paramount in health system strengthening. The limited/lack of key resources in remote areas may result in the facilities inability to offer vital services to the community.

H13. **PATIENT-CENTERED MONITORING FOR TB TREATMENT ADHERENCE IN A LARGE MEXICAN HEALTH JURISDICTION.**

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BACKGROUND

Ciudad Juarez (CJ) is the second largest Mexican city on the US-Mexico border. In 2017, only 86% of individuals starting tuberculosis therapy in CJ had a successful treatment outcome. A major barrier is the need for patients to come to their local health center for directly observed therapy (DOT) doses. Mobile technology for DOT is being increasingly adopted to enhance patient-centered care. In 2017, the first Mexico-initiated use of video DOT technology was launched in CJ, Chihuahua, Mexico.

METHODS

Patients were enrolled between December 2018 and March 2019. Inclusion criteria were >15 years old, stably housed and >1 mile from the health center, no substance abuse, and known susceptibility to all four first line medications. Enrolled patients and TB program staff were trained in use of miDOT (eMOCHA) for monitoring and recording adherence. Smart phones were provided to patients. Monthly reports of adherence were sent to the local health jurisdiction and project coordinators. Outcome measures were percentage of monitored doses/expected doses, percentage with documented culture conversion, and the overall rate of treatment completion.

RESULTS

Forty patients were enrolled. 60% were male, median age =30. Patients completed a median of 90.8% of expected doses, 90% had documented culture conversion.

CONCLUSION

Mobile technology for TB treatment adherence shows promise in Mexico. High rates of adherence are possible and is likely to be well-accepted by patients.

H14. **THE EVALUATION OF NON-CLINICAL INTERVENTIONS AND OUTCOMES IN MODEL-BASED ECONOMIC EVALUATIONS FOR TUBERCULOSIS: A SCOPING REVIEW**

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BACKGROUND

This scoping review seeks to systematically assess the existing literature on model-based economic evaluations on tuberculosis (TB) interventions in order to characterize existing economic evaluations and gauge the extent to which non-clinical interventions and outcomes have been evaluated.

DESIGN/METHODS

A literature search was conducted in MEDLINE, Embase, and PsychINFO databases. Eligible articles used decision-analytic modeling for economic evaluation of TB related interventions. One reviewer screened all articles, and 10% of articles were screened by a second reviewer to ensure accurate application of inclusion criteria. Study information and design were charted and summarized for all included studies, and studies were categorized by intervention type. This study was completed following the Joanna Briggs Institute Methods for scoping reviews.

RESULTS

The database search identified 7,646 unique articles. Following title and abstract screening, 157 full text articles were reviewed, and 97 met the inclusion criteria. The majority of articles were published from 2010 onwards (62%). Five studies included non-clinical interventions, and none reported non-clinical outcomes. The majority of studies considered interventions in the following areas: screening, diagnosis, and drug treatments. The non-clinical interventions identified included smoking cessation strategies and treatment adherence programs.

CONCLUSION

There were few studies that included non-clinical interventions and none that measured non-clinical outcomes (e.g., equity). The burden of TB is significantly impacted by social determinants of health (e.g., nutrition, crowding) and requires the evaluation non-clinical interventions (in addition to single biomedical interventions) in order to effectively set health policy priorities and meet international TB reduction goals.

H15. A PLAN FOR TUBERCULOSIS ELIMINATION IN ARKANSAS: IT'S PAST TIME

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BACKGROUND

Arkansas experienced a dramatic decline in TB incidence from 84.8/100,000 (1953) to 2.6/100,000 (2018). The Arkansas Department of Health (ADH) is committed to the elimination of TB. Current modeling suggests that at the current rate of decline, elimination will not be achieved by the end of this century, resulting in unnecessary illnesses and deaths. A significant barrier to elimination are the 90-100,000 Arkansans with latent TB infections (LTBI) who may progress to active disease. Elimination requires a coherent strategy; we present here the first TB elimination plan in Arkansas.

INTERVENTION

TB elimination will be achieved by reducing the burden of LTBI in the population. This plan features a two-pronged approach: maintain current TB disease activities while expanding high-risk based screening and treatment for LTBI, especially contacts, non-US born, and persons with diabetes. The cornerstone of the plan is the formation of an Arkansas TB Elimination Advisory Committee (ATEAC) comprised of members who share the vision of a TB free Arkansas. This group will meet to discuss implementation efforts, overall progress, and evaluate the plan.

RESULTS

Currently, the elimination plan is undergoing final revisions before publication. Elimination will be achieved at an incidence of 1 case per million population. Relevant stakeholders have endorsed the plan, and thus the plan is pending implementation.

CONCLUSION

Publishing the first plan in Arkansas' history presents an exciting opportunity to accelerate the elimination of TB. Bringing relevant partners together for regular discussion and project evaluation will accelerate the path to our TB elimination goal of the year 2040.

H16. **PATIENT PREFERENCES ACROSS DIFFERENT MODALITIES OF DIRECTLY OBSERVED THERAPY FOR TUBERCULOSIS TREATMENT**

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BACKGROUND

We conducted a randomized cross-over trial comparing in-person directly observed therapy (ipDOT) with electronic DOT (eDOT) for tuberculosis (TB) treatment in four New York City TB clinics. Participants were first randomized to either ipDOT or eDOT for 20 medication doses, then switched observation mode for 20 subsequent doses. We report on DOT preference for treatment following the two cross-over periods.

METHODS

During cross-over completion visits, participants were asked which DOT mode they preferred and reasons for their choice. Study staff documented this information on a visit form. We analyzed chosen preferences. Free-text responses of reasons were thematically analyzed.

RESULTS

Of 216 enrollees, 153 (71%) completed both observation periods. Of these, 145 (95%) provided reasons for DOT preference. We excluded eight participants: five gave no answer; three discontinued TB care. Participants' median age was 40 years (IQR: 27-53); 95 (66%) were male; 131 (90%) were non-U.S. born.

137 (94%) participants chose eDOT for treatment continuation, using live video conferencing (n=69) or recorded videos (n=68). Six participants chose field-based DOT (FDOT); and two chose self-administered treatment. None preferred clinic-based DOT. Participants who chose FDOT were older (median age 70.5, IQR: 65-75.5). Participants preferring eDOT most often made reference to work, school or personal schedules (45%, n=61) and/or mentioned convenience of eDOT (40%, n=55), ease of use (20%, n=27), and not having to travel (20%, n=27).

CONCLUSION

In this study, most persons who experienced both ipDOT and eDOT preferred to complete therapy with eDOT. Further insight into patient preferences may facilitate treatment support strategies.

H17. PERSISTENCE OF EFFECT FROM INTERVENTIONS TO INCREASE DIAGNOSIS AND TREATMENT OF LTBI IN HOUSEHOLD CONTACTS, FOLLOWING A PUBLIC HEALTH INTERVENTION STUDY IN RIO DE JANEIRO, BRAZIL.

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BACKGROUND

Less than 18% of those needing latent TB infection (LTBI) treatment complete it, due to losses in several steps of the cascade-of-care. We conducted a follow-up study 7 months after the conclusion of a cluster randomized trial of a programmatic public health intervention to improve LTBI treatment initiation in household contacts (HHC). We aimed to identify effectiveness and persistence of interventions from healthcare worker's (HCW), HHCs and index-patient's perspective.

METHODS

In two health clinics in Rio de Janeiro, Brazil, semi-structured open-ended questionnaires were administered to HCW, HHC and index-patients regarding knowledge and perceptions about TB and study interventions (initial and in-service training, educational material). The cascade-of-care for LTBI in HHC was analysed for all index patients diagnosed with active TB over 5-months.

RESULTS

Cascade analysis during the trial: 190 HHC were identified and 5 started LTBI treatment per 100 TB patients, and after the interventions, there was no significant difference in HHC identified, but 42 more started treatment (95%CI 22, 63) per 100 index TB patients. In the follow-up study, significantly fewer HHC were identified but the number starting treatment did not change. 19 HCW, 22 HHC and 31 index-patients were interviewed. 61% of HCW said the booklet was one of the most helpful interventions and 56% mentioned initial training. 61% of index patients said all their HHC had been tested for LTBI, 23% said a HHC started LTBI treatment.

CONCLUSION

In this follow-up study, a persistent, and positive effect of the intervention on the number of HHC starting treatment was seen.

I. LTBI

11. THE USE OF INTERFERON-GAMMA RELEASE ASSAYS FOR LATENT TUBERCULOSIS INFECTION SCREENING IN FEDERAL CORRECTIONAL FACILITIES (ALBERTA, CANADA)

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BACKGROUND

The correctional setting presents an opportunity to undertake public health interventions in otherwise hard to reach populations. In 2013, the Province of Alberta, Canada, implemented a latent TB infection (LTBI) screening strategy in federally incarcerated inmates (sentences ≥ 2 years) of following all positive tuberculin skin tests (TSTs) with an interferon gamma release assay (IGRA; QuantiFERON-TB Gold in-tube assay). We evaluate factors associated with TST and IGRA fidelity, identify potential reasons for discordance, and report the outcomes of LTBI treatment.

METHODS

To evaluate the association between demographic and clinical variables and predictors of concordance with the IGRA findings we used one-way ANOVA, Pearson's chi-square test, or Fisher's exact test for expected cell counts ≤ 5 . Thereafter, we examined the contribution of positive predictors from univariate analyses in a multiple logistic regression model. We report outcomes among those offered LTBI treatment.

RESULTS

We analyzed data from 306 inmates, 27 (8.8) female. We observed concordance between the TST/QFT tests in 90 (29.4%). Persons with TST+/QFT-G+ results were less likely to be male, or have a BCG vaccination history, and more likely to be foreign-born ($p < 0.001$). Of the 108 inmates were offered LTBI treatment; 65 (60.1%) accepted and 40 (61.5%) completed in the study period. TST/IGRA discordance has not been associated with disease in follow-up.

CONCLUSION

TST/QFT discordance in Canada among federal correctional facilities and with a low-risk of disease suggests that shift towards IGRA based LTBI screening is warranted. Concordance suggests a targeted screening strategy.

12. **ASSOCIATIONS OF TEST RESULTS AND OTHER CHARACTERISTICS WITH LTBI TREATMENT OUTCOMES**

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BACKGROUND

LTBI care is crucial to TB elimination in the United States (US). This study describes LTBI testing and treatment practices in TB programs.

METHODS

During 2012-2017, a study in 11 states tested participants at high risk for LTBI with two interferon-gamma release assays (IGRAs) and a tuberculin skin test (TST). We included in this analysis clinics whose physicians had access to at least one IGRA and one TST result when treatment was offered and to participants with ≥ 1 positive test. Factors associated with treatment being offered and completed were examined with site-stratified risk ratios (RR) and 95% confidence intervals (CI) and multivariable logistic regression with random intercept for clinic.

RESULTS

Among 6,179 participants with at least one positive test, 3,470 (56%) were offered treatment: 87% (2373/2740) of IGRA+/TST+, 60% (363/602) of IGRA+/TST-, and 26% (734/2837) of IGRA-/TST+. Compared to IGRA-/TST+, an IGRA+/TST+ result was positively associated with offers of treatment in 11/13 clinics [RR range 1.1 (CI 1.1-1.2) to 70.8 (CI 26.7-187.5)]. Among IGRA+/TST+ participants, offers of treatment were significantly more common among close contacts to infectious TB cases (adjusted odds ratio (aOR) 4.5, CI 2.4-8.4) and less common among persons ≥ 65 years vs. 18-44 years (aOR 0.27, CI 0.17-0.42). Homelessness was negatively associated with treatment being offered (aOR 0.48, CI 0.23-1.0) and completed (aOR 0.30, CI 0.17-0.53); 42% of homeless persons were offered and 48% completed treatment.

CONCLUSION

Clinicians are more likely to offer LTBI treatment to patients with positive IGRA results. Strategies are needed to improve LTBI management among homeless populations.

13. **THE LATENT TUBERCULOSIS INFECTION CASCADE-OF-CARE AMONG PEOPLE LIVING WITH HIV: A SYSTEMATIC REVIEW AND META-ANALYSES**

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BACKGROUND

Tuberculosis (TB) preventive therapy (TPT) can reduce TB incidence in people living with HIV (PLHIV), but the proportion initiating treatment, of all those who are eligible is unknown. We conducted a systematic-review (SR) to quantify losses at each step of the LTBI cascade-of-care among PLHIV.

METHODS

We followed methods and search terms used in a previous SR on LTBI cascade-of-care, but with focus on PLHIV. All cohorts including at least 25 participants and reporting two consecutive cascade steps were included. Included studies reported data exclusively among PLHIV or stratified by HIV-status. We used two different frameworks to define the cascades, depending on the use LTBI tests. We meta-analyzed the proportion of PLHIV completing each step of the LTBI-cascade.

RESULTS

A total of 54 cohorts comprising 70,878 PLHIV were included. Completion in each step was similar among the 39 cohorts using LTBI testing and 15 cohorts not using LTBI testing ranging from 68%-85% and 65%-85%, respectively. The cumulative TPT completion was 41% in cohorts that used LTBI tests and 34% in cohorts that did not use tests. Table shows the cumulative retention for each of the cascades, stratified by World-Bank income.

CONCLUSION

Irrespective of LTBI testing, cumulative retention in each cascade step was satisfactory and higher than what has been previously reported for contacts. Retention was similar in programmes that used LTBI testing, as those with simplified management procedures. PLHIV are usually linked to healthcare and TPT has been a recommendation for many years by the WHO and others, which might explain our findings.

Table . Summary table comparing the cumulative retention in the cascade-of-care for different management strategies and resource level^{1,2}

| | <i>Used LTBI tests (N=22 cohorts) High income countries²</i> | <i>Used LTBI tests (N=16 cohorts) Low- & middle-income countries²</i> | <i>Did not use LTBI tests (N=15 cohorts) Low- & middle-income countries</i> | <i>Did not use LTBI tests or chest x-ray (N=11 cohorts) Low- & middle-income countries</i> |
|---|---|--|---|--|
| Step 1: Initial tested/Identified | 91.0% (90.6%, 91.3%) | 83.0% (82.1%, 83.9%) | - | - |
| Step 2: Completed tested/initial tested | 89.2% (88.6%, 89.7%) | 76.6% (75.2%, 77.9%) | - | - |
| Step 3: Medical evaluation /referred for med evaluation | 62.3% (56.6%, 67.3%) | 76.3% (74.3%, 77.9%) | 77.9% (77.2%, 78.7%) ³ | 88.5% (87.7%, 89.3%) ⁴ |
| Step 4: Recommended LTBI treatment/medical evaluation | 56.6% (49.8%, 62.8%) | 64.2% (61.2%, 66.8%) | 60.5% (59.0%, 61.9%) | 69.4% (67.6%, 71.1%) |
| Step 5: Started LTBI treatment /recommended | 42.7% (34.9%, 50.3%) | 52.6% (48.8%, 56.0%) | 39.4% (37.5%, 41.2%) | 43.2% (40.9%, 45.5%) |
| Step 6: Completed LTBI treatment/started treatment | 29.5% (21.6%, 36.0%) | 41.7% (37.9%, 45.3%) | 33.6% (31.7%, 35.7%) | 36.7% (34.4%, 39.1%) |

Notes

1. The value for each level is calculated as the product of the value from the preceding step, multiplied by the pooled estimate for that step (from fixed-effects analysis).
2. One study was multicenter and included sites from different regions and results were not stratified by center, therefore excluded from these analyses.
3. Step 3: Symptom screen (with or without chest x-ray) /Identified
4. Step 3: Symptom screen/identified
5. Referred – in studies that used LTBI tests, this was adjusted to include only those with positive LTBI tests.

14. **PREVALENCE OF LATENT TUBERCULOSIS (LTBI) IN A POPULATION OF MEDICAL STUDENTS IN MONTERREY MEXICO.**

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BACKGROUND

Latent tuberculosis infection (LTBI) is a persistent immune response state to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifest active TB. People with LTBI have no signs or symptoms of TB, but are at risk of active TB when their immune conditions are deficient. The highest risk factor is infection with the human immunodeficiency virus (HIV). Other comorbidities and conditions associated with the reactivation of LTBI are classified as high, moderate, light, low and very low risk, depending on the associated risk factors. Medicine students has been poor studied about the risk of acquire TB infection during medical career.

DESIGN/METHODS

This report corresponds to a Cross-Sectional study carried out in an educational institution in northern Mexico where the frequency of LTBI in medical students in the first years of the career where compared with the proportion of LTBI in students from the last years of the career. Students from the last years of career have contact with patients while students from the first years have not contact.

RESULTS

Medical students showed a frequency of 20.1% of LTBI, then, proportions of LTBI in students from first years showed a proportion of 9.3% of LTBI while those from the last years of career showed a frequency of 50% of LTBI. These differences were statistically significant.

CONCLUSION

In a medical school in northern Mexico, medical students in the first semesters of the career have less LTBI than students in the last semesters of the career who are in contact with patients.

15. **GLOBAL TB PREVENTIVE THERAPY (TPT) ADHERENCE: TIMELY LESSONS FROM ESWATINI**

Grande SW, Adams LV, Maseko TSB, Talbot EA, deGijssel D, Mikal J, Simelane ZZ, Achili A, Mkhontfo M, Haumba SM.

BACKGROUND

Eswatini has one of the highest rates of TB/HIV co-infection in the world, despite guidelines-based national strategies to improve care delivery and prevent TB transmission. A recent study of integrated, patient-selected TPT delivery showed surprisingly high completion. This prompted the need to identify contextual and unseen factors that contributed to this high rate, with an aim to extend to similar settings.

METHODS

Among people living with HIV in Eswatini who participated in an observational study comparing modes of TPT delivery, community-based participatory research guided the development of semi-structured questionnaires for administration by trained interviewers at the participant's healthcare facility. Observational and field note data were analyzed. Qualitative data were analyzed using content analysis.

RESULTS

Between June and October 2017, we interviewed 150 participants, and analyzed responses from the 136 who remembered receiving a choice of their TPT delivery method. Fifty-seven percent were female and the median age was 42. Sixty-five percent chose to receive facility-based TPT. TPT treatment completion was linked to four key concepts: 1) adherence was positively impacted by community education; 2) disclosure of status served to empower participant completion; 3) mode of delivery perceptions positively impacted adherence; and 4) choice of treatment delivery was seen as helpful but not essential for treatment completion.

CONCLUSION

Achieving high rates of TPT completion in Eswatini required community-engaged education and outreach in coordination with care delivery systems. National TB programs in similar high-burden settings should adapt these lessons to improve TPT adherence and ultimately reduce the burden of TB.

16. CIVIL SURGEON LATENT TB INFECTION REPORTING IN CALIFORNIA

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BACKGROUND

Civil surgeons perform latent tuberculosis infection (LTBI) testing for persons applying to adjust their immigration status to permanent residency. As of October 1, 2018, civil surgeons were required to report LTBI to local health departments (LHDs) and advise applicants with LTBI that treatment prevents active TB. Civil surgeons in all LHDs except San Diego and San Francisco use CalREDIE (California's electronic disease reporting system) for LTBI reporting. CDPH and LHDs conducted outreach to >1000 civil surgeons about new requirements and reporting mechanisms. We aimed to assess reporting of LTBI and LTBI treatment to inform additional outreach.

METHODS

We analyzed LTBI reports from civil surgeons to CalREDIE during Oct 1, 2018–Aug 19, 2019.

RESULTS

California LHDs received 2,207 LTBI reports from at least 216 civil surgeon offices in 38 LHDs. Five LHDs accounted for 75% of reports. CalREDIE received 780 (35%) reports of treatment referral and 414 (19%) reports of treatment initiation. Isoniazid for 9 months was the most commonly reported regimen (n=191, 46%), followed by 4 months of rifampin (n=104, 25%) and 12 weekly doses of isoniazid and rifapentine (n=85, 20%).

CONCLUSION

Hundreds of civil surgeons across California reported LTBI using CalREDIE during the first year of new requirements. However, an estimated 100,000 persons apply for status adjustment each year in California. It is likely that a majority of LTBI in this population is not yet being reported. Continued outreach to civil surgeons to maximize reporting and LTBI treatment is needed to increase TB prevention in this population.

17. **GAPS IN STUDY DESIGN FOR IMMUNE PARAMETERS RESEARCH FOR LATENT TUBERCULOSIS INFECTION. A SYSTEMATIC REVIEW.**

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BACKGROUND

The objective was to determine immune parameters (IP) associated with LTBI, compared to active TB and healthy individuals using previously published literature.

DESIGN/METHODS

We conducted a systematic search using Google Scholar and PubMed databases, combining the MesH terms: latent tuberculosis, *Mycobacterium tuberculosis*, cytokines, and biological markers; with the free terms, biomarkers and cytokines. Spanish, English and Portuguese articles comparing the concentration of IP associated with LTBI, either in plasma/serum or in vitro, in adults, non-immunocompromised, versus individuals with TB or without *M. tuberculosis* infection between 2006-july/2018-july were included. Two blinded reviewers carried out the searches, read the abstracts and selected the articles for analysis. Participant's information, diagnostic criteria, IP, detection methods, and biases were collected.

RESULTS

We analyzed 37 articles (of 637 abstracts), which reported on 87 IP. 22, 5, and 2 IP were increased in active TB, LTBI, and healthy individuals, respectively. We found high heterogeneity between studies including failure to account for the time/illness of the individuals studied; varied samples and protocols; different clinical classification of TB; different laboratory methods for IP detection, which in turn leads to variable units of measurement and assay sensitivities; selection bias regarding TST and booster effect. None of the studies adjusted the analysis for the effect of ethnicity on the association between IP and the different stages of TB.

CONCLUSIONS

Studying IP in LTBI is important in order to prioritize preventive treatment. Heterogeneous study populations, samples and experimental conditions, and pooling of LTBI at various times, prevented identification of biomarkers associated with recent infection. PROSPERO-CRD42017073289.

18. **MANAGEMENT OF LATENT TUBERCULOSIS INFECTION (LTBI) USING 3-MONTH RIFAPENTINE AND ISONIAZID (3HP) IN AN INNER-CITY POPULATION WITH PSYCHOSOCIAL BARRIERS TO TREATMENT ADHERENCE AND COMPLETION**

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BACKGROUND

In Canada, preventive therapy for LTBI has meant long durations and frequent dosing. This contributes to poor adherence and completion rates. In response, a shortened treatment regimen, once weekly rifapentine plus isoniazid for 3 months (3HP), is now available, though there has been no formal evaluation of its use. This study explores perceptions of latency and the need for preventive therapy, and barriers and facilitators to treatment adherence and completion in inner-city clients offered 3HP.

DESIGN/METHODS

This qualitative descriptive study involves semi-structured individual interviews. Unstably housed or homeless individuals in Edmonton and Fort McMurray, Alberta, Canada offered directly observed preventive therapy (DOPT) with 3HP are eligible. The data were systematically organized and analyzed using latent content analysis.

RESULTS

Preliminary analysis of six interviews reveals that LTBI and the need for preventive therapy is poorly understood. Facilitators to treatment uptake and completion were a desire to achieve health, fear of death related to TB, and self-motivation to complete therapy. Participants noted the ease of regimen, limited side effects, and positive aspects of DOPT during their treatment. Competing priorities, side effects, and pill burden were reported as barriers to completing therapy. Participants reported feelings of stigma and disease-related shame connected to LTBI and TB.

CONCLUSIONS

Results from this study can help formulate and refine LTBI treatment programs in Canada, especially among underserved populations. This research may support advocacy efforts related to the provision of shorter treatment regimens and interventions that address the stigma and shame related to diagnoses of LTBI and TB.

19. **LATENT TUBERCULOSIS INFECTION REPORTING TO CDC; THE IMPLEMENTATION PROCESS IN ARKANSAS – 2019**

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BACKGROUND

Although reporting of active tuberculosis (TB) to the CDC began in 1953, that of latent tuberculosis infection (LTBI) was only recently implemented, in July 2019. Arkansas is 1 of 5 jurisdictions that received a supplemental grant from the CDC to launch LTBI reporting for the first time ever. LTBI has been reportable in Arkansas for the past 30 years. In this report, we outline the implementation plan to report LTBI to CDC.

RESPONSE

In 2014, Arkansas deployed an electronic health record (EHR) system in all 75 counties and all LTBI cases were computerized. Furthermore, since 2013, Arkansas has maintained the database for treatment outcomes of the 12-dose, once a week, Isoniazid/Rifapentine regimen (3HP) for LTBI. This project was sponsored by CDC. We constructed a master list of all LTBI cases reported in the period 2014-2019 using an Access database. The surveillance form provided by CDC consisted of 28 variables that included a unique state case number, patient demographics and clinical and treatment outcomes. Data were stored in a CDC-derived Web-enabled RedCap database by a team of 3 research analysts.

RESULTS

From January – December 2018, approximately 800 LTBI cases have been reported. Determining the descriptive epidemiology of LTBI in Arkansas using data for 2014-2019 will be the next step.

CONCLUSION

The launch of LTBI reporting to CDC has been successful in Arkansas. Implementation should be generalizable in jurisdictions where LTBI is reportable. The critical challenge in this effort is manpower.

Acknowledgements: CDC Supplemental Grant CDC-RFA-PS20-2001

110. **PRIORITIZING USE OF RIFAMPIN DURING A SHORTAGE IN ONTARIO: DEVELOPING A RESOURCE FOR PREVENTIVE TREATMENT OF LATENT TB INFECTION**

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BACKGROUND

In Canada and globally, rifampin is a critical drug for treating active tuberculosis (TB). However, recent evidence also supports the use of rifampin for the preventive treatment of latent TB infection (LTBI). Interest is growing in rifampin, taken daily for four months, as a shorter alternative to isoniazid taken daily for nine months for treating LTBI. In the summer of 2019, Ontario and other jurisdictions experienced a rifampin supply shortage.

RESPONSE

To help prioritize the use of rifampin during the 2019 supply shortage, Public Health Ontario (PHO) developed a resource for frontline health care providers (i.e., prescribers) and public health units in Ontario on options for preventive treatment of LTBI during the shortage. Developing this resource involved timely consideration of stakeholder needs; available evidence and guidelines; and consultation with Ontario TB experts and public health decision-makers.

RESULTS AND LESSONS LEARNED

A risk-based, evidence-informed resource was developed and distributed to Ontario TB prevention and care stakeholders for use during the rifampin shortage. It considered groups at increased risk of progression to active TB, identifying the highest and second priority groups in whom to consider LTBI treatment with rifampin, as well as lower priority groups in whom other regimens or temporary deferral of treatment initiation could be considered.

CONCLUSION

During the 2019 rifampin shortage in Ontario, PHO developed a timely tool to support preventive treatment of LTBI, in consultation with key partners. Lessons learned may help Ontario and other jurisdictions prepare for future drug supply shortages.

111. **LATENT TUBERCULOSIS INFECTION IS ASSOCIATED WITH INCREASED RISK OF INCIDENT DIABETES MELLITUS AMONG US VETERANS**

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BACKGROUND

Cross-sectional US data from 2011-2012 demonstrated patients with diabetes had twice the prevalence of latent TB infection (LTBI) compared to those without diabetes, but whether LTBI contributes to diabetes risk is unknown. We determined if LTBI increased incidence of diabetes using longitudinal Veterans Health Administration data.

DESIGN/METHODS

We conducted a retrospective cohort study among veterans who received care at VAMC between 2000-2015. Eligible veterans included all patients without pre-existing diabetes who received a tuberculin skin test (TST) or interferon-gamma release-assay (IGRA). We excluded veterans with history of active TB and those diagnosed with diabetes within 2-years after TST/IGRA test date. Veterans were followed from LTBI test date until diabetes diagnosis, death, or 2015. LTBI was defined as TST or IGRA positive. Incident diabetes was defined by ICD-9 codes AND diabetes drug prescription.

RESULTS

Among n=574,111 eligible veterans, there were 2,535,149 person-years (PY) of follow-up (median 3.2 years). LTBI prevalence was 6.6% and diabetes incidence rate (IR) was 766 per 100,000PY. Diabetes IR (per 100,000PY) was greater in veterans with LTBI (IR 1012) compared to those without LTBI (IR 744, p<0.01); hazard ratio (HR) 1.4 (95%CI 1.3-1.4). Adjusting for age, BMI, HIV, and other confounders, veterans with LTBI had increased diabetes incidence (aHR 1.2, 95%CI 1.2-1.3) compared to those without LTBI. Among LTBI veterans, those without LTBI treatment had increased diabetes incidence compared to no LTBI treatment (aHR 1.3, 95%CI 1.1-1.5).

CONCLUSION

Comprehensive longitudinal data from veterans across the US indicate LTBI may increase diabetes incidence, but treatment for LTBI may reduce diabetes risk.

112. **LACK OF UTILITY OF ANNUAL TUBERCULOSIS (TB) SCREENING IN HIV CLINIC PATIENTS BY INTERFERON GAMMA RELEASE ASSAY (IGRA) IN A LOW TB INCIDENCE AREA**

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BACKGROUND

In August 2012, the URMHC HIV clinic replaced annual TB skin test based screening with QuantiFERON®-TB Gold In-Tube (QFT-GIT). This study aims to determine usefulness of annual TB screening of HIV patients after baseline testing in low TB incidence setting of Western NY.

METHODS

Records of HIV infected patients ≥ 18 years of age with at least one QFT-GIT performed between August 2012-October 2018 were reviewed to obtain data on clinical and demographic characteristics, results of screening tests, and follow up of positive results.

RESULTS

From August 2012-October 2018, 1439 patients had QFT-GIT. Median age was 48.2 years (range 18.0-82.0), 1,028 were male, median CD4 count was 555 cells/ul and 59% had <40 HIV copies/ml. At baseline 79 (5.4%) had positive QFT-GIT result (median 1.040 IU/ml, range 0.37- >10), and 23 (1.6%) had indeterminate results. 1377 had negative result and of these 1,010 had follow up QFT-GIT (median 2, range 1-6 tests) during 3,302 person years of follow-up. 29 patients had positive QFT-GIT (1.13 convertors/100 person years). Median change in IGRA value was 0.68 IU/ml (range 0.18-2.12) from last negative IGRA to positive IGRA. 11 convertors had chest X-Ray, which were normal, one had treatment for latent TB several years earlier, and 4 received treatment for latent TB, though no TB exposures were identified.

CONCLUSION

Annual screening for tuberculosis using the QFT-GIT in this HIV infected population failed to identify anyone with active TB, and only 4 of 29 convertors were given treatment for latent TB; no clear TB exposures were identified for this group.

113. **“‘LATENT’? IT’S ONE OF THOSE WORDS THAT IS NOT CLEAR ENOUGH.”**

Parmer J, Allen L, Dowling M, Tatum K, Macario E, Picard R, Walter T, Brackett A.

BACKGROUND

In 2016, the United States Preventive Services Task Force recommended testing populations that are at increased risk for latent tuberculosis (TB) infection (LTBI), including non-U.S.-born persons. A better understanding of current knowledge and awareness levels of TB/LTBI among people born in countries where TB is more common, and their understanding of terms and statistics commonly used by the TB community, is needed to inform future TB/LTBI communication efforts.

DESIGN/METHODS

In 2019, the Centers for Disease Control and Prevention (CDC) conducted 15 in-person focus groups in five U.S. cities, with people born in Mexico, the Philippines, India, Vietnam, China, or Guatemala (top countries of birth by number of U.S. cases). Participants examined TB/LTBI terminology for clarity, understandability, and effectiveness. Participants also discussed awareness and understanding of the Bacille-Calmette Guérin vaccine, as well as commonly used statistics used to describe TB/LTBI risk and prevalence.

RESULTS

Although most participants were familiar with TB, very few were aware of LTBI. Participants had mixed reactions to the term “latent” and provided several alternative terms to help elucidate the meaning of the word. The word “reactivation” was familiar to nearly all participants, but the concept as it relates to LTBI and TB disease was unclear. Using numbers instead of percentages to describe risk and prevalence was almost unanimously preferred.

CONCLUSION

The findings highlight the importance of matching TB/LTBI information to the health literacy and numeracy skills of high-risk populations. Increased and improved patient education and community engagement are needed to address the TB information needs of non-U.S.-born high-risk populations.

114. **COST EFFECTIVENESS OF 3 MONTHS OF WEEKLY RIFAPENTINE AND ISONIAZID IN A CANADIAN ARCTIC SETTING**

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BACKGROUND

The incidence of tuberculosis (TB) in Nunavut, Canada is over 50 times higher compared with the general Canadian population, with the burden of disease falling disproportionately among Inuit. Novel interventions, such as shortened preventive treatment are urgently needed.

METHODS

A Markov model was developed reflecting local practices for latent tuberculosis infection treatment in Iqaluit, Nunavut. This was used to estimate the incremental cost effectiveness (2019 Canadian dollars/quality adjusted life year) of 3 months of weekly rifapentine and isoniazid (3HP) compared to standard therapy consisting of 9 months of twice weekly isoniazid. Results were projected over a 30-year time horizon. Model parameters were derived from retrospectively collected programmatic data, a local feasibility study of 3HP and from published literature. Costs were estimated from the perspective of the Nunavut health care system and were obtained primarily from local, empirically collected data with additional values obtained from published literature. Discounting of 3% annually was applied to costs and utilities.

RESULTS

The 3HP regimen was found to be dominant (both cost saving and more effective) over standard therapy and both TB cases and TB deaths were reduced (Table 1). Deterministic sensitivity analyses supported the robustness of this finding with 3HP dominant in nearly all such analyses. Variables related to the 3HP completion rate, 9H initiation rate and risk of severe adverse events were the most influential on the incremental cost effectiveness ratio.

CONCLUSION

Our analysis suggests that in a remote Canadian arctic setting 3HP is both cost saving and more effective than standard isoniazid monotherapy.

Table 1. Cost-effectiveness model outcomes.

| | 9H | 3HP | Difference (9H – 3HP) |
|---|---------|--------|-----------------------|
| <i>Clinical Outcomes</i> | | | |
| Total quality adjusted life years | 20.13 | 20.14 | 0.00* |
| Disutility due to adverse events | -0.01 | -0.01 | 0.00 |
| Disutility due to TB disease | -0.04 | -0.04 | 0.00 |
| TB cases, per 1000 patients | 30.20 | 28.95 | -1.25 |
| TB deaths, per 1000 patients | 2.47 | 2.37 | -0.10 |
| <i>Cost Outcomes (2019 Canadian \$)</i> | | | |
| Total cost | 1276.37 | 879.84 | -396.52 |
| Costs of latent TB infection treatment | 712.34 | 337.65 | -374.69 |
| Costs of adverse events | 154.08 | 139.41 | -14.67 |
| Costs of TB disease treatment | 240.37 | 233.21 | -7.16 |
| Other costs** | 169.58 | 169.58 | 0.00 |

* due to rounding, values differ from those expected based on numbers listed in table.

**primarily related to surveillance of patients who decline treatment. TB = tuberculosis; 9H = 9 months of twice weekly isoniazid; 3HP = 12 weeks of weekly rifapentine and isoniazid.

115. **EXTERNALLY VALIDATING THE TSTIN3D IN A POPULATION OF IMMIGRANTS IN A LOW INCIDENCE REGION: A DATA LINKAGE, POPULATION-BASED STUDY**

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BACKGROUND

TSTin3D, a tool for estimating risk of active tuberculosis (TB) in individuals with latent TB infection, has been in use for over a decade now, but its predictive performance has never been evaluated.

METHODS

Immigrants who had positive TST and/or IGRA results from 1985 to 2015 were identified using immigration and TB registry data from the Canadian province of British Columbia. Comorbid conditions at the time of testing (i.e., HIV infection, diabetes, cancer, chronic kidney disease requiring dialysis, and use of immunosuppressant) were identified from physician claims, hospitalization, vital statistics, outpatient prescription dispensations, and kidney and HIV registries. The risk of developing active TB within 2- and 5-year periods were estimated using the TSTin3D and the estimates were evaluated using model-based performance indices and through graphical methods.

RESULTS

A total of 40,098 individuals met study criteria. Generally, the TSTin3D algorithm assigned higher risks to demographic and clinical groups that are known to have higher risks of active TB. Concordance estimates ranged from 0.65 to 0.67 in 2- and 5-year timeframes. Ratio of expected to observed counts (E/O) suggests that TSTin3D over predicts actual risks and that over prediction increases over time (3.5% and 12.1% in a 2- and 5-year period, respectively). Calibration plots suggest that over prediction increases towards the upper end of the risk spectrum.

CONCLUSIONS

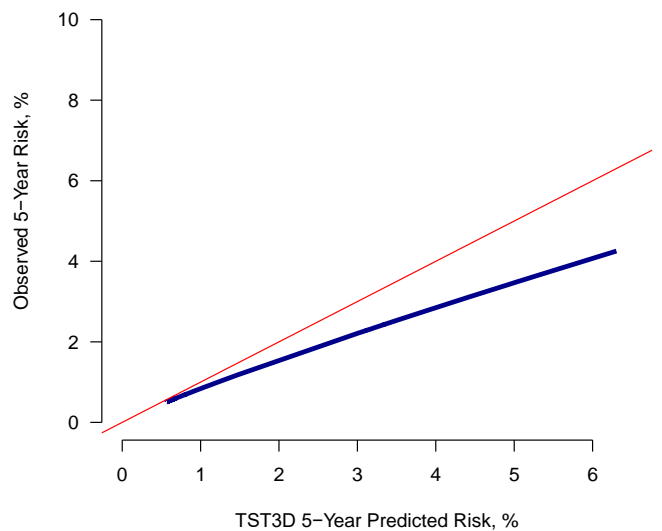
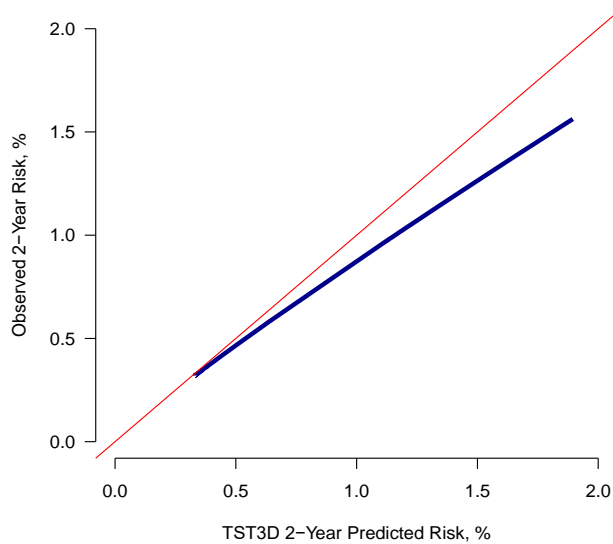
TSTin3D has adequate ability to discriminate between people who developed and did not develop active TB. However, further work is needed to improve its predictive accuracy and calibration, and to facilitate interpretation.

Predictive performance of the TSTin3D algorithm

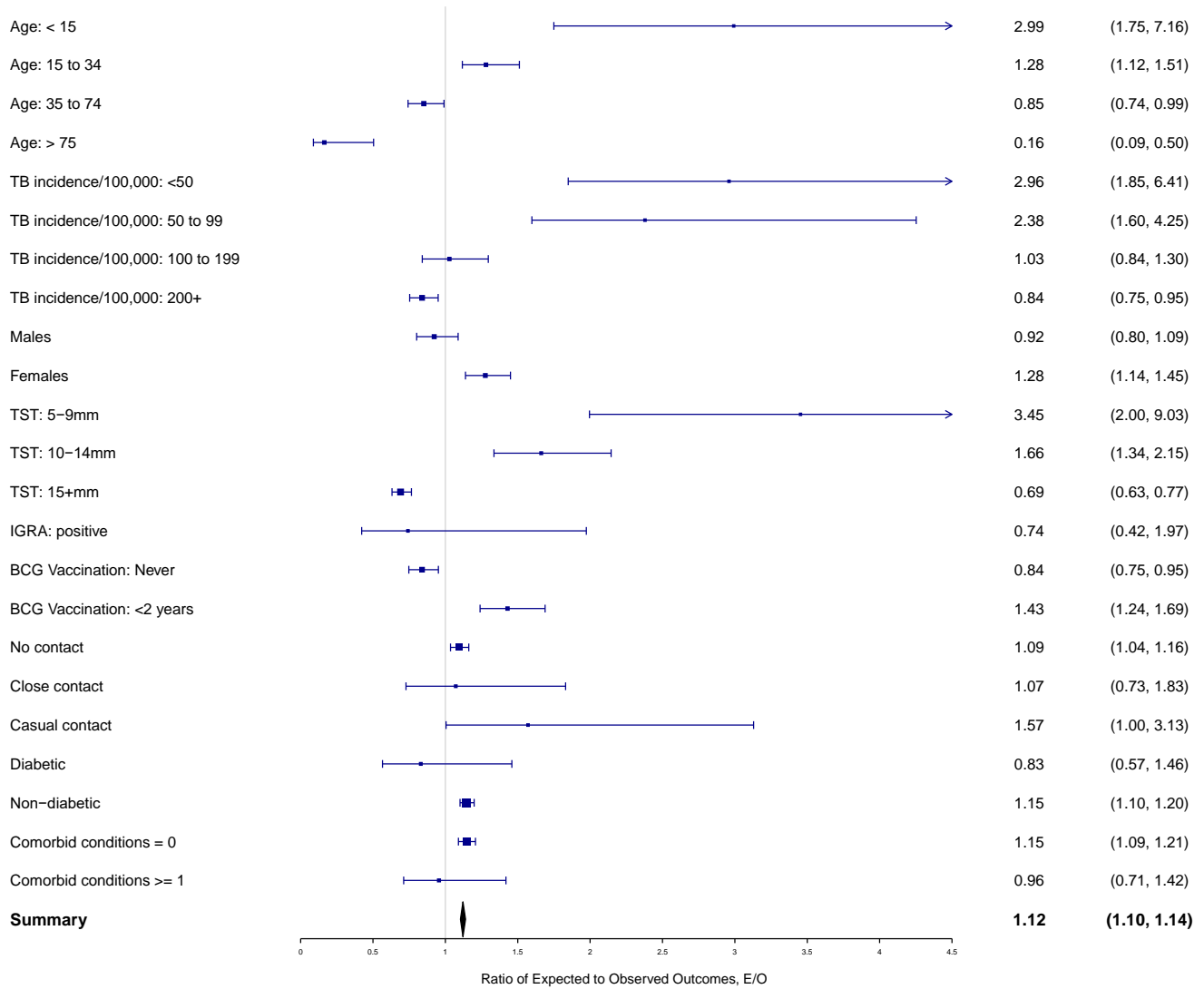
| Performance Index | 2-year | 95% CI | 5-year | 95% CI |
|-------------------|--------|------------|--------|------------|
| Somers' D | 0.29 | 0.20, 0.37 | 0.32 | 0.26, 0.39 |
| Uno's C | 0.65 | 0.60, 0.69 | 0.67 | 0.64, 0.70 |
| E/O | 1.04 | 1.03, 1.04 | 1.12 | 1.11, 1.14 |

Note: The regular concordance statistics (Harrel's C) can be derived from Somers' D using this formula: $D/2 + .5$. Uno's C is an estimate of concordance that is weighted by the censoring distribution.

Calibration plot



Ratio of the number of individuals predicted by TSTin3D will have active TB to the observed number of individuals who developed active TB within 5 years



116. **QUANTIFERON-TB GOLD PERFORMANCE IN CONTACTS OF INFECTIOUS TUBERCULOSIS PATIENTS, NEW YORK CITY**

Ramachandran J, Trieu L, Ahuja S. New York City Department of Health and Mental Hygiene, Long Island City, NY, USA.

BACKGROUND

There is little information about how QuantiFERON-TB Gold (QFT) performs in contacts to infectious tuberculosis (TB) patients, the highest-risk population for progression to TB disease. We aim to determine if QFT is appropriately detecting TB infection in contacts and identify contact characteristics associated with having a positive QFT result. We also examine QFT results among prevalent and incident cases identified during contact investigation.

DESIGN/METHODS

Contacts of infectious NYC TB patients verified between 2011-2015 and without prior TB disease or infection were included. Descriptive analyses and multivariate logistic regression were used to evaluate the association between contact characteristics and having a positive QFT result.

RESULTS

Overall, 6,944 contacts were QFT tested; 1,492 (21%) tested positive, 5,423 (78%) tested negative, and 26 (0%) had indeterminate results. Odds of testing positive were higher among contacts who were born outside the US (aOR 2.58, 95% CI 2.17-3.08), male (1.18, 1.04-1.35), ages 45-64 (1.80, 1.44-2.26), over age 65 (2.62, 1.95-3.53), had close exposure (1.35, 1.13-1.62), or were household contacts (1.91, 1.65-2.20). Among 5,423 patients with a negative test, 9 (0.2%) were diagnosed with TB disease during (prevalent case) or subsequent (incident case) to contact evaluation. Of all prevalent (n=37) and incident (n=16) cases tested with QFT, 5 (14%) and 4 (25%) tested negative, respectively.

CONCLUSION

The contact characteristics associated with a positive QFT result are consistent with known risk factors for TB infection. Additionally, of the contacts with negative QFT results, only 0.2% developed future TB disease, supporting the validity of test results in this population.

117. **TARGETED TESTING AND TREATMENT OF LATENT TUBERCULOSIS INFECTION IN A LARGE SOUTH TEXAS HOMELESS POPULATION**

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BACKGROUND

In 2017, 9,029 TB cases (rate of 2.8 cases per 100,000) were reported in the United States with Texas reporting the second highest number of cases 1,127 behind California at 2,057.

More than 80% of US TB cases are associated with reactivation of longstanding, untreated latent TB infection (LTBI) and experts recognize that testing for and treating LTBI in high-risk populations is the most effective way to prevent TB disease.

INTERVENTION

Activities aimed at identifying and treating LTBI in a large urban homeless population using Interferon gamma release assay (IGRA) blood testing were developed. Implementation required partnerships between public health, the largest homeless campus in south Texas, and clinics providing services to the homeless. Incentives were incorporated to encourage treatment completion.

RESULTS

Through 4.5 years of testing, 11,082 homeless individuals were IGRA tested with a positivity rate of 6.6% (700 positives). Of these, 103 (40.7%) were lost to follow-up, 263 (37.6%) completed medical evaluation, and 105 (39.9%) elected to begin treatment. Six cases of active TB disease were identified. Of those initiating treatment, 81 (77.1%) are expected to complete treatment. 3 months of 3HP is the most common regimen (79%) followed by 4 months of RIF (20%) with one patient receiving 9 months of INH (.01%).

CONCLUSIONS AND KEY RECOMMENDATIONS

The testing and treatment model has evolved based on significant social and structural barriers to care experienced by the population. Incentives support treatment completion; however, achieving high LTBI treatment completion rates among the homeless continues to pose significant challenges requiring innovative approaches to support treatment completion.

118. **LATENT TUBERCULOSIS INFECTION AMONG PATIENTS WITH AND WITHOUT DIABETES MELLITUS: RESULTS FROM A HOSPITAL CASE-CONTROL STUDY IN ATLANTA**

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BACKGROUND

National surveillance data from the US indicates diabetes is associated with latent tuberculosis infection (LTBI). Little is known about US regional differences in LTBI prevalence among patients with diabetes. We aimed to compare the prevalence of LTBI among patients with diabetes and healthy controls without diabetes from Atlanta.

METHODS

We conducted a case-control study in a large hospital in Atlanta from 2016-2019. Eligible cases included adult (≥ 21 years) HIV-negative patients with newly diagnosed (within 3-years) type-2 diabetes and had no prior history of tuberculosis (TB) disease. Eligible controls included adult family members/friends of cases with no prior diagnosis of pre-diabetes/diabetes, HIV, or TB disease. Eligible controls were screened for diabetes by point-of-care glycated hemoglobin (HbA1c) and those with HbA1c $\geq 5.7\%$ were excluded. LTBI was measured by Quantiferon-Gold-in-Tube. Logistic regression was used to estimate the odds ratio of LTBI comparing cases to controls.

RESULTS

We enrolled 98 cases; 119 potential controls were screened and 34 (28.6%) were enrolled as controls (HbA1c $< 5.7\%$), 83 (69.7%) had HbA1c $\geq 5.7\%$ and 2 (1.7%) had indeterminate QFT results. At screening, median HbA1c was 6.0 (IQR 5.8 – 6.2) among excluded controls. LTBI prevalence among cases was 9.2%; and among controls was 14.7% (prevalence difference 5.5% 95%CI -7.7, 18.7). After adjusting for age and sex, the adjusted odds of LTBI among cases were 0.45 (95% CI 0.13, 1.71) times the controls.

CONCLUSION

In Atlanta, we did not find a clinically meaningful difference in LTBI prevalence among adults with diabetes compare to family members without diabetes.

119. **EPIDEMIOLOGY OF LATENT TUBERCULOSIS INFECTIONS IN PACIFIC ISLANDERS LIVING IN THE UNITED STATES**

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BACKGROUND

Little is known about LTBI prevalence and risk factors among U.S.-affiliated Pacific Islanders (USAPI). We examined the epidemiology of LTBI among USAPI living in the United States who were enrolled in a study conducted by the Tuberculosis Epidemiologic Studies Consortium.

DESIGN/METHODS

During 2012 – 2017, participants at high risk for LTBI infection or for progression to TB disease were enrolled in 11 states. Participants received a tuberculin skin test (TST) and two interferon gamma release assays (IGRAs) at the time of enrollment. We restricted analysis to participants who identified a Pacific island country or territory as place of birth. We describe the USAPI population enrolled and LTBI test results, and use chi-square tests to assess risk factors associated with positive results.

RESULTS

Among 455 USAPI, 300(66%) were from Marshall Islands, 151(33%) were from Federated States of Micronesia (FSM), 3(1%) were from Palau and 1 was from American Samoa. Among those with valid IGRA and TST results, 83(19%) were TST+/IGRA+, 257(60%) were TST-/IGRA-, 50 (12%) were TST+/IGRA-, and 38 (9%) were TST-/IGRA+. The proportion of participants who had both a TST positive and at least one IGRA positive was higher in Marshallese than those from FSM (23% vs 9%, P<0.05). Among Marshallese, age was associated with IGRA+/TST+ and the highest proportion among those 25-44 years of age (54%, P<0.05).

CONCLUSIONS

The prevalence of LTBI varied by Island country of origin and was highest among those from the Marshall Islands. Attention needs to be given to this high-risk population when addressing TB elimination in the US.

120. **INTER- AND INTRA- LABORATORY VARIABILITY ASSESSMENT OF THE QUANTIFERON®-TB GOLD PLUS TUBERCULOSIS ASSAY IN US HEALTH CARE PERSONNEL**

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BACKGROUND

Approved in the U.S. in 2017 for detection of latent tuberculosis, QuantiFERON®-TB Gold Plus's (QFT-Plus) inter-laboratory and inter-operator variability remains unreported. We assessed agreement and variability of results by evaluating QFT-Plus at multiple independent sites and employing different operators within each site.

DESIGN/METHODS

Whole blood was collected from 85 Veterans Health Administration employees with prior QuantiFERON-Gold-In-Tube (QFT-3G) results during annual or pre-placement tuberculosis testing. Matched samples were analyzed in 3 independent laboratories by 6 different operators and result concordance was determined using Cohen's kappa statistic.

RESULTS

QFT-Plus results agreement across all 6 operators was moderate ($k=0.77$). Thirty-eight percent of subjects (31/82) had positive results with 6-test agreement. By operator pair comparison, 5-of-6 operators showed the greatest agreement with the other operator working in their lab ($k=0.75-0.95$). Averaging agreement across all pairwise comparisons yielded strong agreement for operators 1,2,3&4 (0.81-0.83) and moderate average agreement for operators 5&6 (0.71-0.77). The percent agreement between any two QFT-Plus operators ranged from 83% (68/82) for operators 6&4 to 98% (80/82) for operators 3&4. The top 3% agreement values came from comparisons involving operators 1-4 (95-98%); the lowest 3% involved operator 6 (83-85%) (see Table 1).

CONCLUSION AND RECOMMENDATIONS

While comparisons between laboratorians indicated high inter-operator agreement, operators agreed most closely within their lab. Two laboratories had nearly perfect agreement between four operators, while the 3rd lab was notably different despite standardization of all equipment. This indicates that training and education contributes significantly to variability and suggests that standardization and automation of the QFT-Plus procedure will provide the most accurate and reliable results.

Table 1. Qualitative comparison of inter-operator variability using QFT-Plus Results. Bolded κ -scores indicate inter-lab and overall comparisons. Numbers in parentheses are the percent agreement. Numbers in brackets are standard deviations of averaged κ -values. OP = operator.

| | | Site A | | Site B | | Site C | |
|---------|-----|------------------|-----------------|------------------|----------------|------------------|-----------------|
| | | OP1 | OP2 | OP3 | OP4 | OP5 | OP6 |
| Site A | OP1 | 1 | | | | | |
| | OP2 | 0.90 (95) | 1 | | | | |
| Site B | OP3 | 0.85 (93) | 0.80 (90) | 1 | | | |
| | OP4 | 0.90 (95) | 0.85 (93) | 0.95 (98) | 1 | | |
| Site C | OP5 | 0.78 (89) | 0.81 (90) | 0.76 (88) | 0.76 (88) | 1 | |
| | OP6 | 0.71 (85) | 0.71 (85) | 0.71 (85) | 0.67 (83) | 0.75 (89) | 1 |
| Overall | | 0.77 (78) | | | | | |
| Average | | 0.83 [0.083] | 0.81 [0.071] | 0.82 [0.091] | 0.83 [0.11] | 0.77 [0.022] | 0.71 [0.030] |

121. **COMPARISON OF TEST CONVERSIONS BY TUBERCULIN SKIN TEST AND INTERFERON GAMMA RELEASE ASSAYS AMONG CLOSE CONTACTS TO PERSONS WITH INFECTIOUS TUBERCULOSIS IN THE UNITED STATES**

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BACKGROUND

Close contacts to persons with infectious TB have elevated risks of infection with *Mycobacterium tuberculosis* and progression to TB disease. Uncertainty remains about whether tuberculin skin test (TST) or interferon gamma release assays (IGRAs) better detect infected contacts. We assessed test conversions, negative at baseline and positive at retest 8 - 10 weeks later (for TST, <5mm at baseline; ≥5mm at retest), and factors associated with conversion among close contacts.

DESIGN/METHODS

The Tuberculosis Epidemiologic Studies Consortium enrolled persons at high risk for infection and/or progression to TB disease, including close contacts (≥8 h of exposure), in 11 states, July 2012-May 2017. Participants received 2 IGRAs, QuantiFERON-TB Gold In-Tube and T-SPOT. TB, and TST. Factors associated with test conversions were identified with chi-square and Fisher's exact tests.

RESULTS

Among 559 contacts with baseline and follow-up results, 415 (74%) were negative for all 3 tests at baseline. Test conversions at follow-up showed 14 (3.4%) positive on all 3 tests, 23 (5.5%) by TST only, 5 (1.2%) by QFT only, and 1 (0.2%) by T-SPOT only. Higher proportions of contacts exposed to smear positive compared with smear negative index cases converted by QFT-GIT (12% vs 4.7% cases, $p<0.05$) and T-SPOT (5.5% vs 0.8%, $p<0.05$) but not TST (13.2% vs 8.8%, $p=0.2$); results showed similar patterns by test type for contacts exposed to cases with cavitory versus non-cavitory disease.

CONCLUSIONS

IGRA conversion results were significantly associated with sputum smear positivity and cavitory disease in the index case; TST results were not.

122. **DESCRIBING THE TUBERCULOSIS INFECTION CARE CASCADE BASED ON ELECTRONIC HEALTH RECORD DATA AMONG PERSONS WITH RISK FACTORS FOR TUBERCULOSIS**

Vonnahme LA¹, Zlot A², Todd J², Schmidt T², Oakley J², Puro J², Ayers T¹. ¹Centers for Disease Control and Prevention, Atlanta, GA; ²OCHIN, Portland, OR, USA.

BACKGROUND

Progression from latent TB infection (LTBI) to TB disease is preventable with treatment. The LTBI care cascade begins with identifying high-risk populations for screening. In collaboration with the OCHIN (formerly Oregon Community Health Information Network), a large network of safety-net clinics, we constructed an LTBI care cascade using an electronic health record (EHR) database.

DESIGN/METHODS

We extracted 2012–2016 OCHIN EHR data. We determined whether patients had risk factors for TB or not and then we calculated the percent tested for TB infection and those with a positive result. We then classified patients as having LTBI, based on a combination of characteristics including diagnostic results, ICD codes, and treatment regimens. We compared patient records with TB risk factors to those without risk factors using chi-square tests.

RESULTS

Of 2.2 million patient records, 63.2% had at least one risk factor for TB, of whom 114,814 (8.3%) were tested; 10,590 (9.2%) had positive TB infection test results. Among patient records without any risk factors, 36,375 (4.5%) were tested and 1,534 (4.2%) were positive. We identified significantly more LTBI in 28,468 (2.1%) patient records with TB risk factors compared to 5,506 (0.7%) without TB risk factors ($p < 0.0001$).

CONCLUSION

OCHIN community clinics include a large proportion of individuals with TB risk factors; however, testing for TB infection is infrequent. Low-risk populations continue to be screened. LTBI prevalence was higher among those with risk factors. Resources should be directed to increase screening and treatment among high-risk populations, including those who attend community clinics.

123. **IDENTIFYING PERSONS WITH TUBERCULOSIS INFECTION IN ELECTRONIC HEALTH RECORD DATA TO IMPROVE TUBERCULOSIS INFECTION SURVEILLANCE**

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BACKGROUND

Over 80% of tuberculosis (TB) cases in the United States are attributed to reactivation of latent TB infection (LTBI). Centralized electronic health records (EHR) are an unexplored data source to identify persons with LTBI. With OCHIN (formerly Oregon Community Health Information Network), we developed an algorithm for identifying persons with TB infection or disease using an EHR cohort.

DESIGN/METHODS

We evaluated variables related to TB diagnostic tests, International Classification of Diseases (ICD) 9 and 10 codes, and treatment regimens for patients with an OCHIN clinic encounter between 2012 to 2016. We classified patient records into categories: definite TB, probable TB, possible TB, definite LTBI, probable LTBI, possible LTBI. We assessed our classification algorithm using contingency tables.

RESULTS

The cohort included 2.2 million patients; 170,574 (8%) had TB-related data available for classification. We classified <0.5% as definite or probable TB, 1.2% possible TB, 15.7% definite or probable LTBI, and 4.2% as possible LTBI. We classified 78% and 98% of patients in TB disease and LTBI categories, respectively, based on combined treatment regimens, ICD codes, and diagnostics. Among those prescribed a TB disease treatment regimen, 57% had a TB disease ICD code; 82% had no diagnostic test. Among those prescribed a LTBI treatment regimen, 84% had an LTBI ICD code; 50% had no diagnostic test.

CONCLUSION

Our hierarchical algorithm demonstrates that EHR data sets are viable sources for LTBI surveillance and can be applied to other EHR cohorts. Our algorithm highlights inconsistencies in recording TB versus LTBI ICD codes and limited recording of diagnostic tests.

124. **WHAT ARE THE RISKS AND BENEFITS AT AN INDIVIDUAL LEVEL OF TPT IN PLHIV?**

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BACKGROUND

Tuberculosis preventive therapy (TPT) is a lifesaving treatment in people living with HIV (PLHIV). The objective of this review was to quantify the potential risks and benefits of provision of TPT to PLHIV and identify research gaps.

METHODS

MEDLINE and CENTRAL were searched from database using keywords related to PLHIV, TPT and TPT outcomes. Outcomes included incidence of TB and mortality, TPT-related adverse events (AE) of grade 3 or higher, and development of drug-resistance. In analyses, outcomes were stratified by treatment regimen and age, and meta-analysed, if appropriate.

RESULTS

A total of 64 studies in PLHIV (36 RCTs; 28 cohorts) were included; 51 included adults, 13 included children and 2 included pregnant women. All TPT regimens reduced the rate of developing TB (pooled risk reduction: 40-80% compared to no TPT) and overall mortality (pooled risk reduction: 10%-80% compared to no TPT) in both children and adults. AE, particularly hepatotoxicity, were common with isoniazid; the pooled proportion of AE of grade 3 or higher was 7-9%. An RCT in pregnant women reported two deaths directly attributable to isoniazid. Little evidence exists on the development of drug resistance related to TPT and comparative safety and efficacy of isoniazid and rifamycin-containing TPT regimens.

CONCLUSION

TPT is effective in reducing TB incidence and overall mortality in PLHIV. Isoniazid may be detrimental in pregnant women, however, more information is needed on alternative regimens. Research is urgently needed to identify the optimal rifamycin-containing TPT regimen for PLHIV and to clarify the risk of emergent drug-resistance.