

END TB



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ABSTRACT COMMITTEE

Sarah Brode, MD (Chair)

West Park Healthcare Centre
Toronto, ON, Canada

Shama Ahuja, PhD, MPH

New York City Department of Health and
Mental Hygiene
New York, NY, USA

Rajita Bhavaraju, PhD, MPH

NJMS Global Tuberculosis Institute at Rutgers
Newark, NJ, USA

E. Jane Carter, MD

Brown University
Providence, RI, USA

Victoria Cook, MD

British Columbia Centre for Disease Control
Vancouver, BC, Canada

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Richmond, CA, USA

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Geisel School of Medicine at Dartmouth
Hanover, NH, USA

Geetika Verma, MD

University of Alberta
Edmonton, AB, Canada

Shu-Hua Wang, MD, MPH & TM

Ohio State Wexner Medical Center
Columbus, OH, USA

ABSTRACTS FOR ORAL PRESENTATION

Yield of Semi Active Case Finding (SACF) for Tuberculosis in Cambodia

Ms. Amanda Quan

University of Ottawa School of Epidemiology and Public Health, Ottawa, ON, Canada

Patient's Perceptions of Patient-Provider Interactions Across Different Methods of Directly Observed Therapy (DOT)

Mr. Marco Salerno

Columbia University, New York, NY, USA

Implementation of Universal Whole-Genome Sequencing for Detection of Drug Resistance and Epidemiologic Investigation in a Local Tuberculosis Program Setting

Ms. Jeanne Sullivan Meissner

New York City Department of Health and Mental Hygiene, Queens, NY, USA

Age-Period-Cohort Analysis of Tuberculosis Rates Among Elderly Patients in New York City, 2001-2015

Dr. Steffen Foerster

New York City Department of Health and Mental Hygiene, Queens, NY, USA

Incidence and Significance of Thromboembolic Disease in Critically Ill Pulmonary TB Patients

Dr. Angela Lau

University of Alberta, Edmonton, AB, Canada

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Ms. Hannah Alsdurf

McGill University, Montreal, QC, Canada

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Poster Session 1

A. EPIDEMIOLOGY

A1. HOMELESSNESS AMONG TUBERCULOSIS CASES: A TWO COUNTY COMPARISON

Agarwal S, Nguyen DT, Graviss EA. Houston Methodist Hospital, Houston, TX, USA.

BACKGROUND

Tuberculosis (TB) cases disproportionately occur among homeless individuals in the United States (US) and Texas (TX). Our objective was to identify and compare characteristics associated with homelessness among confirmed TB cases in the two most heavily populated TX counties, Dallas and Harris.

METHODS

Data from the Centers for Disease Control and Prevention TB Genotyping Information Management System (TB GIMS) was used to evaluate the characteristics of homeless TB patients between 01/01/2010–12/31/2017 in Harris and Dallas counties. Multivariate logistic regression was used to analyze and evaluate the characteristics associated with homeless status among the TB cases in Dallas and Harris counties.

RESULTS

Of the 10,103 newly diagnosed TB cases, 543 (5.4%) were reported as being homeless in the year preceding TB diagnosis. Dallas and Harris counties accounted for n=215 (39.6%) and n=125 (23.0%) of homeless TB cases in TX, respectively. The most common GENType among homeless TB cases in Dallas and Harris counties was G1058 (44.0%) and G00010 (49.5%), respectively. Hispanic and White ethnicities, being an inmate at a correctional institution, smear positivity, and culture positivity were associated with homelessness in Dallas County. Age ≥ 45 , Hispanic ethnicity, excessive alcohol use, and being an inmate at a correctional institution were associated with homelessness in Harris County (Table 1).

CONCLUSION

Different demographic and laboratory characteristics including differing common GENTypes indicate that each county needs individual strategies to control and prevent TB among the homeless in the 2 most populous counties in TX.

Table 1. Characteristics Associated with Homelessness among TB Cases in Dallas and Harris Counties, Multiple Logistic Regression Analysis

Covariate	Dallas		Harris	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Demographics				
Age 45+	1.37 (0.82 - 2.28)	0.23	2.17 (1.12 - 4.18)	0.02
Asian ¹	0.13 (0.01 - 1.17)	0.07	3.67 (0.59 - 22.87)	0.16
Hispanic ¹	0.11 (0.05 - 0.21)	<0.001	0.51 (0.25 - 1.04)	0.06
White ¹	0.53 (0.32 - 0.86)	0.01	1.08 (0.60 - 1.95)	0.79
Risk factors				
Excessive Alcohol use	-	-	3.00 (1.71 - 5.24)	<0.001
Inmate at correctional facility	0.48 (0.23 - 0.99)	0.048	3.50 (1.77 - 6.95)	<0.001
Diabetes	0.37 (0.13 - 1.01)	0.05	-	-
Clinical/laboratory Factors				
SP SMEAR	0.54 (0.32 - 0.91)	0.02	-	-
SP Culture	1.92 (1.04 - 3.56)	0.04	0.63 (0.27 - 1.51)	0.30
Chest X-Ray: Abnormal	-	-	2.24 (0.58 - 8.69)	0.24
Diagnosis Verified by Positive Culture/ NAA	-	-	0.42 (0.15 - 1.16)	0.09
AUC	0.753		0.730	

¹ Reference category: Black/ African American; “-” covariate not included in the model

A2. **OVERVIEW OF TB MORTALITY IN GUYANA**

Edwards A, Khan D, Mohanlall J, Rayside C. National Tuberculosis Programme, Ministry of Public Health, Guyana.

BACKGROUND

The World Health Organization estimated 18 per 100 000 population to TB deaths in Guyana for the year 2017. Ranking highest in TB mortality in the Caribbean and Latin America, Guyana's TB mortality burden still remains a critical action item on Guyana's TB agenda.

METHODS

The certifications of all deaths are done through the use of the *registration of death forms*. These forms are forwarded to the Ministry of Public Health, Statistical Unit where they are sorted as per disease classification of death in keeping with the International Classification of Disease, of which Tuberculosis is grouped A15 –A19. A manual perusal of the forms 2016-2018 (August) resulted in the extraction of data relevant to description of the population whose death resulted in generating TB mortality rates.

RESULTS

Of 145 TB deaths, 61.2% were males, 29.4% females and 9.4% were unknown sex. 2016 reported 62(43%) TB deaths, 2017 55(38%)TB deaths and 2018 30(21%) of TB deaths as of August 2018. The mean age for the deaths was 43.38 years with standard deviation of 15.1 years; the minimum age was 13 years and maximum age of 83 years. 43% of the cases were TB bacteria positive, while 45% of all the deaths were co infected with HIV and a separate 25.4% had other medical illness, with hypertension being the most popular with 31%.

CONCLUSION

TB mortality is fueled by a number of contributing factors, it is critical to have tailored interventions to address those issues which can translate to the reduction of TB mortality in Guyana.

A3. **AGE-PERIOD-COHORT ANALYSIS OF TUBERCULOSIS RATES AMONG ELDERLY PATIENTS IN NEW YORK CITY, 2001-2015**

Foerster S, Silin M, Ahuja SD. New York City Department of Health and Mental Hygiene, Queens, NY, USA.

BACKGROUND

Aging is a well-recognized risk factor for tuberculosis (TB). In New York City (NYC), elderly persons have the highest incidence rates (13 per 100,000 in 2017). Therefore, a better understanding of trends in local TB epidemiology in this population can improve TB control strategies.

DESIGN/METHODS

We calculated incidence rates by 5-year age groups for 2,193 confirmed cases aged ≥ 65 years across three five-year periods between 2001 and 2015. We conducted age-period-cohort analyses to estimate age-specific, cohort-specific annual percentage change in disease incidence rates and non-linear deviations from temporal trends as indicators of period and cohort effects.

RESULTS

The incidence of TB among the elderly in NYC decreased from 20 to 11 per 100,000 between 2001 and 2015, but patterns varied by age group and nativity. Among US-born, incidence rates declined 9% per year across all age groups ($p < 0.001$), and cohort effects were absent. In contrast, among non-US-born elderly there was no consistent trend over time across age groups. Instead, rates declined among 65-74-year-olds over time, but were stagnant or increased among older groups. Significant cohort effects ($p < 0.01$) suggest that non-US-born persons born after 1940 showed reduced rates across all periods. Recent increases in incidence rates occurred among non-US-born elderly from several countries, including China, India, Philippines, and Haiti.

CONCLUSION

Changes in disease incidence can be driven by age, period, or cohort effects, which has implications for effective public health strategies. Our findings suggest that high-risk cohorts among elderly foreign-born persons can be targeted for LTBI testing and treatment to help prevent TB.

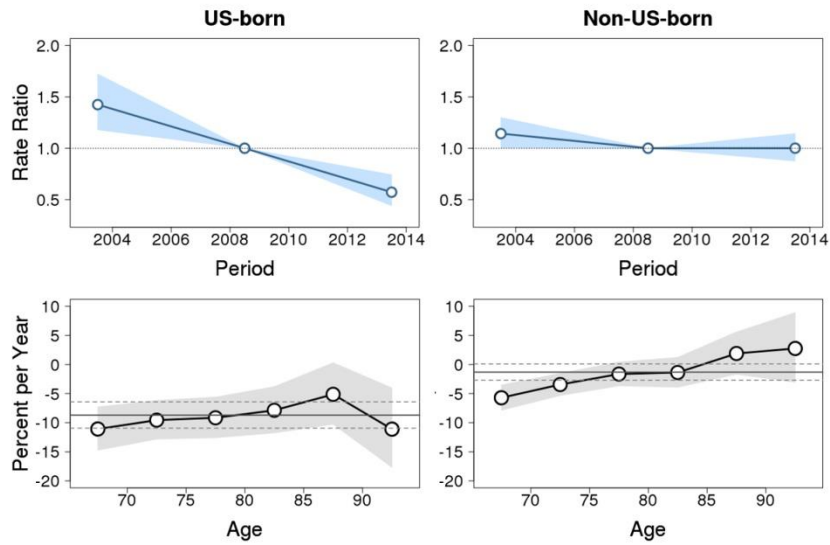


Figure 1: Differences between US-born and non-US-born elderly TB patients in New York City in the ratio of age-specific incidence rates relative to the reference period (top row), and annual percentage change in the expected age-specific incidence rates over time, adjusting for period and cohort effects (bottom row). Circles give point estimates and shaded areas represent 95% point-wise confidence intervals based on age-period-cohort modeling. The horizontal solid line in the bottom panels gives the “net drift”, i.e. the annual percentage change in expected age-standardized incidence rates over time, along with its 95% confidence interval (dashed lines). Significant deviations of age-specific rates of change (“local drifts”) from net drift occur among non-US-born because of cohort effects.

A4. **HOUSEHOLDS CONTACTS OF TB PATIENTS: HOW MANY SHOULD WE EXPECT TO IDENTIFY?**

Fregonese F¹, Campbell JR¹, Oxlade O¹, Benedetti A^{1,2}, Menzies D^{1,2}, Fox G³. ¹McGill University Health Center Research Institute; ²McGill University, Montreal, QC, Canada; ³Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia.

BACKGROUND

Identifying household contacts of TB patients is an essential step in the cascade of care for Latent Tuberculosis Infection (LTBI). The aim of this study was to estimate the number of expected household contacts per index case, using published data.

METHODS

Data were extracted from a previously published systematic review and meta-analysis on the yield of TB in contact investigations. Studies included in the original review reporting the number of household contacts and index cases and starting in 1990 or later were eligible. Generalized linear mixed methods were used to estimate the number of household contacts identified per index case and its associated 95% CI.

RESULTS

Eighty-five studies conducted in 40 countries, were included. Most studies (89%) were set in low/middle-income countries (LMIC) and in urban areas (87%). Sixty-one studies included data for contacts of all ages, with a median (1st and 3rd Quartile) number of 148 (72; 366) TB cases and 542 (242; 1918) contacts. LMIC countries had an increased number of household contacts per index case (3.8 (95% CI 3.3, 4.4) vs. 2.4 (95% CI 1.8, 3.4)). Forty studies had information on contacts who were ≤ 15 years of age: the number of household contacts ≤ 15 years old in LMIC settings was 1.7 (95% CI 1.4, 2.1).

CONCLUSION

In all settings, the number of expected contacts can be used to help healthcare workers optimize contact investigation. More studies reporting the number of contacts identified are needed, especially in high-income countries to improve precision around estimates.

A5. **USE OF ELECTRONIC HEALTH RECORDS TO IDENTIFY THE FREQUENCY OF TUBERCULOSIS EXPOSURE AND TESTING IN THE OUTPATIENT SETTING**

Gelman H¹, Thanassi W², Zeliadt S¹, Winston C³. ¹Veterans Administration (VA) Center of Innovation for Veteran-Centered and Value-Driven Care, University of Washington, Seattle, WA; ²VA Palo Alto Health Care System, Stanford Hospital and Medical Center, Palo Alto, CA; ³Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

Our goal was to use electronic health records (EHR) in a national health system setting to determine feasibility of identifying patients who have been exposed to tuberculosis disease and consequent testing patterns.

DESIGN/METHODS

Veteran's Health Administration's EHR was queried using ICD9/10 codes (V01.1, Z20.1) to identify persons with exposure to tuberculosis (contacts). Testing for tuberculosis infection was recorded when it followed the first appearance of an exposure ICD 9/10 code. Testing data included fourteen ICD9/10 and CPT/HCPCS codes (R76.11, 795.51, V74.1, Z11.1, 86580, 86480, 86481, 86585, 0010T, 3455F, 3510F, G9359, G9360, G9932). Pharmacy data, laboratory tests, medical records, and skin test order histories were also interrogated.

RESULTS

Among 6.4 million Veterans seen in outpatient care between 2007 and 2017, we identified 13,471 individuals who had documented tuberculosis exposure without documentation of a prior history of TB. We confirmed that 7,348 (54.5%) received a subsequent tuberculosis test within the VA health system. The use of blood tests in this cohort increased from <2% of tests in 2008 to >48% by 2017.

CONCLUSIONS/RECOMMENDATIONS

EHRs can be used to identify tuberculosis contacts and related tests, as well as opportunities for improvements in care. Data mining for tuberculosis exposure, testing, treatment and disease is exceptionally complex because of multiple demographic risk factors, inconsistent provider coding, and the multitude of non-specific ICD9/10 and CPT codes assigned to tuberculosis infection and testing. Documentation of post-exposure tuberculosis testing in EHRs, especially skin testing, may be incomplete, but we identified encouraging trends in appropriate test use within the Veterans Health Administration.

A6. **MULTIPLE TREATMENTS FOR TUBERCULOSIS IN THE CENTRAL AREA OF A METROPOLIS, 2008-2016: PROFILES, CAUSES AND CHARACTERISTICS**

Hamburger FG, Rujula MJP. Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil.

BACKGROUND

A significant proportion of Brazilian patients with tuberculosis require more than a single treatment. It is important to understand better these cases in order to reduce the burden of tuberculosis.

DESIGN/METHODS

Cross-sectional epidemiological study with secondary data obtained from TBWeb system of São Paulo State Health Department. Inclusion criteria: reported and treated as a tuberculosis case in the central region of São Paulo City at least twice between 2008-2016. Exclusion criteria: lack of information about outcome. Demographic, epidemiological and clinical data were analyzed with SPSS 21.0 in order to verify variables associated with different outcomes.

RESULTS

Among 4105 cases of tuberculosis in central São Paulo region, 570 cases in 249 patients were retreatments. Of the 249 patients: 72.3% male; mean age 37.2 ± 14 years; 48.9% with positive serology for HIV. The most common reasons for retreatment were: abandonment of previous treatment (59.4%); relapse (28.1%); and treatment failure (10%). Drug sensitivity was tested in 120 patients and n=45 presented some degree of drug resistance. The outcome of the 249 patients was: cure (46.5%); abandonment (26.5%); and death (12%). HIV+ status and previous abandonment were associated with worse outcomes (p-value <0.001). Retreatment due to previous treatment failure was associated with cure (p-value <0.001).

CONCLUSION

There is not a single profile for patients with multiple treatments in the studied area. They are an heterogenous group, with different needs to be met by the health system, including availability of drug sensitivity tests to adjust treatment and strategies to increase treatment adherence.

A7. **CASE FATALITY AMONG INDIAN TUBERCULOSIS PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Huddart S^{1,2}, Svadzian A^{1,2}, Nafade V^{1,2}, Satyanarayana S³, Pai M^{1,2}. ¹Department of Epidemiology, Biostatistics and Occupational Health, McGill University; ²McGill International TB Centre, Montreal, QC, Canada; ³Center for Operational Research, International Union Against Tuberculosis and Lung Disease, Delhi, India.

BACKGROUND

More than a quarter of the global TB deaths occur in India. Patient mortality is an important marker of care quality as prompt diagnosis and appropriate treatment should prevent deaths both during and after treatment. This systematic review seeks to estimate the case fatality ratio (CFR) for Indian TB patients.

METHODS

We searched Medline, Embase and Global Health for eligible papers published between 2006 and 2017. The treatment and post-treatment CFRs were extracted and, when sufficiently homogeneous, pooled using Normal-Binomial Generalized Linear Mixed Models. Pooling was also performed in key patient subgroups.

RESULTS

A total of 125 relevant studies were identified. The overall treatment CFR was 0.06 (95% CI: 0.04, 0.07). The CFR was higher for HIV+ [0.11 (0.08, 0.15)] and DR-TB patients [0.12 (0.08, 0.17)]. We found similar CFRs for adult [0.05 (0.03, 0.08)] and pediatric [0.04 (0.02, 0.09)] patients. The public sector CFR was 0.05 (0.04, 0.07) but only 4 of 125 (3.2%) papers described privately treated patients, precluding a pooled estimate for this strata. Out of 125 studies, 78 (62.4%) had limited generalizability, 31 (24.8%) had selection bias, and 6 (4.8%) had short follow-up times.

CONCLUSION

Our study shows that overall, Indian TB patients experience a CFR equal to that called for in the WHO End TB strategy. However, the CFR is not well described or is unacceptably high for important vulnerable groups. This work highlights the need for more high quality patient follow-up, especially in India's large private healthcare sector.

A8. EPIDEMIOLOGICAL STUDY IN SUSPICIOUS PATIENTS OF TUBERCULOSIS IN THE STATE OF MEXICO, YEAR 2017

Mendoza F, Vazquez K, Diaz JI, Widrobo L, Velazquez IR, Ramirez MDG, Jimenez JM. Laboratory of Public Health of State of Mexico, Toluca, Mexico.

BACKGROUND

Tuberculosis (TB) is one of the priorities in the WHO 2030 agenda. Describe the epidemiological constants presented by TB in the State of Mexico (EdoMex) and the comorbidities associated with the disease, establish patterns of behavior in the face of antibiotics.

METHODOLOGY

During 2017, 1176 samples were received with presumptive TB diagnosis. The diagnosis was made following the Diagnostic Algorithm. For the statistical analysis, the Chi2 test was performed with a 95% Confidence Interval (95% CI) and significant results $P \leq 0.05$.

RESULTS

The prevalence was 25.9%; the 0.85% of the samples were positive to MNTB. 29.16% of the patients presented comorbidity with Diabetes Mellitus (DM) and HIV. The Risk Factors (OR) associated with the prevalence of TB the following factors: 1) Comorbidity: $P = 0.017$ (OR = 1,742) in HIV positive patients. 2) Cause of Study: (diagnosis or control): $P = 0.0001$ (OR = 1.617), in patients who send samples for Control. 3) In Drug Resistance: It was observed: DM and TB patients showed resistance to Streptomycin (7), Isoniazid (3), Rifampizine (2), Ethambutol (1) and Pyrazidamide (10), while resistance to drugs observed in patients with only HIV are Streptomycin (2) and Pyrazidamide.

CONCLUSIONS

The number of patients with HIV and TB is lower (16) than that observed in patients with DM and TB (98), and the highest number of cases observed with treatment failures are patients with DM (37) to those observed with HIV positive (5). Considering that the DM does not allow compliance with the 2030 Agenda on TB.

A9. **ES MAYOR LA INCIDENCIA DE TUBERCULOSIS TODAS FORMAS Y PULMONAR CON COMORBILIDADES EN GUANAJUATO VS MÉXICO, 2015?: TASAS AJUSTADAS**

Leos LC¹, González FE², Lara E², Sulca JA³. ¹Instituto de Salud Pública del Estado de Guanajuato; ²Universidad de Guanajuato; ³Centro Nacional de Prevención y Control de Enfermedades, Guanajuato, Mexico.

ANTECEDENTES

Durante el 2015, en Guanajuato (Gto) se observa en la práctica mayor frecuencia de tuberculosis todas formas (TbTF) y pulmonar (TbP) asociadas a enfermedades, a diferencia de México. Esto generó la inquietud de conocer los datos mediante tasas ajustadas, para posteriormente analizar posibles causas por las cuales Gto presenta distintas características que el país.

INTERVENCIÓN

Estudio descriptivo retrospectivo de incidencia acumulada anual de tuberculosis todas formas con comorbilidades (DM, VIH, desnutrición, alcoholismo y otras) para el 2015 en el Estado de Guanajuato registrados en Sistema Nacional de Vigilancia Epidemiológica. Cálculo de ajuste de tasas por método directo con base Epidat versión 4.2 y población estándar OMS 2000-2025.

RESULTADOS

Se incluyeron un total de 163 casos de Gto y 20 mil 628 de México. La tabla 1 muestra en Guanajuato 39.4% de TbP-DM vs 26.8% de México, TbP-VIH 5.8% vs 4.7% y TbP-alcoholismo 7.1% vs 5.3% respectivamente. La Tasa ajustada (TA) de TbTF con comorbilidad en Gto fue 3,45 IC 95% (2,93-3,99) y en México fue 7,99 IC95% (7.79-8.16). La TA de TbP con comorbilidad en Gto fue 2.86 IC 95% (2,40-3,39) y en México fue 6,85 IC95% (6.70-7.01).

CONCLUSIONES

Las tasas ajustadas en TbTF y TbP fueron menores en Guanajuato que en México. Estos resultados de TA, permitirán analizar la implementación de estrategias en Guanajuato dirigidas a pacientes con antecedentes de DM y VIH principalmente, al contrario de lo que se había observado en la práctica.

Tabla. 1. Comorbilidades en Tuberculosis Pulmonar, no Pulmonar y Todas Formas 2015

	Guanajuato (Estatad)						México (Nacional)					
	TbP		Tb no P		Tb Todas Formas		TbP		Tb no P		Tb Todas Formas	
	Total	%	Total	%	Total	%	Total	%	Total	%	Total	%
Enf. No transmisibles												
Diabetes Mellitus	95	39.4	9	6.9	101	27.2	4409	26.8	359	8.6	4768	23.1
Neoplasias	0	0	3	2.3	3	0.8	42	0.3	27	0.6	69	0.3
Desnutrición	15	6.2	5	3.8	20	5.4	1719	10.4	274	6.6	1993	9.7
Otras	20	8.3	16	12.2	39	10.5	2590	15.7	900	21.6	3470	16.8
Enf. Transmisibles												
VIH	14	5.8	14	10.7	28	7.5	766	4.7	538	12.9	1324	6.4
Adicciones												
Alcoholismo	17	7.1	3	2.3	20	5.4	865	5.3	136	3.3	1001	4.9
Drogas intectables	0	0	0	0	0	0	178	1.1	28	0.7	206	1
Ninguna												
Sin enf. Asociadas	80	33.2	81	61.8	161	43.3	5890	35.8	1907	45.7	7797	37.8
Total	241	100	131	100	163	100	16459	100	4169	100	20628	100

Fuente. SINAVE 2015

A10. RISK OF ACTIVE TB AMONG FOREIGN-BORN INDIVIDUALS WITH CLOSE CONTACTS TO PEOPLE WITH PULMONARY TB

Puyat JH, Shulha H, Romanowski K, Chiang L, Johnston J. BC Centre for Disease Control, Vancouver, BC, Canada.

BACKGROUND

The risk of developing active tuberculosis (TB) among contacts of people with pulmonary TB is well described in the literature. However, there is limited information about the risk of active TB among contacts in migrant populations in a low incidence region.

METHODS

In this retrospective study, we used linked immigration and TB registry data from British Columbia, Canada, to identify individuals born outside of Canada who were exposed to a person with culture-confirmed pulmonary TB, and to determine who among the exposed were subsequently diagnosed with active TB. Using descriptive analyses, we estimated the risk of active TB, stratified by type of contact (non-household versus household) and size of tuberculin skin test induration (<9mm versus >10 mm). Everyone that received treatment for latent TB infection were excluded from analysis.

RESULTS

A total of 4,321 contacts (80.55% non-household; 19.45% household) were identified, 50 of whom developed active TB (19 or 0.54% of non-household and 31 or 3.65% of household contacts) within 1 (64%), 2 (66%), 3 (73%), 4 (76%), and 5 (87%) years. In those with <9 mm induration, active TB was diagnosed in 0.16% and 1.94% of non-household and household contacts, respectively, versus 0.96% and 4.91% in those with >10 mm induration.

INTERPRETATION

The risk of active TB is 7 times higher in household contacts compared to non-household contacts, and 2 to 6 times higher, depending on type of contact, in those with larger induration relative to those with smaller induration.

A11. LONG-TERM ALL-CAUSE MORTALITY AMONG PATIENTS TREATED FOR TUBERCULOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Romanowski K¹, Baumann B², Basham CA^{1,2}, Rose C^{1,2}, Ahmad Khan F³, Fox G^{4,5}, Johnston J^{1,2}. ¹BC Centre for Disease Control; ²University of British Columbia, Vancouver, BC; ³Research Institute of the McGill University Health Centre, Montreal, QC, Canada; ⁴Woolcock Institute of Medical Research; ⁵University of Sydney, Sydney, Australia.

BACKGROUND

Accurate estimates of long-term mortality following tuberculosis (TB) treatment are lacking. This systematic review and meta-analysis aimed to establish the mortality rate among TB survivors, and examine differences in mortality risk by diagnosis type, study characteristics, co-prevalence of HIV, and demographics.

METHODS

We systematically searched EMBASE, MEDLINE, and the Cochrane Database of Systematic Reviews for cohort studies published between 1997 and 2018. Selected studies reported mortality estimates for patients with TB as well as a valid control group representative of the general population. Random-effects meta-analysis with inverse variance weighting was used to obtain pooled standardized mortality ratios (SMRs).

RESULTS

Data from 10 studies were included, comprising 40 781 individuals and 6922 deaths. The pooled SMR for all-cause mortality among the patient population, compared to the control group, was 2.91 (95% CI 2.21, 3.84). When restricted to those with confirmed treatment completion or cure, the pooled SMR was 3.76 (95% 3.04, 4.66) among treated patients, compared to the control group. Effect estimates were similar when stratified by TB type, sex, age, and country income category. Causes of mortality were extracted for 3,388 deaths that occurred post-treatment. Almost one third (29.6%) of mortality was attributed to cardiovascular disease (CVD) while malignancy was the second leading cause of death (26.2%).

CONCLUSION AND RECOMMENDATIONS

People treated for TB have significantly increased mortality following treatment when compared to age and sex standardised control populations. Multidisciplinary interventions that address both biomedical and social factors of TB may substantially impact the long-term prognosis in this population.

A12. **CHARACTERISTICS OF ELDERLY TUBERCULOSIS PATIENTS IN NEW YORK CITY, 2001-2015**

Silin M, Foerster S, Ahuja SD. New York City Department of Health and Mental Hygiene, Queens, NY, USA.

BACKGROUND

The elderly have an increased risk for tuberculosis (TB) due to longer lifetime exposure, immune senescence, and comorbidities that increase the risk of progression from latent infection to active TB. We describe demographic, clinical and risk factors of elderly TB patients in New York City (NYC) and identify differences between United States (US)-born and Non-US-born patients.

DESIGN/METHODS

We extracted NYC TB registry data for 2,193 elderly (≥ 65 years) patients confirmed in NYC between 2001 and 2015. We report overall descriptive statistics and assess differences by birth in the US using Pearson's chi-square and Fisher's exact tests.

RESULTS

Elderly TB patients were predominantly male (60%) and 50% were ≥ 75 years old. Non-US-born patients accounted for 72% of all cases; among these, top countries of birth were: China (35%), Philippines (6%), and Haiti (5%). Eighty-two percent of non-US-born patients were in the US for >5 years before diagnosis. Non-US-born patients were more likely to refuse HIV testing (42% vs. 32%), have culture-confirmed TB (84% vs. 77%), have first-line drug resistance (15% vs. 7%), and were less likely to have cavities on chest X-rays (12% vs. 18%). US-born patients were more likely to have experienced homelessness (6% vs. 1%), abused alcohol (13% vs 3%), used drugs (7% vs. 1%), smoked tobacco (13% vs. 9%), and die prior to treatment start or completion (32% vs. 20%)(all $p < 0.05$).

CONCLUSION

Elderly TB patients in NYC differ in a number of characteristics, which can help understand local TB epidemiology, and improve TB prevention and control efforts in this high-risk group.

A13. IMPLEMENTATION OF UNIVERSAL WHOLE-GENOME SEQUENCING FOR DETECTION OF DRUG RESISTANCE AND EPIDEMIOLOGIC INVESTIGATION IN A LOCAL TUBERCULOSIS PROGRAM SETTING

Sullivan Meissner J¹, Knorr J¹, Modestil H¹, Ahuja SD¹, Nilsen D¹, Dworkin F¹, Osahan J¹, Rakeman, J², Escuyer V³, Halse TA³, Shea J³, Musser K³. ¹New York City Department of Health and Mental Hygiene (NYC DOHMH), Queens; ² Public Health Laboratory, NYC DOHMH, New York; ³Wadsworth Center, New York State Department of Health, Albany, NY, USA.

BACKGROUND

Whole-genome sequencing (WGS) of *Mycobacterium tuberculosis* isolates can be used for species identification, prediction of drug resistance, high-resolution genotyping, and analysis of single nucleotide polymorphisms (SNP) to characterize and compare TB strains.

INTERVENTION

In 2016, the Wadsworth Center, New York State Department of Health (NYS DOH) implemented universal WGS for culture-positive TB cases in NYS. Identification, predicted first- and second-line drug susceptibility profiles, and spacer oligonucleotide typing results are communicated to New York City (NYC) through the NYS electronic laboratory reporting system. Since 2017, high-quality SNP analysis has been conducted weekly to identify potential clusters and support high-priority investigations.

RESULTS

Between March 1, 2016 and June 30, 2018, WGS results were available for 1,064 (97%) culture-positive NYC TB cases. WGS identified 877 (82%) drug-susceptible and 187 (18%) drug-resistant isolates, including 31 multidrug-resistant and three extensively drug-resistant strains. Concordance between conventional drug susceptibility testing (DST) results and WGS-predicted susceptibility and resistance was 98%. Since 2017, SNP analysis was applied in 20 false positive investigations and informed cluster prioritization, investigation and outbreak response for 134 cases.

CONCLUSIONS

WGS enables rapid species identification and detection of first- and second-line drug resistance, ensuring that healthcare providers in NYC initiate effective treatment regimens quickly. Concordance between conventional DST and WGS-predicted drug resistance is high. Use of existing electronic reporting mechanisms has facilitated timely, standardized reporting of WGS results. SNP analysis has been instrumental in identifying or refuting potential laboratory contamination events, differentiating TB strains to refute transmission and focus epidemiologic investigations, and detecting potential outbreaks and cross-jurisdictional transmission.

A14. **TUBERCULOSIS RATES AMONG NON-U.S.–BORN PERSONS IN THE UNITED STATES BY COUNTRY OF BIRTH**

Tsang CA, Langer AJ, Kammerer JS, Navin TR. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

The U.S. Centers for Disease Control and Prevention (CDC) recommends screening for tuberculosis (TB) infection in populations at increased risk, including persons born in countries with TB incidence rates >20 cases /100,000 population; however, this approach assumes that expatriates in the United States are representative of the overall country-of-birth (COB) population in terms of TB risk. To evaluate this assumption, we calculated U.S. TB rates by COB.

METHODS

We calculated U.S. rates by COB for 2012–2016 using CDC surveillance data and U.S. Census Bureau population estimates. The Census Bureau aggregates COBs with small U.S. populations into larger regional population estimates. We compared U.S. rates with COB rates reported to the World Health Organization (WHO) by calculating incidence rate ratios (IRRs) for each COB. IRRs >1.0 indicate a higher COB rate than U.S. rate.

RESULTS

The median IRR was 4.9 (interquartile range 2.4–8.1). Notable outliers included South Africa (IRR=79.2, 95% confidence interval (CI)=59.8–104.8), Lithuania (IRR=53.1, 95% CI=13.3–212.4), and Belarus (IRR=52.9, 95% CI=17.1–164.1) as well as United Arab Emirates (IRR=0.1, 95% CI=0.0–0.2) and Tonga (IRR=0.6, 95% CI=0.3–0.9). Of the 195 countries in the world, 179 had COB rates greater than the corresponding U.S. rate.

CONCLUSION

COB rates are, on average, substantially (a median of five-fold) higher than the corresponding U.S. rates, suggesting that expatriates in the United States are not representative of COB populations. U.S. rates might provide a way to prioritize non-U.S.–born populations in the United States by COB for TB testing and treatment.

B. SYSTEMS

B1. ECHO FOR US-MEXICO BINATIONAL TUBERCULOSIS CONTROL COLLABORATION

Adams F¹, Moser K², Vera-García C², Duran-Pena O³; Fortune D⁴, Munoz M⁵, Luna F⁵, Cervantes J⁶, Assael R⁶, García Aviles MA⁴, Armistad A⁷, Dezan A⁸, Struminger B⁸. ¹New Mexico Office of Border Health, Las Cruces, NM; ²Centers for Disease Control and Prevention, San Diego, CA; ⁴New Mexico Department of Health, Santa Fe, NM; ⁵Ministry of Health National TB Program, Mexico City; ⁶Clinica Medica Internacional, Juarez, Mexico; ⁷University of New Mexico, Albuquerque; ⁸ECHO Institute at the University of New Mexico, Albuquerque, NM, USA.

BACKGROUND

The United States and Mexico share a dynamic border region, due to social and economic ties between the two nations. Coordination of TB care for binational patients is essential for the health of patients and the public in both countries.

INTERVENTION/ RESPONSE

The US-Mexico Binational TB ECHO (teleECHO™ program) was developed as a pilot collaboration between the New Mexico Office of Border Health, the ECHO Institute™ at the University of New Mexico Health Sciences Center, and with support by the Centers for Disease Control and Prevention and the National TB Program in Mexico. Objectives for US and Mexico border states include: 1) increasing understanding of resources available for US-MX binational TB case management; 2) improving systems through discussion of current cases; and 3) improving collaboration and communication on behalf of US-MX binational TB patients. Sessions include simultaneous translation via a live interpreter as well as live captioning in Spanish and English.

RESULTS

A 3-month pilot launched in April 2017. Positive participant feedback led us to extend the program through June 2019. As of September 2018, we have completed 17 teleECHO sessions with 14 patient cases presented and 579 total attendees. The program's reach is greater than anticipated, with participation from non-border states in the United States, Mexico, and Central America.

CONCLUSION

Providing a bilingual virtual platform for discussion of binational TB cases engages multiple stakeholders and offers the opportunity for improved understanding and better care coordination. The unique offering of simultaneous bilingual translation has fostered robust participation from colleagues on both sides of the border.

B2. WHAT ARE THE POTENTIAL SAVINGS OF ELECTRONIC DIRECTLY OBSERVED THERAPY FOR HEALTH DEPARTMENTS? EVIDENCE FROM AN ECONOMIC EVALUATION IN NEW YORK, RHODE ISLAND, AND SAN FRANCISCO

Asay GB¹, Lam CK², Mangan J¹, Romo L³, Gummo C⁴, St. John K⁴, Macaraig M², Keh C³, Marks SM¹, Burzynski J², Bamrah Morris S¹. ¹Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Atlanta, GA; ²Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Queens, NY; ³San Francisco Department of Public Health, Population Health Division, Disease Prevention and Control Branch, Tuberculosis Prevention and Control, San Francisco, CA; ⁴Center for HIV, Hepatitis, STDs, and TB Epidemiology, Division of Preparedness, Response, Infectious Disease, and EMS, RI Department of Health, Providence, RI, USA.

BACKGROUND

Tuberculosis (TB) programs offer various forms of directly observed therapy (DOT) to monitor patients ingesting TB medication. Field- and clinic-based DOT are conducted in-person, while live- and recorded-electronic DOT (eDOT) enables remote observation through video-enabled devices. We assessed DOT costs at three US TB programs – New York City, Rhode Island, and San Francisco.

METHODS

Cost of eDOT software, hardware, vehicle usage, and staffing needed for DOT were collected, retrospectively. Staff for all DOT types documented duration of DOT sessions, and time and distance associated with staff travel for in-person DOT sessions, prospectively October – December 2017. Patient data including weeks of treatment, side effects, type of TB treatment (e.g., drug-resistant disease or latent TB infection), and language assistance were also collected. Using a regression model, we adjusted for correlation among multiple observations conducted by the same staff. Costs were presented in US\$ 2017.

RESULTS

During the study period, 349 DOT sessions were captured from 207 patients: 105(30%) were field-based; 66(19%) clinic-based; 122(35%) recorded-eDOT; and 56(16%) live-eDOT. On average, field-based DOT sessions took longest (12 minutes), while recorded-eDOT sessions were shortest (4 minutes). Mean travel time and distance for field-based DOT was 21 minutes (range: 3-75) and 5 miles (range: 0-38). Overall, sites saved between \$680 and \$2,051 per patient using eDOT over in-person DOT.

CONCLUSIONS

Using eDOT can reduce travel time and expense for TB programs. Higher incidence areas, with ability to scale eDOT, can potentially save more per patient.

B3. PATIENT TIME AND COSTS ASSOCIATED WITH DIRECTLY OBSERVED THERAPY: EVIDENCE FROM NEW YORK CITY, RHODE ISLAND, AND SAN FRANCISCO

Asay GB¹, Lam CK², Mangan J¹, Romo L³, Gummo C⁴, St. John K⁴, Macaraig M², Keh C³, Marks SM¹, Burzynski J², Bamrah Morris S¹. ¹Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Atlanta, GA; ²Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Queens, NY; ³San Francisco Department of Public Health, Population Health Division, Disease Prevention and Control Branch, Tuberculosis Prevention and Control, San Francisco, CA; ⁴Center for HIV, Hepatitis, STDs, and TB Epidemiology, Division of Preparedness, Response, Infectious Disease, and EMS, RI Department of Health, Providence, RI, USA.

BACKGROUND

Standard of care for tuberculosis (TB) treatment includes monitoring patients by directly observed therapy (DOT). Electronic DOT (eDOT) could reduce the cost associated with DOT; however, eDOT and in-person DOT costs to patients are not well known.

DESIGN/METHODS

Using a standardized survey, we collected patient demographics and costs from a convenience sample of patients who had at least one eDOT session in New York City, Rhode Island, and San Francisco from October 2017 through January 2018. Patient costs included the value of time spent in in-person and e-DOT and in learning eDOT software, missed work for travel and clinic visits, costs of technology, patient enablers, and dependent caregiver costs. eDOT costs (US\$ 2017) were compared to those for community based (field-DOT) and clinic-based DOT.

RESULTS

Among 87 participants, 84% used personal phones for eDOT, and reported a \$53 median monthly cell-service cost. Median time for patients to learn the eDOT application was 10 minutes (range: <1 minute-3 days) and median time for eDOT was 3 minutes (range: <1–28 minutes). Patients' reported one-way median travel time to clinic of 30 minutes (range: 10–165 minutes) and out-of-pocket cost \$5.07 (range: \$0–\$35). Patients [15 (17%)] needing dependent care for clinic-based DOT indicated a median of 3 hours of care (range: 1.5-14) for each visit. Recorded eDOT, live eDOT, field-DOT, and clinic-based DOT cost patients \$3.89, \$4.25, \$4.01, and \$26.40 per session, respectively.

CONCLUSIONS

Patients face monetary and time costs with TB treatment monitoring. From the patient perspective, recorded eDOT was the least costly.

B4. PATIENT-CENTERED MONITORING FOR TB TREATMENT ADHERENCE IN A LARGE MEXICAN HEALTH JURISDICTION

Perez H¹, Cervantes J^{1,2}, Barrera G^{1,2}, Campos A³, Assael R^{1,2}. ¹Amor-ProTB, NPO; ²Clinica Medica Internacional, Ciudad Juarez; ³Servicios de Salud de Chihuahua, Dirección de Micobacteriosis, Chihuahua, Mexico.

BACKGROUND

Ciudad Juarez (CJ) is the second largest Mexican city on the US-Mexico border. In 2015, only 63% 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 January 2017 and March 2017. Inclusion criteria were ≥ 18 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 Video DOT Program 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

Ten patients were enrolled. 50% were male, median age =30. Patients completed a median of 88.9% of expected doses, 90% had documented culture conversion.

CONCLUSIONS

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.

**B5. CONSULTATION CALLS TO CALIFORNIA DEPARTMENT OF PUBLIC HEALTH
TUBERCULOSIS CLINICIANS: AN EARFUL ON TB COMPLEXITY**

Feraud J, Katrak S, Barry P, Flood J. Tuberculosis Control Branch, California Department of Public Health, Richmond, CA, USA.

BACKGROUND

California Tuberculosis (TB) Control Branch (TBCB) clinicians provide real-time medical consultation to providers from health departments and community settings via phone and e-mail. To inform training and education needs, we analyzed the clinical call characteristics.

DESIGN/METHODS

Clinical consultations from 2016-2017 were analyzed by call frequency, topic, and complexity. Local health jurisdiction (LHJ) morbidity level (high morbidity: >50 TB cases/year, medium morbidity: 11-50 TB cases/year, and low morbidity: 0-10 cases/year) was also examined. Primary call topic categories were TB disease, latent TB infection [LTBI], infection control and contact investigation; subtopics included treatment, diagnosis, screening, policy/legal, and complexity factors such as drug resistance, immune suppression, and advanced age.

RESULTS

Of 475 clinical calls, 378 (80%) were from California health departments; 159 (42%) from high morbidity jurisdictions, 98 (26%) from medium morbidity jurisdictions, and 121 (32%) from low morbidity jurisdictions. The most common primary topic was TB disease (327, 69%), followed by LTBI (75, 16%); and treatment was the most frequent subtopic. Patients with ≥ 1 complexity factor were the subject of 118 (74%) high morbidity jurisdiction calls vs. 83 (69%) low morbidity jurisdiction calls, with drug resistance (95, 20%), immune suppression (71, 15%), and advanced age (67, 14%) occurring most commonly.

CONCLUSION

TBCB provides a high volume of consultations to healthcare providers across morbidity levels. Questions on TB treatment were most frequent, and often focused on complicated patients. As TB disease declines, clinicians facing complex patients are particularly challenged. Novel strategies to enhance their capacity to treat TB patients with multiple conditions is needed.

B6. POTENTIAL LIMITATIONS OF ELECTRONIC DIRECTLY OBSERVED THERAPY (EDOT): EXCLUSIONS FROM A RANDOMIZED TRIAL OF IN-PERSON DOT VERSUS EDOT FOR TUBERCULOSIS TREATMENT

Goswami ND³, Lam CK^{1,3}, Salerno M^{1,2}, Mangan JM³, Burzynski J¹, Reaves M^{1,2}, Kiskadden-Bechtel S^{1,2}, Bowers S^{1,3}, Dias M^{1,2}, Thomas A³, Henry G¹, Macaraig M¹. ¹Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Queens; ²Division of Pulmonary, Allergy & Critical Care, Columbia University, New York, NY; ³U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

Electronic directly observed therapy (eDOT) use is increasing among U.S. tuberculosis (TB) programs. New York City (NYC), the U.S. Centers for Disease Control and Prevention (CDC), and Columbia University partnered to conduct a randomized controlled trial comparing in-person DOT with eDOT among TB patients at NYC Health Department TB clinics. We quantify interim data on reasons for study exclusion.

INTERVENTION

From July 2017 to August 2018, we screened all persons treated for active TB for study inclusion. Patients who were not enrolled due to exclusion criteria or physician discretion were compared to enrolled patients. Reasons for patient exclusion, which were not mutually exclusive, were analyzed.

RESULTS AND LESSONS LEARNED

Of the 472 TB patients assessed for study participation, 254 (54%) were not interested in further participation, 129 (27%) were enrolled, and 89 (19%) were excluded. Of these 89, only 28 (31%) were found to later receive eDOT in their clinic (non-study setting). Compared to enrolled patients, a higher proportion of excluded patients were over 65 years old (33% vs 12%). Of 103 reasons for patient exclusion cited, common reasons included: (1) prescription of a non-rifampin regimen or injectable anti-TB medication (n=19); (2) physician concerns about comorbid medical conditions with eDOT (n=16) and treatment adherence with eDOT alone (n=20).

CONCLUSIONS AND KEY RECOMMENDATIONS

In this public health setting, many TB patients were not appropriate candidates for eDOT due to patient-specific situations and physician concerns. In line with guidelines advocating patient-centered care, these preliminary data suggest that TB programs should consider providing multiple, patient-specific DOT options.

B7. TUBERCULOSIS IN THE UNITED STATES: MEDICAL EXPERT ADVICE PROVIDED BY FIVE U.S. TB REGIONAL TRAINING, EDUCATION, AND MEDICAL CONSULTATION CENTERS (RTMCCS), 2013–2017

Goswami ND¹, Griffith D², Bhavaraju R³, Lardizabal A³, Lauzardo M⁴, Chen L⁵, Wilson JW⁶, Haley CA⁴. ¹U.S. Centers for Disease Control and Prevention, Atlanta, GA; ²Heartland National TB Center and University of Texas Health Science Center, Tyler, TX; ³Global TB Institute at Rutgers, The State University of New Jersey, Newark, NJ; ⁴Southeastern National TB Center at University of Gainesville, Gainesville, FL; ⁵Curry International TB Center at University of California, San Francisco, Oakland, CA; ⁶Mayo Clinic Center for Tuberculosis, Rochester, MN, USA.

BACKGROUND

In 2017, 9,093 new cases of tuberculosis (TB) were reported in the United States. Although TB incidence is declining, there is an increasing percentage of TB patients with drug-resistance and/or comorbid conditions over the past ten years. With rapidly advancing science, expert consultation is paramount in providing optimal care to TB patients.

INTERVENTION

Data from TB medical consultation services offered through five CDC-funded Regional Training, Education, and Medical Consultation Centers (RTMCCs) across the U.S. from 2013–2017 were prospectively collected in an electronic database and analyzed.

RESULTS AND LESSONS LEARNED

RTMCCs provided 14,586 medical consultations to TB providers. Most consults related to patients with active TB (51%) or latent TB infection (LTBI, 19%), with and the remainder related to contact investigations or other issues. Physicians and nurses were primary users of consultation services, and often embedded in local or state health departments. Common topics asked of the consultation service related to TB medications and treatment choice (n=3,384, 26%) and diagnostic or laboratory questions (n=2,539, 19%). Consultations were about pediatric (17%) and adult (80%) patients.

CONCLUSIONS AND KEY RECOMMENDATIONS

RTMCC medical consultation services were well-utilized over a recent five-year period; consultations represent a snapshot of TB expert advice provided to U.S. healthcare workers. The service has potential for increased reach to providers in private clinics, hospitals, and correctional settings. These data highlight areas where increased data and/or national guidance may impact TB-related clinical practices.

B8. WORDS AND PHRASES USED BY TB-AFFECTED HOUSEHOLDS TO DESCRIBE THE STIGMA OF TB

Huff DL^{1,2,3}, Datta S^{1,2,3}, Bonadonna L^{2,3}, Wingfield T^{1,2,3,4}, Montoya R^{2,3}, Evans CA^{1,2,3}. ¹Infectious Diseases & Immunity, Imperial College London, and Wellcome Trust Imperial College Centre for Global Health Research, London, London, United Kingdom; ²Innovation For Health And Development (IFHAD), Laboratory of Research and Development, Universidad Peruana Cayetano Heredia University; ³Innovacion Por la Salud Y Desarrollo (IPSYD), Asociación Benéfica PRISMA, Lima, Perú; ⁴Institute of Infection and Global Health, Liverpool, United Kingdom.

BACKGROUND

Understanding and reducing tuberculosis (TB) stigma are important for TB elimination, yet TB stigma remains poorly defined and understudied.

METHODS

We sought to describe TB stigma from the perspective of members of TB-affected households in poor communities in Lima/Callao, Peru, by providing derived definitions of the primary TB stigma types affecting them, and associating their responses within these TB stigma types. A survey documented words and phrases used to describe TB stigma, which were then categorized into themes. TB-specific definitions were derived from the stigma literature for the stigma types most commonly impacting members of TB-affected households. The most frequently occurring themes were then associated with TB stigma types by definition.

RESULTS

Members of TB-affected households expressed very similar perceptions of TB stigma. The most frequent responses are shown in the figure and included emotion themes of sadness, fear, embarrassment, and low self-esteem; and behavior themes of isolation, rejection, and discrimination. People with drug-resistant TB tended to express themes of sadness and isolation more frequently than people with drug-sensitive TB and household members without TB disease. In general, themes could not be isolated to any one TB stigma type. Two exceptions were the themes ignorance and contempt.

CONCLUSION

Identifying key themes used by members of TB-affected households to describe TB stigma may be of more value in understanding TB stigma than associating themes with specific types of TB stigma by definition. Creating theme profiles for individual respondents may facilitate psychotherapeutic support groups in reducing TB stigma among TB-affected households.

B9. A SYSTEMATIC REVIEW OF THE EVIDENCE FOR THE CLINICAL EFFECTIVENESS AND COST-EFFECTIVENESS OF USING DIGITAL TECHNOLOGIES TO IMPROVE TREATMENT ADHERENCE AND OUTCOMES IN TUBERCULOSIS

Kumar K^{1,2}, Ghafur S³. ¹Airway Disease Infection Section, National Heart & Lung Institute, Faculty of Medicine, Imperial College London; ²Imperial College Healthcare NHS Trust; ³Centre for Health Policy, Institute of Global Health Innovation, Imperial College London, London, United Kingdom.

BACKGROUND

Tuberculosis (TB) therapy non-adherence leads to poor clinical outcomes and significant financial burden to healthcare services. Digital technologies such as short message service (SMS), smartphone applications, medication monitors, video observed therapy (VOT), ingestible sensors with wirelessly observed therapy (WOT) and social media platforms may offer novel solutions to improve adherence, outcomes and cost savings.

DESIGN/METHODS

MEDLINE, EMBASE, Web of Science, Scopus, CENTRAL, ClinicalTrials.gov, WHO Clinical Trials Registry, WHO publications and the grey literature were systematically searched to identify randomised controlled trials and observational studies with controls that evaluated the clinical effectiveness of using the listed technologies to improve TB treatment adherence and outcomes. Economic studies pertaining to their costs were included.

RESULTS

Sixteen studies were identified. SMS reminders do not improve adherence or outcomes; one study demonstrating improvement in treatment completion rates had a high risk of bias. The one study on smartphone applications does not demonstrate improvement in treatment outcomes. Evidence from two studies shows that medication monitors may improve treatment cure rates and decrease treatment non-adherence. VOT is not associated with improvement in adherence or outcomes. No suitable studies on the clinical effectiveness of WOT or social media platforms were identified. Medication monitors, VOT and WOT may lead to cost savings but comprehensive cost-effectiveness analyses are lacking.

CONCLUSION

Given the current paucity of high-quality evidence, policymakers cannot make definitive evidence-based decisions regarding wider implementation of these technologies. More studies need to be commissioned on using these technologies among TB patients, particularly in low and middle-income countries with the highest TB burden.

B10. WELTEL TB OUTREACH: PILOTING A MOBILE HEALTH INTERVENTION FOR PROVINCIAL TUBERCULOSIS SERVICES

Cook VJ^{1,2}, Gourlay K², Johnston JC^{1,2}, Giffin C¹, Patel P², Enjetti A², Smillie K², Lester RT^{2,3}. ¹BC Centre for Disease Control; ²University of British Columbia, Vancouver, BC, Canada; ³WelTel.org

BACKGROUND

Directly Observed Therapy for individuals living with tuberculosis (TB) is a proposed standard of care, however high resource demands from health care systems prevent adherence. We examined a mobile health (mHealth) intervention as a low-cost alternative to observed therapy for patients in between clinical appointments.

INTERVENTION

WelTel is a centralized, secure, web-based digital health platform allowing communication between healthcare providers and clients via text messaging, phone, or video. WelTel was introduced to the BC TB Outreach program to centralize communication with enrolled patients, who receive regular text-message check-ins. Only SMS and phone calls were used in this pilot. Correspondence history and notes made by healthcare providers were accessible to other providers on the platform. Focus groups were held with outreach workers and nurses to qualitatively assess the feasibility, acceptability and transferability of the platform.

RESULTS AND LESSONS LEARNED

The program succeeded in replacing existing individual provider-to-client messaging practices. Early assessment revealed perceived improvements in continuity of care and communication between patients and clinicians. Clinic and outreach teams noted that language differences and clinical integration were challenges for implementation. The clinic team enrolled more patients than outreach nurses.

CONCLUSIONS AND KEY RECOMMENDATIONS

Digital health technology has potential to enhance tuberculosis services through improving patient care continuity and enhancing management of healthcare resources. We propose a future pilot of mobile video DOT for TB patients requiring more intensive support and monitoring.

B11. ADAPTATION OF THE WORLD HEALTH ORGANIZATION'S TUBERCULOSIS ELIMINATION FRAMEWORK TO GUIDE LOCAL PROGRAM PLANNING

Leung T¹, Burnell C¹, Chong K¹, Fuller J¹, Lechner J¹, Nguyen T¹, Samarita T¹, Sebastian A¹, Seto C¹, Rea E^{1,2}. ¹Toronto Public Health; ²University of Toronto, Toronto, ON, Canada.

BACKGROUND AND REASONS FOR IMPLEMENTATION

In 2014, the World Health Organization (WHO) released *Towards Tuberculosis (TB) Elimination: An Action Framework For Low-Incidence Countries*. We describe our adaptation of this global framework in Toronto, Canada, a large urban city with a TB incidence of 10.0 per 100,000, to support local program planning for TB elimination.

INTERVENTION OR RESPONSE

We compared our local epidemiology with the characteristics of low-incidence countries outlined by WHO to ensure relevance for Toronto. We reviewed WHO's framework and translated the eight priority action areas and essential elements in the context of our local TB program structure and public health jurisdictional responsibilities.

RESULTS AND LESSONS LEARNED

We categorized WHO's eight priority action areas into three streams: (a) Screening, Treatment and Client Support; (b) Surveillance Data Management, and Program Evaluation; and (c) Advocacy, Collaboration, Education, and Policy Development. Within each stream, we identified program activities (e.g. active TB management, contact investigation, molecular epidemiology, advocacy) and outlined activity-specific goals, ongoing/routine work, and prospective initiatives. The outcome of this process was a one-page comprehensive overview of our program, tying our activities to TB elimination actions. The initial framework has since been used as a key planning tool for priority setting, identifying gaps, and establishing a clear five-year program plan.

CONCLUSIONS AND KEY RECOMMENDATIONS

Developing a TB elimination framework at the local level has been useful for focusing our program efforts and may be useful for other TB programs looking for a structured approach to work towards TB elimination.

B12. IMPLEMENTING THE ‘PATIENTS CHARTER FOR TUBERCULOSIS CARE’ IN HIGH INCIDENCE COMMUNITIES AND ACROSS JURISDICTIONAL BORDERS: REFLECTING ON PROCESS

Lynn A^{1,2}, Cardinal-Grant M², Nokohoo M³, Janvier D³, Piche D³, Heffernan C², Long R^{1,2}. ¹School of Public Health; ²Tuberculosis Program Evaluation and Research Unit, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada; ³Community co-investigators from their own Indigenous community.

BACKGROUND AND REASON FOR IMPLEMENTATION OR PROBLEM BEING ADDRESSED

Tuberculosis (TB) in the Canadian Prairies tends to occur in high incidence communities. Historically, patients and communities have not been involved in TB programming. Further complicating matters are the colonialily imposed jurisdictional barriers which define TB programming and fail to reflect the mobile realities of those living within.

INTERVENTION OR RESPONSE

A regional coalition of four high incidence, interconnected communities was formed. This coalition advocates for community and population health supports, aiming at having a downstream effect on TB transmission and progression to disease. It functions as an ethical space that brings together Indigenous and non-Indigenous stakeholders to discuss local community needs, identifying pertinent social determinants of health, such as housing and lack of services, confounding TB elimination efforts. Within the coalition communities participate as equal stakeholders in decision making.

RESULTS AND LESSONS LEARNED

Successes of the regional coalition include addressing colonial-imposed systems that affect health and providing a platform for advocacy. Federal and provincial stakeholders have been responsive to community identified needs. For example, a gap in human resources was identified and stakeholders responded with creation and funding of TB coordinator positions. Local level interventions, including sharing and interpretation of surveillance data and expanded outreach, were identified as community priorities. Challenges include administrative and institutional timeline and funding restrictions, and additional demands placed on community participants.

CONCLUSIONS AND KEY RECOMMENDATIONS

The development of a regional coalition is a way forward, changing the relationship between Indigenous communities, non-Indigenous communities, and government stakeholders. This process may be scalable to other high incidence Indigenous communities in Canada and beyond.

B13. BRITISH COLUMBIA'S (BC) ONLINE TUBERCULOSIS (TB) COURSES: A STEP FORWARD IN ADVANCING TB EDUCATION FOR NURSES

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

BACKGROUND

Nurses play an important role in providing TB care to clients. There was a recognized need to establish provincial access to basic TB education to support safe and competent nursing practice. This led to the development of two evidence-based, accessible and user-friendly online TB educational courses in BC: TB Essentials Course (2014) and the Tuberculin Skin Testing (TST) Course (2016).

INTERVENTION/RESPONSE

The TB Essentials Course offers a broad overview of the biosocial factors involved in TB care in the public health setting. The TST Course builds capacity to competently perform comprehensive TB screening assessment and testing. It complements the practical application of TB testing participants receive in their local work setting. These evidence-based courses, take 1-3 hours to complete, are open-access, self-directed, and include quizzes and activities to consolidate learning.

RESULTS

The Tuberculosis Essentials Course has had 1183 participants complete the course to date. The course evaluation results (n=853) reveal that 94% of participants strongly agree and/or agree that the course prepared them to begin providing TB care. The Tuberculin Skin Testing Course has had 947 participants complete the course to date. The course evaluation results (n=128) reveal that 91 % of participants strongly agree and/or agree that they would recommend the course to a co-worker.

CONCLUSIONS

BC's online TB courses are a widely used and valuable educational resource for nurses. An online education platform can be an effective way to reach health care providers broadly and is a useful tool to support provider TB knowledge and practice.

B14. USE OF SMART-PHONE TECHNOLOGY IN DIRECTLY OBSERVED THERAPY FOR TUBERCULOSIS TREATMENT AT PUBLIC HEALTH – SEATTLE KING COUNTY TB CONTROL PROGRAM

Gardner-Toren K, Mummert L. Public Health - Seattle & King County, Tuberculosis Control Program, Seattle, WA, USA.

BACKGROUND

Directly observed therapy (DOT) has become the universal approach to ensure adherence to tuberculosis treatment. When Public Health – Seattle & King County was facing potential budget cuts and needed to reach increased numbers of geographically dispersed patients with unpredictable schedules, the TB program explored alternative options for DOT in selected patient sub-groups. emocha, a HIPAA compliant telemedicine app, was chosen to address this issue.

INTERVENTION OR RESPONSE

emocha allows patients to upload a video of themselves taking their TB medications. After a patient has initiated treatment and meets the eligibility requirements, they are enrolled and trained by TB staff to use emocha. Through the app, patients can report side effects and see a list of their medications. Patients must clearly show their medications bottles, number of pills, and ingestion. Assigned staff then watch, approve, and provide feedback on video submissions.

RESULTS

Since emocha's implementation in October 2016, 101 patients have been enrolled, of which 64 patients have completed treatment using emocha, 5 have transferred back to in-person DOT, and 32 are currently enrolled. Represented on emocha are patients from 24 different countries ranging from 1-84 years of age with 42% of users above age 50. Patients, on average, used emocha for 67% of overall treatment. Today, 56% of patients are using emocha.

CONCLUSION

The use of smart-phone technology has brought DOT into the 21st century by easing patient burden brought by lengthy treatment regimens and distributing outreach resources more efficiently. Telemedicine programs, like emocha, will continue to be instrumental in local TB control efforts.

B15. **PATIENT'S PERCEPTIONS OF PATIENT-PROVIDER INTERACTIONS ACROSS DIFFERENT METHODS OF DIRECTLY OBSERVED THERAPY (DOT)**

Salerno M^{1,2}, Kiskadden-Bechtel S^{1,2}, Reaves M^{1,2}, Bowers S^{1,3}, Hill A³, Thomas A³, Dias M^{1,2}, Lam CK^{1,3}, Burzynski J¹, Macaraig M¹, Goswami ND³, Mangan JM³. ¹Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Queens; ²Division of Pulmonary, Allergy & Critical Care, Columbia University, New York, NY, USA; ³U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

As the use of digital technologies to support tuberculosis (TB) treatment adherence expands, their impact on patient-provider interactions warrants evaluation.

METHODS

We are conducting a randomized controlled trial comparing traditional in-person directly observed therapy (ipDOT) with electronic DOT (eDOT) for TB treatment, in four TB clinics throughout New York City. Employing a crossover study design, participants are scheduled for 20 medication doses with ipDOT and 20 doses with eDOT.

Following the two observation periods, participants complete a questionnaire to report the frequency staff discussed patients' questions and concerns, provided needed information, ensured understanding, and displayed empathy. Positing that participants' most recent experiences may influence their answers, responses were categorized by type of DOT used immediately before completing the questionnaire.

RESULTS

Since July 2017, 129 participants have been enrolled and 67 (52%) completed both observation periods as scheduled. Participants median age is 37 years (range: 18-86); 66% (n=44) are male; 91% (n=61) are non-U.S.-born.

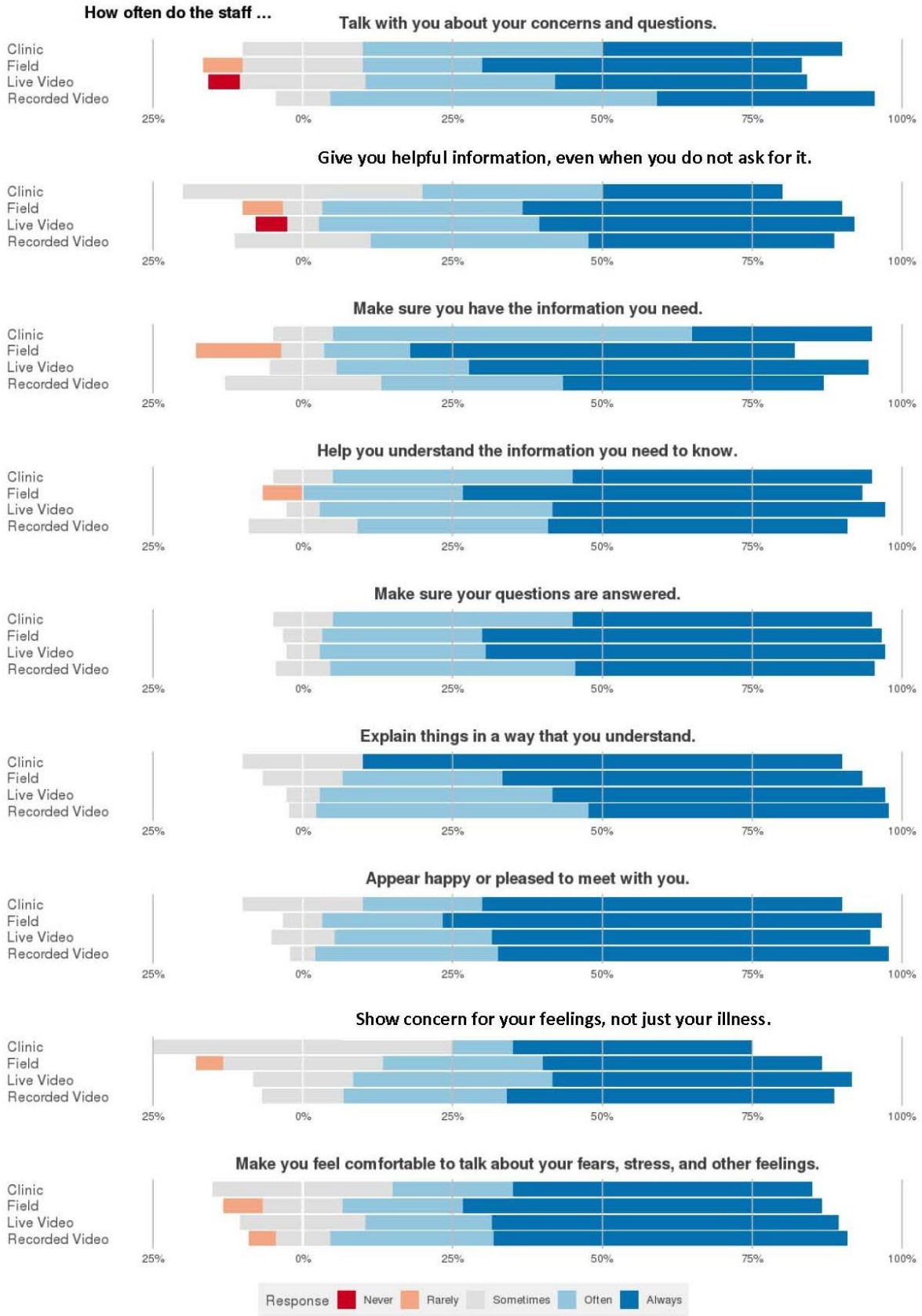
Before responding to the questionnaire, 10 (15%) participants used clinic-based DOT, 15 (22%) used field-based DOT, 19 (28%) used eDOT with live video conferencing and 23 (34%) with recorded videos.

Among all forms of DOT, 73-93% of participants answered either "always" or "often" to 7 of 9 questions.

Participants on clinic-based DOT were more likely to answer "sometimes" when asked if staff provided information unsolicited (40%), or displayed concern for participants' feelings (50%). Participants on field-based DOT more often responded "always" to questions. (Figure 1)

CONCLUSION

Relative to patient-provider interactions, preliminary findings suggest all DOT methods are performing acceptably.



B16. USING VIDEO ADMINISTERED DIRECT OBSERVATIONAL THERAPY TO INCREASE TREATMENT COMPLIANCE TO MEDICATION FOR LATENT TUBERCULOSIS INFECTION

Taylor A¹, Molina S¹, Agustin T¹, Silvas F¹, Davis B¹, Marr S¹, Perez-Velez C¹, Oren E². ¹Pima County Health Department, Tucson, AZ; ²San Diego State University, San Diego, CA, USA.

BACKGROUND

Tuberculosis is the leading infectious disease cause of death globally. Completing treatment thoroughly for latent tuberculosis infection (LTBI) is imperative in preventing progression to active disease. The Pima County Health Department needed a method to efficiently manage LTBI patients on a regimen of rifapentine and isoniazid once a week for 12 weeks.

INTERVENTION

The objective of this project was increase treatment initiation and completion rates through use of direct observational therapy by video (VDOT). Patients enrolled in the VDOT trial, had access to the internet, had a device or borrowed one, and were non-contagious. The patients completed a satisfaction survey on the use of VDOT compared to other modalities, completing both Likert and open-ended questions.

RESULTS

Of the 27 LTBI patients who participated in the VDOT study from January – August 2018, 100% completed treatment compared to a 75% baseline completion rate of traditional DOT LTBI patients (2017). Prior to the VDOT option, the treatment initiation rate was 68% for traditional DOT LTBI patients (2017). After introducing the VDOT option, the treatment initiation rate increased to 83% during the period of the pilot study. Eighty-three percent of patients surveyed agreed or strongly agreed that VDOT is more convenient than traditional DOT. In addition, 78% found VDOT to save time and 84% found it easier to use.

CONCLUSION

Given the findings, VDOT use in the future may include a record-and-forward video platform. VDOT is expected to enhance the capacity of case management through ease of use and convenience for both the patient and staff.

B17. TEN-YEARS INTO THIRD-PARTY BILLING FOR TB SERVICES IN MASSACHUSETTS: INITIAL ANALYSIS OF IMPACTS AT MULTIPLE LEVELS

Tschamp C^{1,2}. ¹Heller School for Social Policy and Management, Brandeis University, Waltham; ²Medical Advisory Committee for the Elimination of TB (MACET), Boston, MA, USA.

BACKGROUND

The Massachusetts (MA) TB control program consists primarily of a network of public-private, contracted “TB clinics.” In response to fiscal pressure from federal and state budget cuts, third-party billing (T-PB) for TB services began statewide in 2009. MA has since experienced reductions of 18% in the TB case rate, 33% in TB clinics, and 30% in dedicated nurse-case managers, and a 30% increase in complex cases.

METHODS

I combined TB programmatic document review, qualitative data from a convenience sample of six experts, literature regarding price’s impact on utilization, and microeconomic theory to assess impacts of T-PB from multiple perspectives.

RESULTS

Individual access: Third-party billing decreased the quantity of TB services by suppressing individual demand through financial and non-financial disincentives. As much as 25% of TB visits are not insured, which reduced negative financial impacts.

City/town public health: T-PB did not apply to several services provided outside the TB clinics.

TB clinic provider organizations: During integration, T-PB increased labor costs, caused production disruption, and decreased quality of services by diverting skilled labor away from essential surveillance and control functions. T-PB increased reimbursement rates only for services provided to insured patients.

State TB program: Initial implementation disruption was followed by a new steady state.

CONCLUSION

Initial analysis indicated third-party billing was beneficial from a financial perspective at the state TB program level and at some provider-level organizations. T-PB was neutral or negative from both financial and non-financial perspectives at the individual level. Third-party billing alone cannot end the erosion of TB prevention and control infrastructure.

B18. KNOWLEDGE, ATTITUDE AND PRACTICE OF NURSE STUDENTS IN SAINT MARC, CENTRAL HAITI TOWARDS TB

Vandal S. DSNI, Miragoane, Nippes, Haiti.

BACKGROUND

Haiti has the highest TB incidence and a high HIV prevalence in the Caribbean; and in Haiti Saint Marc has the Highest HIV and coinfection TB/HIV in the country, 22% in 2017; since some local patients prefer to go outside for HIV or TB care, we conduct survey to understand the behavior of the providers and the population to affected patients.

METHOD

Nursing students from the 2 nursing schools were invited to participate, and after verbal consent, had to fill out the validated and already used in the country; students who don't live in Saint Marc , or not present during the survey day, or sick, or refuse to participate were excluded.

RESULTS

497 students filled out the questionnaire, their mean age was 23 years, and 76% complete secondary school, 91% live in or nearby Saint Marc; 90% know TB signs, 65% clearly how TB is transmitted; 100% the treatment is free, and 43% where are the TB clinics in the zone; 34% think that evil is involved in the transmission, 85% TB could be cured; 45% don't the link between HIV and TB; 85% would not want people to know if they have TB, 56% would only provide financial support to a family with TB.

CONCLUSION

These finding show that providers attitude toward TB or HIV or Coinfected TB/HIV affected patient are linked to lack of knowledge, to better understand the disease, deeper training and more comprehensive advocacy are needed to reverse stigmatization that constraint patients to move for available care.

B19. TUBERCULOSIS CONTROL PROGRAMS IN REFUGEE CAMPS IN RWANDA AND TANZANIA

Wen XJ¹, Nability SA¹, Tromble EE¹, Mumporeze J², Sultana Z², Dassanyake L³, Johnson MT³, Maina AGK⁴, Burton A⁵, Migambi P⁵, Cookson ST¹. ¹U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA; ²United Nations High Commissioner for Refugees, Kigali, Rwanda; ³United Nations High Commissioner for Refugees, Kigoma, Tanzania; ⁴United Nations High Commissioner for Refugees, Geneva, Switzerland; ⁵Rwanda BioMedical Center, Kigali, Rwanda.

BACKGROUND

Refugees are vulnerable to tuberculosis (TB) because of overcrowding and food aid dependency. We assessed the camps using the TB evaluation tool with the goal of improving it and of revising the WHO/UN Refugee Agency's field manual for TB control among refugees.

INTERVENTION

In late 2017-early 2018, we assessed three camps each in Rwanda and Tanzania hosting Burundi and Congolese refugees using the TB program evaluation tool for resource-limited settings. The tool contains laboratory, health education, clinical-case management for adults and children, and data management components. Grading was based on proportion of items achieved per component, >85% "excellent", 70-84% "good", 50-69% "passing", and ≤ 49% "failing". We assessed gaps in TB detection using originating or host country TB incidence/notification rates (NR), using the latter for refugees residing in camps >5 years.

RESULTS AND LESSONS LEARNED

Camps received excellent scores across laboratory and data management components with scores of "good" for clinical-case management for adults, but only "passing" for children. Health education scores varied, with average of "good". Congolese living in camps >5 years, in both host countries had NRs similar to Rwanda's, between 49-58/100,000, but below Tanzania's NR. Newly-arriving refugees from Burundi to both host countries had NRs between 22-66/100,000 -- below Burundi's NR (73/100,000) and WHO's estimated incidence (118/100,000).

CONCLUSIONS AND KEY RECOMMENDATIONS

The assessment found all components passed but child clinical-case management performed the poorest. Tanzania's detection gap was greater than Rwanda's, but both countries need improved contact tracing and greater TB education of staff/refugees. These methods/findings will be used to revise the tool and manual.

C. TRANSMISSION/INVESTIGATION

C1. RISK FACTORS ASSOCIATED WITH PROLONGED AIRBORNE ISOLATION

Abbott A, Kalyatanda G, Seraphin MN, Lauzardo M. University of Florida, Gainesville, FL, USA.

BACKGROUND

Patients suspected of having active Tuberculosis (TB) are placed on airborne isolation. Tuberculosis is ruled out for most. Pitfalls of isolation have included increased rates of adverse effects, delay in obtaining procedures and patients having a negative perspective about their care.

METHODS

We analyzed data on 74 patients placed on isolation between 2014 and 2015. The main outcome was days on respiratory isolation, categorized around the median value. We investigated clinical and demographic risk factors associated with prolonged respiratory isolation using logistic regression.

RESULTS

The sample is predominantly male (74.3%), White (56.8%), and U.S.-born (81.1%), with 43.2% between the ages of 30-59 years. Median duration of isolation was 2 days, range (0-39 days). In multivariable analyses, patients who had a latent TB infection (LTBI) test done at the hospital were more than seven times as likely to be on isolation beyond 2 days (OR=7.87, 95% CI: 1.26, 48.96). Those with fever seemed to be almost six times more likely to be on isolation for more than 2 days (OR=5.64, 95% CI: 0.95, 33.39), however, the results did not reach statistical significance (P=0.0569).

CONCLUSION

We observed that having an LTBI test (purified protein derivative, interferon-gamma release assay) performed in the hospital significantly prolonged airborne isolation. Sputum smears were not obtained in almost half of cases involving LTBI testing, suggesting the LTBI test was used to evaluate for active TB. This improper use of testing can be detrimental to patients and to public health.

C2. COSTS OF DIFFERENT STRATEGIES FOR TUBERCULOSIS SCREENING AND DIAGNOSIS IN PRISONS

Arias C¹, López L¹, Marin D¹, Nieto E², Keynan Y³, Rueda ZV¹. ¹Universidad Pontificia Bolivariana; ²Universidad de Antioquia, Medellín, Colombia, ³University of Manitoba, Winnipeg, MB, Canada.

BACKGROUND

The high tuberculosis (TB) prevalence in prisons, delay in diagnosis and overcrowding contribute to the risk of TB transmission within prisons. Our aim was to estimate and compare the costs of passive case finding (PCF) and two active case finding strategies, one with sputum smear (ACF-S) and/or culture (ACF-S&C) in one prison in Medellín, Colombia.

METHODS

We obtained information between 2009 to 2017. Costs were estimated in USD based on institutional financial perspective. An inventory of activities and human and material resources were used for each activity for each year of each strategy PCF, ACF-S, and ACF-S&C. Costs included: personnel (physician, nurse, technician) and materials: supplies of stationery, flipcharts, billboards, pencils, sputum smear and culture. Costs associated with active TB management were not estimated.

RESULT

The annual cost of ACF-S&C had the highest cost (PCF US\$6,687.4; ACF-S US\$34,769.1; ACF-S&C US\$49,092.9) but identified more people with respiratory symptoms (mean of screened people: PCF: 154; ACF-S: 1066; ACF-S&C: 844) and more TB cases (ACF: 24-50 cases, PFC: 7-26 cases). When we compared the cost of screening per person, the cheapest strategy was ACF-S (PCF: 43.46; ACF-S: 34.43; ACF-S&C: 58.551), however this strategy it will identify only 75% of TB cases.

CONCLUSION

ACF is associated with higher upfront cost compared to PCF, but it identifies more TB cases, which may allow to halt TB transmission within prisons. Since ACF identifies greater proportion of active TB cases and without increased associated costs this approach to ACF should be adapted in prisons.

C3. **POSSIBLE TRANSMISSION MECHANISMS ASSOCIATED WITH MIXED TUBERCULOSIS INFECTIONS IN A HIGH HIV-PREVALENCE COUNTRY**

Baik Y¹, Zetola NM², Moonan PK³, Modongo C², Boyd R⁴, Finlay A³, Click ES³, Oeltmann JE³, Shin SS⁵.

¹University of California, Los Angeles, Los Angeles, CA; ²University of Pennsylvania School of Medicine, Philadelphia, PA; ³U.S. Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis; ⁴U.S. Centers for Disease Control and Prevention, Division of Tuberculosis Elimination Atlanta, GA; ⁵Sue & Bill Gross School of Nursing, University of California Irvine, Irvine, CA, USA.

BACKGROUND

Concurrent infection with multiple strains of *M. tuberculosis* (MTB), referred to as mixed-infection, challenges traditional clinical and epidemiologic paradigms. HIV-associated immunosuppression may increase the risk of mixed-infection. Our study explored possible transmission mechanisms associated with mixed-infection in a population-based, molecular epidemiology study in Botswana —the KOPANYO study.

DESIGN/METHODS

During 2012–2016, all registered tuberculosis (TB) patients in Gaborone and Ghanzi districts were eligible for enrollment. We considered mixed infection as multiple repeats of alleles at two or more loci within 24-locus MIRU-VNTR results in baseline sputum culture. We compared MIRU-VNTR results of putative mixed-infection with non-mixed MIRU-VNTR results to identify possible precursor strains of each mixed-infection. Possible precursor strains were classified as part of ongoing transmission if found in two or more patients, including the mixed-infection patient; and reactivated strain, if occurred only in the mixed-infection patient, suggesting reactivation of remotely acquired infection.

RESULTS

Among 2137 TB patients, 1218 (57%) were HIV-infected. MIRU-VNTR detected 885 different strains, of which 37 (4.2%) were mixed-infections. Twenty-three strains (62%) had patterns consistent with a combination of ongoing transmission cluster and reactivated strains, 10 (27%) with multiple reactivated strains, and 4 (11%) with multiple ongoing transmission. Among the 37 patients with mixed infection, 22 (59%) were HIV-infected, ranging from 50–61% across the possible transmission patterns.

CONCLUSIONS

We attributed a high proportion of mixed-infections to a combination of ongoing transmission and reactivated strains. Public health interventions that reduce multiple exposures to TB may also reduce the prevalence of mixed TB infections.

C4. **LESSONS FROM IMPLEMENTING AN INCIDENT COMMAND SYSTEM IN A CONGREGATE SETTING CONTACT IDENTIFICATION**

Batista M, Jones C, Ledezma E, Simmons T. Texas Department of State Health Services, San Antonio, TX, USA.

BACKGROUND

Contact identifications (CI) in congregate settings are challenging due to the need to identify and screen a large number of contacts who gathered and shared the same space for a period of time. In February 2018, the Texas Department of State Health Services (DSHS)-Public Health Region 8 (PHR 8) initiated a CI when a person diagnosed with tuberculosis was identified at a school in Kendall County, Texas. As a result, 206 school contacts were screened and tested in one of the largest CI's conducted in PHR 8.

METHODS

PHR 8 staff in collaboration with the school district reviewed the individual's schedule. Contacts with 6+ hours of exposure a week, or immunocompromising conditions, were screened during two testing events. An incident command system (ICS) was implemented in order to assist with planning and operations. Conferences with school staff and student's parents were held before the testing events to address questions, concerns, provide tuberculosis education and address the media. The PHR 8 tuberculosis program provided leadership with multiple DSHS programs contributing personnel to the CI and testing process.

RESULTS

The implementation of an ICS structure manned with personnel from various PHR 8 programs made this investigation successful. This region-wide effort allowed for the successful screening of 195 contacts, resulting in a 94.7% evaluation rate.

CONCLUSION

It takes a well-organized team in order to successfully perform large-scale tuberculosis testing events. Making use of various PHR 8 personnel as well as an ICS structure was an effective strategy for this CI and should be considered standard practice.

C5. CONTACT TRACING SPEED AND INCLUSION

Chen Y, Hoepfner V, Osgood N. University of Saskatchewan, Saskatoon, SK, Canada.

BACKGROUND

Completing contact tracing (CT) within one month is a costly task. It would be helpful to reduce costs if outcomes could be maintained with longer durations. The objective was to determine the effect of longer CT duration with lower percentage traced on cumulative TB cases.

DESIGN/METHODS

An agent-based simulation model was constructed using historical Saskatchewan data applied to a hypothetical population of 15000. Seven experimental scenarios with completion times ranging from 1 to 18 months at 50% traced, and two control – no contact tracing, and 100% traced in 1 month – were constructed. 100 run Monte Carlo ensembles measuring cumulative TB cases over 20 years were conducted for each scenario. The statistical significance of each scenario was established using a two-sided Mann-Whitney test across each pair of scenarios.

RESULTS

Completing 50% CT within 1 month resulted in a 17% increase in TB cases over 20 years compared to 100% within 1 month. Extending the 50% CT duration from 1 month to 18 months resulted in a 17% increase in TB cases. The corollary was that 50% CT duration of 15 months compared to 1 month did not result in a significant increase in TB cases.

CONCLUSIONS

Cumulative TB cases are similar when completing 50% CT within 15 months compared to 1 month. The dominant variable in CT is the percent of contacts that are traced. Further investigation is needed to determine the full impact of increasing percent of contacts traced over longer CT periods.

C6. **MULTIDISCIPLINARY EFFORTS TO DECREASE THE TIME TO DISCONTINUATION OF AIRBORNE ISOLATION FOR PATIENTS WITH SUSPECTED ACTIVE PULMONARY TUBERCULOSIS IN AN URBAN TERTIARY MEDICAL CENTER BY MEANS OF A NEW ELECTRONIC ORDERING SET**

Eddy JJ, Becker S, Daniel G, Fleming K, Gaur N, MacMurdo S, Miller NS, O'Donnell C, Orr B, Tull C, Fagan M. Boston Medical Center, Boston, MA, USA.

BACKGROUND

Airborne isolation rooms are frequently used at Boston Medical Center to rule-out infectious tuberculosis (TB) in suspect patients. Inefficiencies in electronic medical record (EMR) ordering practices and in the induction/collection of sputa appeared to be contributing to unnecessarily long periods under airborne precautions, prolonging hospital stays and making airborne rooms inaccessible to other patients.

INTERVENTION

A multidisciplinary panel representing physicians, respiratory therapy (RT), and nursing was convened in the Fall of 2016 to assist information technology in devising a new EMR order set for TB rule-out. Orders were streamlined, options were created for both expectorated and induced samples, and simultaneous nucleic acid amplification testing (NAAT) was incorporated. The timing of sputum collections considered meal delivery times, RT staffing, and microbiology lab testing algorithms. Chart review was undertaken of TB rule-outs in 3-month periods before and after the roll-out of the new order set on March 1st, 2017.

RESULTS

The mean length of time for discontinuation of airborne precautions (i.e., hours between 1st sputum collection and 3rd sputum acid-fast smear result) on non-ICU wards was compared before and after order set implementation. The mean time for all rule-outs decreased by 7.2 hours (52.5 to 45.4 hours, N=65, CI -0.5 to 14.9, p=0.07). However, the decrease was 11.8 hours (52.5 to 40.7 hours, N=46, CI 2.1 to 21.5, p=0.02) in the subset of patients for whom the order set was actually used by providers.

CONCLUSIONS

Simple interventions using information technology may effectively address complex logistical problems involving tuberculosis prevention and control.

C7. **WHOLE GENOME SEQUENCING AS A TOOL TO UNDERSTAND AND QUANTIFY ACTIVE TUBERCULOSIS ARISING FROM LOCAL TRANSMISSION**

Guthrie JL¹, Cherian SS², Kong C³, Roth D⁴, Jorgensen D³, Rodrigues M³, Walker T⁵, Foster D⁵, Henry B^{1,6}, Cook VJ^{4,7}, Johnston J^{4,7}, Tang P⁸, Gardy JL^{1,4}. ¹School of Population and Public Health; ²Department of Pathology and Laboratory Medicine, University of British Columbia; ³British Columbia Centre for Disease Control Public Health Laboratory; ⁴British Columbia Centre for Disease Control, Vancouver, BC, Canada; ⁵Nuffield Department of Medicine, John Radcliffe Hospital, Oxford, UK; ⁶Office of the Provincial Health Officer, Ministry of Health, Victoria; ⁷Department of Medicine, University of British Columbia, Vancouver, BC, Canada; ⁸Department of Pathology, Sidra Medical and Research Center, Doha, Qatar.

BACKGROUND

British Columbia (BC) has committed to reducing TB incidence rates by 50% by 2022 as part of its Provincial TB Strategy, and reducing local transmission through targeted, evidence-based interventions has been identified as an important objective within the strategy.

DESIGN

A total of 2,290 clinical *Mycobacterium tuberculosis* (*Mtb*) isolates collected in BC (2005–2014), were first genotyped by 24-locus MIRU-VNTR. The 974 clustered isolates and 247 isolates of special interest, such as drug-resistant isolates and serial isolates from the same individual, were directed to whole genome sequencing (WGS) using the Illumina HiSeqX. Genotype and WGS results were linked to case-level clinical and demographic data to characterize the epidemiology of tuberculosis transmission in BC.

RESULTS

The proportion of isolates clustered decreased from 42% using MIRU-VNTR to 26% with WGS using a 20-SNP threshold. Among persons born outside Canada, only 8% of cases clustered by WGS, and clusters in this group were often small. In contrast, 77% of Canadian-born TB cases represent local transmission, with 11 large outbreaks (11–72 cases/cluster) identified. Although WGS data suggested a significant degree of geographic structure to transmission, we detected individual transmission-events across large distances (>1,000 km).

CONCLUSIONS

This study demonstrates the value of WGS for large population-based studies, providing a benchmark transmission estimate against which we can compare future progress towards elimination within BC's TB program. Routine use of WGS will significantly improve our understanding of TB transmission, and provide the evidence necessary to develop more effective care and treatment strategies.

C8. INNOVATION IN FIELD EPIDEMIOLOGY: USING SOCIAL MEDIA AND WHOLE GENOME SEQUENCING TO ENHANCE A TUBERCULOSIS OUTBREAK INVESTIGATION

Knorr J, Modestil H, Ahuja SD, Sullivan Meissner J. New York City Department of Health and Mental Hygiene, Queens, NY, USA.

BACKGROUND

The New York City (NYC) Bureau of Tuberculosis Control (BTBC) conducts universal genotyping and routinely investigates tuberculosis (TB) genotype clusters using chart review, patient interview, spatial analysis, and queries of non-BTBC medical and social service databases. The Centers for Disease Control and Prevention began conducting whole genome sequencing (WGS) for large TB outbreaks in 2013.

INTERVENTION

In 2015, BTBC identified a quickly-growing TB outbreak within an endemic strain first identified in NYC in 1997; few known links existed among outbreak patients. BTBC requested WGS analysis and used social media to help establish epidemiologic links.

RESULTS

From October 2012 to January 2018, BTBC identified 13 cases with matching conventional genotyping results. Preliminary investigation and WGS results identified a subset of nine cases likely linked by recent local transmission, including two counted outside NYC. All nine patients were United States-born; eight (89%) were male; median age was 28 years (range 19-59); 89% had known history of marijuana use; two patients had previously-identified contact links; eight had links to a multi-unit apartment complex. Among four (44%) patients with Facebook profiles identified, two listed each other as a “friend” and three shared a common friend. An additional two were linked to previously-identified cluster patients through Facebook profiles of their associates.

CONCLUSION

Identifying social contacts through traditional contact investigation and patient interview was unsuccessful in this group of mostly young men. Social media has been invaluable for elucidating relationships and identifying previously unknown links between patients. WGS helped focus the outbreak investigation by further differentiating this TB strain.

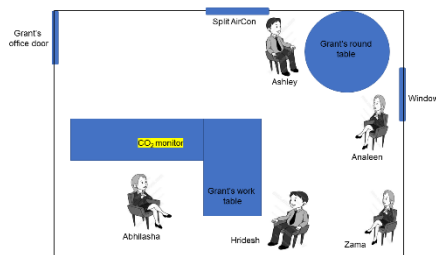
C9. COOL BUT DANGEROUS – INCREASED TB TRANSMISSION RISK RESULTING FROM GLOBAL WARMING

Nardell EA¹, Mishra H², Nathavitharana R³, Sampson AJ², Theron G². ¹Brigham & Women's Hospital, Boston, MA, USA; ²Stellenbosch University, South Africa; ³Beth Israel Deaconess Medical Center, Boston, MA, USA.

BACKGROUND

Climate change has resulted in a steep increase in air conditioner (AC) use. In India, for example, between 2010 and 2015, ductless AC sales tripled. Ductless (split system) AC cools and dehumidifies but provides no outside air exchange. Moreover, for efficient AC use windows must be closed. We demonstrated the effect of ductless AC on *rebreathed air fraction* as estimated by ambient CO₂ measurements in an occupied room before and after turning on ductless AC and closing the windows.

DESIGN/METHODS



5 volunteers occupied an administrative office for the 1st and 3rd hour of a 3-hour study while CO₂ was monitored in the center of the room (Figure 1, left).

Phase 1 – office occupied, window open, AC off;

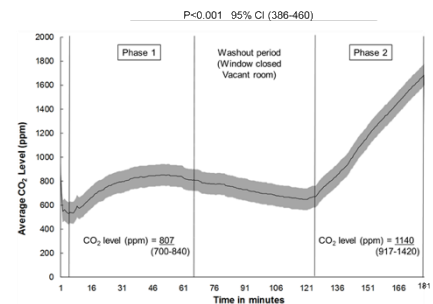
Washout period– room empty, window closed

Phase 2 - office occupied, AC on, window closed.

The study was repeated 3 times.

RESULTS

CO₂ levels rose (Figure 2, right) from just under 600 ppm to just over 800 ppm with the window open. After an hour where levels returned to baseline in the empty room, CO₂ levels soared when the room was again occupied with the AC on, but the window closed, reaching 1420 ppm at the end of the hour without signs of plateauing.



CONCLUSION

Ductless AC is saving lives from heat exhaustion, but also ocultly increases the risk of airborne infection due to closed windows and resulting increased rebreathed air fraction – in this case approximately doubling ambient CO₂ during just a 1-hour observation period. Adding germicidal UV air disinfection is one viable solution.

C10. YIELD OF TUBERCULOSIS (TB) CONTACT INVESTIGATION (CI) PROGRAM IN CAMBODIA

Quan AM¹, Song N², Eang C², Zwerling A¹. ¹School of Epidemiology and Public Health, University of Ottawa, ON, Canada; ²FHI 360, Cambodia.

BACKGROUND

Cambodia experiences a 326/100,000 TB incidence more than a third of TB cases remain undiagnosed. Traditional approaches, such as passive case-finding, have failed to illicit the desired impact on long-term TB incidence. We reported the yield of cases diagnosed through a USAID funded Challenge TB (CTB) program to improve and promote CI in Cambodia.

DESIGN/METHODS

From January 1st 2016- December 31st 2017, CTB supported the National TB program's CI program where close contacts of known TB index cases were screened to identify presumptive TB patients. CTB supported travel and training for health centre (HC) staff and village health support groups. Diagnostics were completed by HC staff through sputum collection, GeneXpert where available, and CXR.

RESULTS

Among the 2334 index cases identified, 45,463 contacts were found, of which 38,948 (86%) underwent screening. 10,708 (27%) symptomatic individuals were identified, 1,813 (17%) TB diagnoses were made. Only 293 (16%) had bacteriologically-confirmed (smear positive) TB, the remaining 1,520 individuals were diagnosed using CXR and clinical evaluation. The program's overall number needed to screen (NNS) to find one person with any form of TB was 22. NNS to find a single bacteriologically-confirmed pulmonary TB case was 133.

CONCLUSION

Our findings suggest that systematic screening of index cases' close contacts followed by geneXpert or smear microscopy and CXR is feasible. When using more inclusive parameters, our NNS of 22 was relatively low compared to other reported ACF methods. The majority of individuals were clinically diagnosed and there is a risk of over diagnoses and overtreatment.

Table 1: CI program results by year, age and diagnoses type

Results by year:	Age group	# of household and neighbour contacts	# of screened household and neighbour contacts	# of symptomatic ¹ contacts	# of BK+ bacterially confirmed TB cases	# of BK-clinically diagnosed TB cases	All Ages	
							BK+ Dx	BK-/Clinical Dx
2016	<15 years of age	5692	4801 (84%)	1071 (22%)	9	191	49	295
	>15 years of age	9300	7078 (76%)	2053 (29%)	40	104		
2017	<15 years of age	10546	9713 (92%)	2385 (25%)	7	622	244	1225
	>15 years of age	19925	17356 (87%)	5199 (30%)	237	603		

C11. YIELD OF SEMI ACTIVE CASE FINDING (SACF) FOR TUBERCULOSIS IN CAMBODIA

Quan AM¹, Song N², Eang C², Zwerling A¹. ¹University of Ottawa, Ottawa, ON, Canada; ²CENAT, Cambodia.

BACKGROUND

TB prevalence rate among the elderly in Cambodia is three times higher than that of the general population, proactive screening strategies targeting this high-risk group could be optimal and urgently require evidence to support national scale up. We reported the yield of cases found through a USAID funded Challenge TB (CTB) SACF program that targeted the elderly population.

DESIGN/METHODS

From January 1st 2016 to December 31st 2017, CTB supported National TB Program's SACF program that targeted the elderly population visiting pagodas or mosques on pre-determined holy days. CTB supported travel and training of health centre (HC) staff and village health support groups so they could conduct TB screening and TB education activities at the pagodas and mosques.

RESULTS

TB was diagnosed in 943 (7%) of the 13,809 symptomatic individuals identified through the screening program. Overall, 755 (80%) individuals had smear-positive TB, and an additional 181 individuals were diagnosed using CXR and clinical evaluation. The program's overall number needed to screen (NNS) to find one person with any form of TB was 25. NNS to find a single bacteriologically-positive pulmonary TB case was 31.

CONCLUSION

Our findings suggest that systematic screening of a high-risk group followed by GeneXpert smear microscopy and Xpert or CXR is feasible. NNS to identify one smear-positive case of 31 is relatively lower compared to other reported ACF methods in Cambodia. Lower risk of overdiagnoses and overtreatment since many cases were bacteriologically confirmed.

Table 1: SACF program results by year

	# of participants	# of TB suspects ¹	# of BK+ bacterially confirmed TB cases	# of BK- clinically diagnosed ² TB cases	Total # of TB diagnoses
2016	8796	524 (6%)	97 (75%)	30 (25%)	130
2017	14554	8565 (59%)	658 (81%)	151 (19%)	813

C12. EVOLUTION OF THE INFECTION CONTROL IN HAITI'S FACILITIES

Richard M¹, Valesco ML². ¹National TB Program (NTP); ²La Direction Sanitaire du Sud-Est (DSSE), Haiti.

BACKGROUND

Though Haiti has the Highest HIV prevalence, TB incidence and coinfection TB/ HIV rate in the Caribbean Infection control measures were unknown until the 2010 earthquake; with CDC support to the Haiti's NTP, infection control interventions were assessed, and local professionals were trained to continue the process; what permit to the NTP to start by 2015 to implement these measures in the country. Since then, very few are known about this implementation, to appreciate the progress, the NTP decided to evaluate implementation in July 2018.

METHOD

A validated and approved questionnaire was submitted and filled out by the 268 TB facilities of the country; questions were grouped into administrative, environmental and individual protection measures; forms were collected by and sent to central level for data entry and analysis with epi info 3.5

RESULTS

Over 268 sites, 165 complete the form, 97 have a functional committee, 78 have already implemented at least all the administrative interventions, 59 administrative and regularly individual protection, 38 facilities rehabilitated or rebuilt improve ventilation; 23 use UVGI to compensate poor ventilation; 5 report the result of their own yearly staff evaluation for infection control. Private, High volume, non for profit, were more likely to implement the 3 measures.

CONCLUSION

Despite a lot challenges, infection control have been implemented and expanded to the country, but a lot efforts are needed improve the extension to support response to end TB by 2050 in the island.

C13. ESTIMATING PROBABILITY OF DIRECT TRANSMISSION BETWEEN TUBERCULOSIS PATIENTS USING SPATIAL, DEMOGRAPHIC, AND CLINICAL CHARACTERISTICS

Van Ness S¹, Lee R², Horsburgh, Jr. CR³, Sebastiani P¹, Jenkins HE¹, White LF¹. ¹Boston University Department of Biostatistics; ²Harvard T.H. Chan School of Public Health; ³Boston University School of Public Health Department of Epidemiology, Boston, MA, USA.

BACKGROUND

Serial interval estimation (time between symptom onset in primary and secondary cases) is important to understand infectious disease dynamics but requires linking direct transmission cases, which is harder for tuberculosis than other diseases. We aimed to develop a model to predict direct transmission between pairs of cases.

DESIGN/METHODS

We used a subset of cases with genetic and contact tracing data to develop a gold standard of transmission events. We built a model to estimate the direct transmission probability using a Bayesian classification method with demographic, spatial and social risk factor data, using the gold standard dataset to identify predictors of transmission. Through simulations, we assessed three different approaches to defining links: true transmission, a 2-SNP threshold, and a 2-SNP threshold plus confirmed contact.

RESULTS

In simulation assuming the gold standard is the truth, the area under the curve (AUC) was 88% (standard deviation 2.7) using informative covariates, compared to 67% (1.7) with random covariates. Additionally, 28% (3.8) of the time, the true infector had the highest probability (versus 5.6% [2.3] with random covariates). Using SNP threshold with confirmed contact, the AUC was 86% (3.3) and the true infector had the highest probability 27% (4.6) of the time. With only SNP threshold, the AUC and percentage correct were 85% (3.7) and 23% (4.8) respectively.

CONCLUSIONS

This is a novel way to infer transmission in any dataset with a subset of cases with rich contact tracing and/or genetic data. The estimated probabilities could be used for serial interval estimation and inferring potential transmission trees.

C14. EVALUATION OF TUBERCULOSIS (TB) INFECTION PREVENTION AND CONTROL MEASURES WITHIN TB CLINICS IN GUYANA 2017

Williams R, Mohanlall J, Khan D. National Tuberculosis Programme, Ministry of Public Health, Guyana.

BACKGROUND

Prevention and control measure implemented in healthcare facilities forms part of an active method to reduce the spread of diseases. In Guyana, Tuberculosis (TB) is an infectious disease with public health relevance, and as such, it is essential to have adequate TB control and prevention measures in place. Therefore, this study reviewed relevant data that provide a clearer understanding of TB control measures within the TB clinics in 2017.

METHOD

Data retrieved for further evaluation from the Tuberculosis risk assessment checklist provided by the Standards and Technical services department to monitor Tuberculosis prevention and control measures within the TB clinics in Guyana based on the World Health Organisation (WHO) guidelines. In 2017, TB control and prevention risk assessment visits were conducted per quarters to all of the TB clinics within all ten administrative regions. However, for this study a selection of one site per region was reviewed.

RESULTS

Of the ten TB clinics included in this study, the notable findings were as followed: For Managerial control, all ten clinics failed to meet the specified requirements. Also, six clinics meet the administrative control requirements. Five of the ten meet most of the environmental control measures and seven sites meet the personal protective and equipment (PPE) requirements.

CONCLUSION

It was noted that there is room for improvement in the implementation of TB control and prevention measures within the healthcare setting. However, strategic planning and effort must be put in place to improve managerial control at all sites.

D. LTBI

D1. **CONNECTIONS, CONTENT, AND CONVERSATIONS: COMMUNICATING CDC'S UPDATED LATENT TB INFECTION TREATMENT RECOMMENDATIONS**

Allen L, Bowman S, Parmer J, Sera-Josef C, Sessions M, Yadav C. U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

In June 2018, the U.S. Centers for Disease Control and Prevention (CDC) released updated recommendations for the use of once-weekly isoniazid-rifapentine for 12 weeks for the treatment of latent tuberculosis (TB) infection (3HP). 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 patient education materials in multiple languages that state and local health departments could co-brand. CDC also updated and re-launched existing web content and materials to ensure consistent guidance and messages.

RESULTS AND LESSONS LEARNED

In the two months following publication of the recommendation and supporting materials, visits to the patient education materials webpage and downloads of the patient brochure more than doubled. All updated webpages saw an increase in visits, including over 17,000 unique visits to the latent TB infection treatment regimens page. Engaging content on Twitter and Facebook also helped drive traffic to CDC resources. Proactive outreach strategies led to articles in both traditional and partner publications.

CONCLUSIONS AND KEY RECOMMENDATIONS

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

D2. **HOW LABOUR INTENSIVE IS LATENT TB MANAGEMENT? USING TIME AND MOTION STUDIES TO ESTIMATE LABOUR NEEDS FOR LTBI SCALE-UP**

Alsdurf H¹, Oxlade O², Menzies D², ACT4 Trial team. ¹McGill University, Epidemiology; ²McGill International TB Centre, McGill University, Montreal, QC, Canada.

BACKGROUND:

Time and motion (TAM) studies have been used to precisely quantify the time required for specific work activities, such as assembly line workers. We have used TAMs in a novel way: to quantify the increase in healthcare workers (HCW) time spent on management of latent tuberculosis infection (LTBI) following LTBI program strengthening and expansion (ACT4 Trial).

INTERVENTION/RESPONSE:

HCW involved in TB care at the 24 ACT4 health facilities were invited to participate. Those who agreed were followed for a full work day, noting each of their daily activities, which were quantified into pre-determined categories such as LTBI services. To assess changes in their workload, HCW were followed before and after the intervention. Based on the number TB patients treated at ACT4 facilities, increased time on LTBI was extrapolated regionally to estimate total work-force time required for LTBI program scale-up.

RESULTS AND LESSONS LEARNED:

A total of 140 HCW in five countries participated in the baseline TAM (before LTBI program strengthening). Data was available for 69 of these HCW after the intervention was implemented. For these workers there was a 7% increase in the proportion of time, corresponding to an additional 30 minutes per work day, spent on LTBI-related activities at intervention sites on average.

CONCLUSIONS AND KEY RECOMMENDATIONS:

We found that there has been a significant increase in the proportion of HCW time spent on LTBI-related activities in ACT4 intervention sites. Expressed per TB patient - this increased workload can be extrapolated to estimate workforce requirements following similar LTBI programme strengthening and expansion in other settings.

Table 1: Comparison of the mean change in percent of HCW¹ time spent on all LTBI-related activities by type of site

		Phase 1	Phase 2	Mean Change	Difference in Change	
Type of Site	N	Mean Percent of Time	Mean Percent of Time	Δ Percent of Time (Phase 2 – Phase 1)	Δ Change in Percent of Time (Intervention – Control)	P-value
Intervention	(29)	18%	25%	7% (-48%, 59%)	11% (1%, 23%)	0.05
Control	(40)	22%	18%	-4% (-95%, 61%)		

¹Data presented for HCW who participated in TAMs during both Phase 1 and Phase 2

D3. IMPROVING THE LATENT TUBERCULOSIS CASCADE OF CARE FOR HOUSEHOLD CONTACTS THROUGH PARTICIPATION IN THE ACT4 STUDY: EXPERIENCES AT THE CALGARY TUBERCULOSIS CLINIC

Bedingfield N¹, Fisher D¹, Oxlade O², Valiquette C², Fregonese F², Menzies D². ¹University of Calgary, Calgary, AB; ²McGill International TB Centre, Montreal, QC, Canada.

BACKGROUND

The ACT4 trial is an international pragmatic cluster randomized trial directed at evaluating and strengthening the latent tuberculosis infection (LTBI) cascade of care amongst household contacts of individuals with infectious TB. The Calgary TB Clinic is a participating site, serving a predominantly foreign-born population.

INTERVENTION/RESPONSE

Baseline assessment consisted of quantitative evaluation of the LTBI cascade over 6-months (using pre-existing registries) and questionnaires on barriers administered to patients and health care providers. Registry analysis showed 130 household contacts were identified for 32 infectious patients, 43 of whom initiated LTBI Treatment (LTBIT) for a ratio of 1.3 contacts initiating LTBIT/patient. Significant losses in the pathway occurred at Mantoux assessment and physician LTBIT recommendation. From 37 questionnaires, convenience and communication were identified as important patient barriers to retention in care. Four solutions were implemented in Fall 2017: evening clinics, a nursing education session, prescribing guidelines, and a patient education pamphlet.

RESULTS

Post-implementation registry assessment is ongoing and reported to staff and management quarterly. In quarter 1 there was a 1.6-fold increase in patient volume, and only 16 LTBIT initiations per 25 infectious patients (ratio:0.64). Quarters 2 and 3 showed improvement over baseline with 13 contacts initiating LTBIT for 9 infectious patients (ratio:1.44), and 25 contacts initiating LTBIT for 15 infectious patients (ratio:1.67). Process evaluation revealed that pamphlet usage was poor, evening clinics were popular amongst contacts, and solutions directed at provider practice change required reinforcement.

CONCLUSION

Successful health services solutions require continual monitoring, refinement and long term collaboration between TB programs and researchers.

D4. **LATENT TUBERCULOSIS PREVENTIVE THERAPY OUTCOMES AMONG END-STAGE KIDNEY DISEASE PATIENTS**

Chiang L^{1*}, Kumar D^{2*}, Romanowski K¹, Levin A^{3,4,5}, Djurdjev O⁶, Morshed M^{1,7}, Sekirov I^{1,7}, Cook VJ^{1,2}, Johnston J^{1,2}. ¹British Columbia Centre for Disease Control; ²Department of Medicine, University of British Columbia; ³Department of Medicine, Division of Nephrology, University of British Columbia; ⁴British Columbia Provincial Renal Agency; ⁵Centre for Health Evaluation and Outcomes Research, St. Paul's Hospital; ⁶Department of Measurement and Reporting, Provincial Health Service Authority; ⁷Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada.

*Co-first authors.

BACKGROUND

Chronic kidney disease (CKD) is an established risk factor for active tuberculosis (TB). While systematic screening and treatment of latent TB infection (LTBI) is strongly recommended among this population, the medical complexity of CKD patients may preclude the use of LTBI therapy. In this study, we aimed to investigate the outcomes of end-stage kidney disease (ESKD) dialysis patients in British Columbia (BC), Canada.

DESIGN/METHODS

We identified ESKD patients in the BC Provincial Renal Agency (BCPRA) database that started dialysis between Jan. 1, 2001 – Mar. 31, 2017 and linked associated LTBI treatment data from the BC Centre for Disease Control (BCCDC) TB database. Treatment outcomes, occurrences of adverse events (AEs), and deaths during course of treatment, were assessed through retrospective chart review.

RESULTS

A total of 272 dialysis patients were prescribed LTBI therapy; 199 (73.2%) were hemodialysis (HD) patients, 175 (64.3%) were male, and 191 (70.3%) were from medium to high incidence TB countries. The median age was 65 (IQR 56-73). Overall, 214 (78.7%) completed LTBI therapy. At least one AE was identified in 102 (37.5%) patients. One (0.4%) patient was hospitalized due to an AE, while 16 (15.7%) required drug discontinuation. No deaths were associated with LTBI therapy. Out of the 102 patients that experienced AEs, 74 (72.6%) completed LTBI therapy.

CONCLUSION

Through close outpatient monitoring, the majority of ESKD patients in this cohort were able to safely tolerate and complete LTBI therapy. Notably, the treatment completion rate of this cohort remained relatively high despite challenges associated with therapy.

D5. REPEATABILITY OF T-SPOT IN SPLIT SAMPLES UNDER IDENTICAL CONDITIONS

Feng P¹, Wu Y², Cattamanchi A³, Chen M¹, Katz D¹, Ayers T¹ for the CDC Tuberculosis Epidemiological Studies Consortium (TBESC). ¹Centers for Disease Control and Prevention; ²Northrop Grumman, Atlanta, GA; ³University of California San Francisco, San Francisco, CA, USA.

BACKGROUND

The T-SPOT[®].TB test (T-SPOT), an interferon-gamma release assay, quantifies T cell responses, as spot counts, to *Mycobacterium tuberculosis* antigens for latent tuberculosis infection (LTBI). To date, no studies, outside of the manufacturer, have assessed its repeatability to help guide clinical practice.

DESIGN/METHODS

Immunocompetent persons ≥ 15 years old at high risk for LTBI or progression to TB disease were enrolled at local health department TB clinics in 10 states. A single blood draw from each participant was split into two samples that were processed simultaneously at a central laboratory. Spot counts of ≥ 8 were considered positive. We assessed agreement with percent concordance and Cohen's kappa with 95% confidence intervals (CI) for dichotomous results; and Lin's concordance correlation coefficient (CCC) with 95% CI and Bland-Altman plots for continuous results.

RESULTS

Of the 538 pairs, 93% (502/538) were concordant ($\kappa=0.79$, 95% CI=0.73, 0.86); 90 (17%) were positive by both samples and 412 (76%) were negative by both; and 36 (7%) were discordant. Ninety-one percent (487/538) had continuous results. The median absolute difference in spot counts among concordant pairs was 1 (IQR=1–3) and 8 (IQR=6–14) among discordant pairs. Overall, the CCC was 0.81 (95% CI=0.77, 0.83). The Bland-Altman plots showed an increase in absolute difference as the average number of spots increased.

CONCLUSIONS

Because all other factors were held constant, these results reflect the inherent variability of the T-SPOT. Although the discordance is relatively low, clinicians should be aware that the interpretation of samples with counts near 8 spots could change if repeated.

D6. **ISONIAZID PREVENTIVE THERAPY PROTECTS AGAINST TUBERCULOSIS AMONG HOUSEHOLD CONTACTS OF ISONIAZID-RESISTANT PATIENTS**

Huang CC^{1,2}, Becerra MC², Grandjean L³, Lecca ML⁴, Calderón R⁴, Contreras C⁴, Yacato R⁴, Galea J⁵, Zhang Z², Murray M¹. ¹Harvard Medical School, Department of Global Health and Social Medicine; ²Brigham and Women's Hospital, Boston, MA, USA; ³ Wellcome Centre for Clinical Tropical Medicine, Imperial College London, London, United Kingdom; ⁴Socios En Salud, Lima, Peru; ⁵School of Social Work, University of South Florida, Tampa, FL, USA.

BACKGROUND

WHO recommends the use of isoniazid (INH) only, or INH and rifapentine therapy, to treat latent tuberculosis infection (LTBI) in group with high risk of tuberculosis progression. The recent rise of INH and multi-drug resistant (MDR) tuberculosis has complicated the choice of LTBI treatment regimen. We examine the risk of disease progression of household contacts (HHCs) exposed to sensitive, INH-resistant, or MDR tuberculosis who received INH as part of routine tuberculosis management.

DESIGN/METHODS

Of a 36-month recruitment period in Lima, Peru, we enrolled 4,500 index tuberculosis patients and their 14,044 HHCs. We measured the incident tuberculosis of the HHCs over a one-year follow-up. HHCs were offered INH preventive therapy (IPT) if they were ≤ 19 years-old. We used a Cox frailty proportional hazards model to evaluate whether the effect of IPT on tuberculosis progression varied by the resistance profile of the index case. We repeated the analyses in a second independent dataset.

RESULTS

Among 4,216 under 19 years of age, 2,106 HHCs (50%) initiated IPT at enrollment. We found that the protective effect of INH against tuberculosis progression was stronger in HHCs exposed to drug-sensitive (HR[95%CI]=0.2[0.20-0.50]) or MDR-TB (0.26[0.08-0.77]) than in those exposed to mono-INH-resistant (0.80[0.23 to 2.79]). In the second independent dataset, we found that none (0/76) of MDR-TB exposed HHCs who received IPT developed tuberculosis, compared to 3%(8/273) of those who did not received IPT.

CONCLUSION

We found that IPT protected against TB among contacts of MDR-TB patients. This finding suggests that INH may have role in the management of MDR-LTBI.

D7. EVOLVING APPROACHES TO REDUCE THE RESERVOIR OF MYCOBACTERIUM TUBERCULOSIS AT AN ACADEMIC MEDICAL CENTER

Talbot E^{1,2}, Moir W², Boyle P³, Dube M³, Leeman H², McLellan R¹. ¹Dartmouth College, Hanover; ²New Hampshire Department of Health and Human Services, Concord; ³Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA.

BACKGROUND

U.S. healthcare institutions offer treatment to health care workers (HCW) with a history of positive latent tuberculosis infections (LTBI) testing, but uptake is poor. Institutions then enroll these HCW into surveillance programs that administer an annual TB symptom screen questionnaire, which also typically have low response rates and infrequently yield clinically actionable information. We attempted to resolve the LTBI status of HCWs in the LTBI surveillance program at a large academic medical center.

INTERVENTION

We analyzed the LTBI surveillance program dataset to identify the subset of HCWs with no record of completing treatment. We emailed a link to a web-based survey to offer free confirmatory testing and treatment. Trained staff contacted each respondent to facilitate the intervention cascade.

RESULTS

219 (49%) of 444 HCWs responded to the questionnaire: 94 (43%) reported having completed treatment for LTBI or active tuberculosis and 35 (16%) declined confirmatory testing or treatment. To date, 55 (25%) have requested confirmatory testing, of which 12 completed: 10 were negative and two positive. The two employees with positive confirmatory testing have been offered treatment, with one accepting and one undecided.

CONCLUSION

Preliminary results of this quality project indicate that web-based surveys, confirmatory testing and personalized outreach are effective and easily implemented to manage the reservoir of LTBI at an academic medical center. We recommend this approach as more useful than the traditional but low impact annual symptom screens.

D8. UNDERSTANDING PATIENT ATTRITION IN THE LATENT TB INFECTION CASCADE OF CARE AMONG HOUSEHOLD CONTACTS OF PULMONARY TB PATIENTS

Paulsen C¹, Long R¹, Oxlade O², Fregonese F², Valiquette C², Menzies D². ¹University of Alberta, Edmonton, AB; ²McGill University, Montreal, QC, Canada.

BACKGROUND

Research to improve the impact of latent TB infection (LTBI) treatment has focused predominantly on improving adherence. However, there are many steps prior to the initiation of treatment where patients are lost. This study aimed to identify barriers limiting LTBI diagnosis and treatment initiation among close household contacts of pulmonary TB cases.

DESIGN/METHODS

LTBI cascade of care indicators were collected retrospectively for household contacts of all microbiologically confirmed pulmonary TB cases diagnosed from January–October 2017 at the Edmonton TB Clinic. Indicators included: contact identification, screening, medical assessment, and offer of treatment. Standardized questionnaires were administered to 10 healthcare workers, 10 index cases, and 17 adult household contacts from June–August 2018. Questionnaires captured TB knowledge, attitudes and barriers to LTBI diagnosis and treatment.

RESULTS

A complete assessment and initiation of appropriate treatment occurred in 86% of close household contacts (104/121). Greatest losses occurred at initial screening (6) and initiation of treatment (8). Questionnaires indicate patients are satisfied with and trust the clinic, with 70% (19/27) reporting no improvements needed. Those with recommendations for improvement suggested appointment reminders, better translation services, and more home care options. Staff echoed the need for multilingual educational material, in addition to shorter-course regimens, and extended clinic hours.

CONCLUSION

Losses were identified at different stages in the LTBI cascade of care. Next steps will be implementation of targeted activities to improve patient outcomes. These include: expanded information sheets in multiple languages; text-message appointment reminders; and promotion of shorter-course regimens. Continued evaluation of the cascade of care is ongoing.

D9. **INCREASING LATENT TUBERCULOSIS INFECTION TESTING AND TREATMENT IN IMPERIAL COUNTY, CALIFORNIA: BASELINE ASSESSMENT AT A LOCAL COMMUNITY CLINIC**

Schmitt M^{1,2}, Shah N³, Asfaha S³, Kriner P², Baig A⁴, Perez H⁴, Mochizuki T³. ¹University of Arizona, Tucson, AZ; ²Imperial County Public Health Department, El Centro; ³California Department of Public Health, Richmond; ⁴Clinicas de Salud del Pueblo, Brawley, CA, USA.

BACKGROUND

Imperial County(IC), California has the highest rate of tuberculosis(TB) in the state at 21.2/100,000(CDPH, 2018). California is scaling up latent tuberculosis infection(LTBI) testing and treatment in community settings to prevent TB disease.

INTERVENTION

A clinic in IC serving a high-risk population was chosen. Providers completed a Likert-scale survey, 1(strongly disagree) to 7(strongly agree), to identify barriers and facilitators in LTBI care. Patient charts were abstracted to understand current LTBI practices from screening to testing and treatment; data was entered into RedCap and analyzed using Stata.

RESULTS

Five of 10(50%) providers completed the survey. Providers reported a low level of comfort with short-course regimens for treating LTBI(median=3) and reported there was not adequate time during visits to address LTBI(median=4). All reported improving LTBI care was a clinic priority(median=7). Of 142 charts abstracted, 103(73%) were adults and 39(27%) were pediatric patients. Median age was 42(range 0-87); 131(92%) identified as Hispanic/Latino; 84(59%) spoke Spanish as their primary language. Among Hispanic/Latino patients, 13(14%) adult and 21(58%) pediatric patients were tested for LTBI. Of those tested, 7(19%) had a positive result and all had a chest x-ray to rule-out TB. Of those with a positive result, 5(71%) started treatment with isoniazid; one completed and three were still on treatment.

CONCLUSION

There are opportunities to increase LTBI testing and expand treatment. Further understanding of barriers to adult testing is needed. Next steps include educational trainings for providers and staff and a patient awareness campaign. Follow-up data abstraction will be conducted and expansion to other clinics is being considered.

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D10. **TESTING AND TREATMENT FOR LATENT TUBERCULOSIS INFECTION IN CORRECTIONAL SERVICES CANADA**

Varsaneux O, Smith JM, Sarkesh S, Kom EA, Ma K. Clinical Services and Public Health Branch, Health Services Sector, Correctional Services Canada, Ottawa, ON, Canada.

BACKGROUND

Testing and treatment for Latent Tuberculosis Infection (LTBI) among federal inmates is a significant public health initiative in order to prevent the ongoing transmission of *M.TB* in this closed environment. Inmates with a positive tuberculin skin-test (TST) are offered an interferon-gamma release assay (IGRA) and are referred to medical specialists for treatment.

METHODS

IGRA results were extracted from electronic medical records and reviewed for differences across gender, region, and Aboriginal status and linked to LTBI treatment starts to examine the role of IGRA in treatment recommendations.

RESULTS

There were 1606 IGRA results returned, of which 25% (n=411) were positive and 73.5% (n=1181) were negative (n=16 were indeterminate). IGRA results did not differ by gender (IGRA positive: male, 25%, female 27%; OR 1.1, 95%CI 0.75-1.65) or Aboriginal status (IGRA positive: non-Aboriginal, 25%, Aboriginal 30%; OR 1.25 95%CI 0.93-1.69). Between April 2014 – March 2018, there were 444 treatment starts for LTBI (n=143 were IGRA positive, n=12 were IGRA negative or indeterminate, and n=289 had no IGRA information). Since 2013, 185 inmates with positive IGRA results were not treated for LTBI.

CONCLUSION

IGRA testing can more accurately identify patients with true infection with *M.TB*. Focussing treatment efforts on those most likely to have latent infection prevents progression to active disease and decreases potential transmission.

D11. A PLAN TO SCREEN ALL MARSHALLESE IN ARKANSAS FOR TUBERCULOSIS: PROGRESS, CHALLENGES, AND OPPORTUNITIES

Sonaty GT¹, Adolph SS², Patil N^{1,2}, Hainline Williams S³, Mukasa L^{1,2}. ¹University of Arkansas for Medical Sciences; ²Arkansas Department of Health, Little Rock; ³Arkansas Department of Health Bates Outreach Clinic, Springdale, AR, USA.

BACKGROUND AND PROBLEM

Community-based screening for latent tuberculosis infection (LTBI) has emerged as a strategy to help end tuberculosis (TB) in hard-to-reach populations in low-incidence regions. Since 1986, 8,000-15,000 people from the Republic of the Marshall Islands have moved to Northwest Arkansas. Ongoing TB transmission has been reported among them, with outbreaks in 2004 and 2014. Arkansas Department of Health committed in 2014 to screen all Marshallese for LTBI, regardless of ability to pay. An outreach clinic was established including Marshallese staff, and door-to-door screening was conducted. The objective of this assessment was to describe program progress and identify implementation barriers.

RESPONSE

Sequential explanatory design was used: analysis of program monitoring data informed semi-structured interviews and unstructured observations, conducted in Springdale, AR throughout summer 2018. Key informants included program participants, staff, and community leaders. Content and thematic analysis was used for qualitative data.

RESULTS AND LESSONS LEARNED

From January 2014 through July 2018, 2,079 (13.9-26.0%) Marshallese were reached for LTBI screening; 1,999 (13.3-25.0%) had valid test results; of those, 341 (17.1%) were positive; of those, 335 (98.3%) initiated treatment and 292 (87.2%) completed treatment. Five of 17 neighborhoods had <10 people screened per TB case. Interviews and observations revealed that cultural norms, stigma, limited knowledge of services, frequent relocation, and logistical factors slowed screening.

CONCLUSIONS AND KEY RECOMMENDATIONS

Active LTBI screening in the community has helped reach a marginalized population, but many are still missed by TB prevention efforts. A community-based TB advisory board should be formed to help develop strategies that can reach the rest of the Marshallese in Arkansas.

D12. **PERFORMANCE OF QUANTIFERON TB GOLD PLUS (QFT PLUS) IN A PUBLIC HEALTH SETTING, KING COUNTY, WASHINGTON**

Sorri Y, Narita M. Seattle-King County Public Health, Seattle, WA, USA.

BACKGROUND

In June 2017, the U.S. FDA approved the use of QFT Plus for detecting latent tuberculosis infection (LTBI). Public Health – Seattle & King County switched from QFT GIT to QFT Plus in November 2017. We examined the performance of QFT Plus on the cohort of patients who were evaluated at the TB Clinic and the Refugee Clinic.

METHODS

Data that was collected on patients who had a QFT Plus test through the TB Clinic and the Refugee Clinic from November 2017 through September 2018 was used. The cohort includes refugees, asylees, close contacts and class B1. Among the positive QFT Plus, discordance between TB1-nil and TB2-nil is defined as only one of the two is ≥ 0.35 and the other being < 0.35 .

RESULT

Of the 1523 patients tested, 314 (20.6%) were QFT-Plus positive, 1199 (78.7%) negative and 11 (0.8%) indeterminate. Of 314 positive results, 281 (90%) were both TB1 – nil and TB2-nil ≥ 0.35 (“concordant”), and 34 were discordant; 15 were TB1+/TB2- and 19 were TB1-/TB2+. There was a strong agreement between TB1 and TB 2 ($\kappa=0.88$, $P<0.0001$). The odds of being positive by QFT Plus was significantly higher for male gender (OR 1.4, 1.12-1.86, $P <0.004$), Class B1 (OR5.7, 4.1-7.9, <0.0001) and household contact (OR 2.9, 1.7-5.0, $P<0.0001$).Among positive results with differences between TB2 and TB1 >0.6 IU, Class B1 (OR 5.5, 2.8-10.6, $P <0.001$) and household contacts (OR 3.0, 1.0-8.7, $P=0.05$) are significantly associated with a greater TB2 response.

CONCLUSION

The difference between TB2 and TB1 which is currently being used in some articles to estimate the CD8+ activation, is associated with Class B1 and household contacts indicating group of individuals that are at higher risk of progression to active TB.

D13. **FACTORING PREVIOUS TREATMENT INTO ESTIMATES OF TUBERCULOSIS INFECTION PREVALENCE, UNITED STATES, 2011-2012**

Vonnahme LA, Haddad MH, Navin TR. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

National Health and Nutrition Examination Survey (NHANES) point estimates suggest 13.3-14.1 million persons in the United States have latent tuberculosis infection (LTBI). These estimates, however, do not adjust for persons previously treated for tuberculosis (TB) disease or LTBI, and thus, who might not require treatment. We used treatment history to refine national estimates of persons with untreated LTBI.

DESIGN/METHODS

Using a complex survey design analysis of 2011-2012 NHANES data, we ascertained the prevalence of self-reported previous treatment for TB disease or LTBI among persons with a current positive test for *Mycobacterium tuberculosis* infection (i.e., tuberculin skin test ≥ 10 mm or positive interferon-gamma release assay). We stratified results by nativity (U.S.-born vs. non-U.S.-born).

RESULTS

Among NHANES participants with a positive test, a weighted 11.9% (95% CI: 8.5%–15.3%), corresponding to 2.4 million in the U.S. population, reported prior treatment for TB disease or LTBI. Among U.S.-born persons with a positive test, 12.7% (7.5%–17.9%), or 1.2 million persons, reported prior treatment for TB disease or LTBI. Similarly, 11.3% (8.0%–14.5%) of non-U.S.-born, or 1.1 million persons, reported prior LTBI treatment for TB disease or LTBI.

CONCLUSION

To reflect untreated LTBI, previous point estimates of LTBI prevalence may need to be reduced by approximately 12%, to 10.8-12.0 million, to reflect the number of persons with LTBI who require treatment for the condition. Prevalence of prior treatment did not differ by nativity, emphasizing the need to implement current guidelines to increase screening and treatment for LTBI among persons born in countries with higher TB burdens.

Poster Session 2

A. PEDIATRICS

A1. **THE IMPACT OF INTERFERON GAMMA RELEASE ASSAY TESTING (IGRA) IN A PEDIATRIC CLINIC IN MANITOBA**

Barbari MA, Consunji-Araneta R. Children's Hospital of Winnipeg, Winnipeg, MB, Canada.

BACKGROUND

Majority of referred tuberculosis (TB) contacts had BCG vaccine administered at birth. A positive tuberculin skin test (PPD) could represent TB infection versus a vaccine related reaction.

The interferon gamma release assay (IGRA) is a surrogate marker of TB infection and is more specific than PPD in BCG vaccinated populations. The Canadian TB Standards recommends IGRA testing for people who received BCG after infancy.

DESIGN/METHODS

We tabulated demographic, epidemiologic, immunologic, and clinical information of pediatric TB contacts (2014 -2017) and compared PPD measurements and IGRA results.

RESULTS

Forty-six of 145 patients who were referred to the clinic as TB contacts (2014-2017) and were tuberculin positive were tested with IGRA. All patients had BCG vaccine. These patients had poor compliance to isoniazid (INH) treatment, had vague exposure histories, medication intolerance, unread or unsure PPD measurements, or missed their 8-week post contact PPD tests. IGRA was done to determine their risk to develop TB disease if treatment was discontinued, or whether INH treatment was indicated.

IGRA was positive in only 12/46 IGRA tested patients. Their PPD measurements ranged from 0mm-23mm.

IGRA negative patients had PPD reportedly ranging from 0-37mm. Treatment was discontinued in the IGRA negative children.

CONCLUSION

IGRA testing provides better direction for care and improved risk stratification for disease in pediatric TB contacts who have previously been vaccinated. It eliminates the inter- and intra-reader subjective variability in PPD measurements.

A2. WINDOW PROPHYLAXIS FOR CHILDREN EXPOSED TO TUBERCULOSIS

Cruz AT, Starke JR. Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA.

BACKGROUND

Preschool-aged children exposed to adults with potentially contagious intrathoracic tuberculosis are started on monotherapy for prevention during the 'window period,' the time required for tuberculin skin tests (TSTs) or interferon- γ release assays to convert following infection. Treatment is recommended given the risk of rapid disease progression in this cohort. Our goal was to assess the proportion of exposed children who developed infection and disease, as well as to assess safety and tolerability of window prophylaxis.

DESIGN/METHODS

Retrospective cohort study of children (<5-years-old) seen in a large metropolitan pediatric tuberculosis clinic from 2007-2017 in contact with adults with suspected contagious TB (index case). Children were included if they were asymptomatic, had initial TSTs < 5mm, normal physical examinations and chest radiographs, and were started on window prophylaxis.

RESULTS

Window prophylaxis (97% isoniazid, 2% rifampin) was begun for 752 children from 12 health departments. In 41%, the index case cohabitated with the child; 68% were AFB smear-positive. Medications were received daily or twice-weekly under direct observation (DOT) in 99% for a median of 9 weeks (IQR 7-12 weeks). Adverse events (7, 0.9%) were rare; no child developed hepatotoxicity or tuberculosis disease. TST conversion was seen in 37 (4.9%) and was more common when the index case was a parent (OR 3.2, 95%CI: 1.2-8.2), but was not associated with smear or culture positivity.

CONCLUSION

Progression to infection was infrequent and unassociated with microbiological parameters. Thresholds for referral of exposed young children should be low given medication safety and difficulties with risk stratification.

A3. **INTERFERON-GAMMA RELEASE ASSAY TESTING IN CHILDREN UNDER 2 AT A US TUBERCULOSIS CLINIC**

Gaensbauer J. Denver Metro Tuberculosis Clinic/University of Colorado School of Medicine, Denver, CO, USA.

BACKGROUND

Use of interferon-gamma releasing assays (IGRAs) in children <2 may derive many of the same advantages which have led to preference over TST in older children. At the Denver Metro Tuberculosis Clinic, we have begun identifying clinical scenarios for judicious introduction of an IGRA (QuantiFERON-TB Gold (QFT)) for children <2 and sought to evaluate test performance in an initial cohort.

DESIGN/METHODS

We retrospectively analyzed tests obtained between 2012 and 2018, including specific values of antigen, mitogen and negative control, and clinical outcomes. Testing scenarios were categorized to assess test performance within the specific clinical context.

RESULTS

We analyzed 51 QFTs: 2 were positive, none indeterminate, one failed phlebotomy and the remainder were negative. Mitogen tube results were robust, and the two positives had antigen-nil results of 1.30 and 0.53. 13 patients were TST+, 12 of whom were QFT negative. QFT-tested patients were categorized into one of four clinical scenarios: BCG-vaccinated immigrant screening (12-23 months; n=26); primary care screening for travel or family origin in TB endemic countries (12-23 months; n=13); contact evaluation at any age using both IGRA and TST (n=9); and miscellaneous medical work-up (n=3). Among QFT- patients not treated for LTBI, no incident case of TB disease has been identified to date.

CONCLUSION

IGRAs appear to be a reliable tool for identifying LTBI in children <2 years old. Future research should continue to evaluate performance in this age range to maximize the TB diagnostic tool-kit for young children who are highest risk of TB disease following infection.

A4. **FACTORS ASSOCIATED WITH ACCEPTANCE AND COMPLETION OF THERAPY FOR TUBERCULOSIS INFECTION IN IMMIGRANT CHILDREN**

Lamb GS, Cruz AT, Javier M, Starke JR. Baylor College of Medicine/Texas Children's Hospital, Houston, TX, USA.

BACKGROUND

Treatment of tuberculosis infection (TBI) is recommended for children to reduce future risk of TB disease. We describe the factors associated with acceptance and completion of therapy for TBI infection among immigrant children.

METHODS

Retrospective cohort study of immigrant children (<18-years-old) with TBI managed at a children's hospital (2010-2017), evaluating association between treatment completion and demographics, TBI testing, regimen, mode of administration, immigration status, and adverse drug events (ADEs).

RESULTS

218 children were included; 211/218 (96.8%) initiated (45% 9-months isoniazid [9H], 30% isoniazid/rifapentine [3HP], and 25% 4-months rifampin [4R]) and 156/211 (73.9%) completed therapy. Completion of therapy was associated with use of 3HP, and originating from SE Asian countries. ADEs were seen in 26/211 (12.3%) and required a regimen change in 8/26 (30.8%); the most common ADEs were rash (11/26, 42.3%) or nausea/vomiting (9/26, 34.6%). No children had clinical hepatotoxicity. There was no difference in rates of ADEs when comparing regimen used. Completion of therapy was associated negatively with development of ADEs (OR: 13.89, CI: 3.20-60.25), but was not associated with type of immigration status, language preference, use of interpreters, the test of infection used to diagnose TBI, or if medications were administered with health department assistance versus entirely by the family.

CONCLUSIONS

Immigrant children have high rates of acceptance and completion of therapy for TBI. Use of 3HP and originating from SE Asia were associated with higher completion rates. Development of ADEs was associated negatively with completion of therapy.

A5. **EXPERIENCE WITH USING RAPID MOLECULAR TESTING IN DIAGNOSING PULMONARY AND EXTRA-PULMONARY PEDIATRIC TUBERCULOSIS IN A NON-ENDEMIC SETTING - A RETROSPECTIVE CASE SERIES**

Mijovic H, Al-Nasser Y, Al-Rawahi G, Roberts A. BC Children's Hospital, Vancouver, BC, Canada.

BACKGROUND

Children are more likely to present with extra-pulmonary or disseminated tuberculosis (TB). Timely and accurate diagnosis is limited in part by low microbiological detection rates and long time to positive cultures. Xpert® MTB/RIF is a rapid, automated molecular assay that has been validated for diagnosing pulmonary but not extra-pulmonary TB in children. It is not used routinely in non-endemic settings.

DESIGN/METHODS

We conducted a retrospective chart review of children diagnosed with active TB at our facility between 2015 and 2017 in order to compare performance of Xpert testing to acid-fast bacilli (AFB) stain and *Mycobacterium tuberculosis* culture on pulmonary and extra-pulmonary specimens and examine the utility of molecular testing results in diagnosis and clinical decision making. Descriptive statistics was used for analysis.

RESULTS

10 children were diagnosed with active TB, including 6 extra-pulmonary and 2 disseminated disease cases. AFB stain was positive on at least one specimen in 4/10 cases, cultures were positive in 8/10 and Xpert in 7/10 cases. Average time to positive culture was 19 days. All cases positive on Xpert were also culture positive. Xpert diagnosed TB in 4/6 of extra-pulmonary specimens submitted, including pericardial fluid, lymph node tissues and cerebrospinal fluid.

CONCLUSION

Culture and molecular testing demonstrated similar TB detection rates, albeit based on a small patient population. While cultures remain the most reliable diagnostic method, molecular testing in combination with clinical history and biochemical or histopathology markers may facilitate rapid diagnosis and treatment of pulmonary and extra-pulmonary pediatric TB in a non-endemic setting.

A6. **DIAGNOSTIC ACCURACY OF STOOL XPERT MTB/RIF FOR THE DETECTION OF ACTIVE TUBERCULOSIS IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS**

Sulis G^{1,2*}, MacLean E^{1,2*}, Schumacher SG³, Denkinger CM³, Pai M^{1,2}, Khan FA^{2,4}. ¹Department of Epidemiology, Biostatistics and Occupational Health, McGill University; ²McGill International TB Centre, McGill University, Montreal, QC, Canada; ³Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland; ⁴Respiratory Epidemiology and Clinical Research Unit, McGill University, Montreal, QC, Canada.

**these authors contributed equally*

BACKGROUND

Tuberculosis (TB) is a major cause of morbidity and mortality in children, yet its microbiological confirmation is often challenging. Xpert MTB/RIF is currently recommended as the initial diagnostic test for presumptive TB, though appropriate respiratory samples may be difficult to obtain from children. A potentially valid alternative in this population is stool, which is less invasive to collect, although standardized processing methods have not yet been defined.

METHODS

We conducted a systematic review and meta-analysis according to PRISMA guidelines to evaluate the diagnostic accuracy of stool Xpert for childhood TB against (1) a microbiological reference standard (MRF) and (2) a clinical reference standard (CRF). PubMed, EMBASE, Scopus, and Cochrane Library were searched for relevant publications from Jan 1, 2008 to June 15, 2018. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool was applied to assess the risk of bias.

RESULTS

Nine studies (involving 1681 children) were included in qualitative and quantitative synthesis. Pooled sensitivities of stool Xpert compared to MRF and CRF were 67% (95% CI: 52-79) and 22.0% (95% CI: 9-44), respectively; pooled specificities were 99% (95% CI: 98-99) and 100% (95% CI: 66-100). Stool Xpert sensitivity appeared slightly improved among HIV-infected children (pooled estimate: 79%; 95% CI: 68-87). Overall, the risk of bias was rated moderate to high.

CONCLUSION

The high false negative rate of stool Xpert versus both MRF and CRF suggests that, in its current configuration, stool Xpert is unsuitable as a screening test. An optimized stool sample preparation protocol may potentially improve the diagnostic performance.

A7. **PEDIATRIC FIXED DOSE COMBINATION ORAL FORMULATIONS FOR TUBERCULOSIS**

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

BACKGROUND

Childhood tuberculosis (TB) represents approximately 20% of the total disease burden in low-resource countries, with treatment nonadherence cited as a major barrier to the control of TB. Patient acceptability of daily treatments is critically important to effectively fight TB; however, there are few pediatric formulations of anti-TB drugs which facilitate long-term compliance. To meet the needs for suitable shelf-stable pediatric friendly oral formulations of anti-TB drugs, Luna Innovations and industry partners are working to finalize development of a fixed-dose combination (FDC) formulation that is palatable to children.

DESIGN/METHODS

Luna has created chewable troches containing WHO-recommended anti-TB drugs: Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide (PZA). These troches were made with taste-masking and stability excipients in a base of PEG 1,450. After mixing, the molten solution was poured into bear-shaped molds and allowed to cure. Drug loading and stability was evaluated with High Performance Liquid Chromatography (HPLC).

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 troche's loading efficiency. To test stability, Luna performed 3-month stability testing (ambient and 40 °C) on individual anti-TB drug-loaded troches, including INH. There was no significant correlation between INH drug quantity and time, compared to alternate FDC formulations, indicating drug stability in PEG-based troches.

CONCLUSION

PEG-based troches have been shown to maintain drug stability for up to 3 months in ambient and accelerated conditions for INH loaded troches. Work is ongoing to confirm drug stability and perform pre-clinical evaluation of FDC PEG-based troches.

A8. USE OF IGRA FOR LTBI DIAGNOSIS IN HIGH-RISK CHILDREN IN CALIFORNIA 2 YEARS AND YOUNGER

Wendorf K¹, Lowenthal P¹, Feraud J¹, Cabanting N², Ramos M². ¹Tuberculosis Control Branch, California Department of Public Health; ²Office of Refugee Health, California Department of Public Health, Richmond, CA, USA.

BACKGROUND

New guidelines support using interferon gamma release assays (IGRAs) in children 2 years and older for diagnosis of latent tuberculosis infection (LTBI). However, lack of experience with IGRAs in children <2 years, and concern that IGRAs could be less sensitive than tuberculin skin tests (TSTs) limits their use in young children. Our aim was to identify TB cases among children ≤2 years of age at high risk for TB exposure who were tested for LTBI using IGRA.

METHODS

Retrospective review of domestic TB screening data from California's Refugee Health Electronic Information System for children ≤2 years of age who immigrated to California between October 2013 and December 2016. Children screened were cross-matched with the California TB registry to identify cases of TB disease among this cohort between October 2013 and December 2018.

RESULTS

A total of 1998 children ≤2 were identified; the majority emigrated from countries with high TB incidence (>150 cases per 100,000). Half were tested with an IGRA (n=942 47%); a quarter received TSTs (n=508, 25%); 1% of children had a positive IGRA (n=10) versus 14% with a positive TST (n=70). Fifteen IGRA results were indeterminate (2%). No cases of TB disease were identified during the 3186 person years of follow-up.

CONCLUSION

IGRA positivity was less than TST positivity in high-risk children ≤2 years of age. Despite fewer LTBI diagnoses in the IGRA-tested population, no cases of TB disease among children who tested negative were identified suggesting good negative predictive value in young children.

B. MDR-TB

B1. THE COST OF MULTIDRUG-RESISTANT TUBERCULOSIS IN CANADA

Campbell JR¹, Nsengiyumva P¹, Chiang L², Khadawardi H³, Oxlade O¹, Rasberry H¹, Rea E⁴, Romanowski K², Sabur N³, Sander B⁴, Uppal A¹, Brode S^{3,4}, Johnston JC^{2,5}, Schwartzman K^{1,6}. ¹McGill International TB Centre, Montreal, QC; ²British Columbia Centre for Disease Control, Vancouver, BC; ³West Park Healthcare Centre; ⁴University of Toronto, Toronto, ON; ⁵University of British Columbia, Vancouver, BC; ⁶Montreal Chest Institute, Montreal, QC, Canada.

BACKGROUND

Multidrug-resistant tuberculosis (MDR-TB) requires prolonged treatment, expensive drugs, and close monitoring for treatment side effects. The costs of providing this care; however, are largely unknown. We estimated the health system costs for patients who completed MDR-TB treatment in British Columbia, Ontario, and Quebec, Canada.

METHODS

We chart-reviewed all MDR-TB patients who initiated treatment at the British Columbia Centre for Disease Control (Vancouver), West Park Healthcare Centre (Toronto), and Montreal Chest Institute (MCI) between January 2010 and June 2016 and subsequently completed treatment. Information regarding consumables (e.g. drugs, supplies), services, and personnel time used during diagnosis, treatment, and follow-up was extracted. Quebec costs for each item were used to estimate the total cost per MDR-TB episode in all settings. For comparison with MDR-TB, we also calculated overall costs for 30 patients treated at the MCI for drug susceptible TB (DS-TB) and latent TB infection (LTBI).

RESULTS

Forty-six MDR-TB patients were included. Mean age was 35 (SD 13.4) years, 25 patients (54%) were female, and 4 (9%) had extensively drug-resistant TB. **Table 1** shows TB-related costs by phase of clinical care. Across all sites, the median (Q1, Q3) cost of MDR-TB was \$123 183 (\$94 895, \$160 033) with treatment-related consumables (\$60 654) and hospitalizations (\$42 147) correspondingly accounting for 49% and 34% of costs. The median (Q1, Q3) costs for DS-TB and LTBI were \$3371 (\$2718, \$9397) and \$861 (\$818, \$956), respectively.

CONCLUSION

MDR-TB is very costly to treat and manage in Canada. The high costs of MDR-TB appear to be driven by hospitalizations and treatment-related consumables.

Table 1. Median (Q1, Q3) costs associated with MDR-TB by phase of clinical care and cost category

Phase of Clinical Care	Personnel Cost	Consumables and Service Cost
Diagnosis	\$250 (\$237, \$344)	\$835 (\$770, \$835)
Treatment	\$8 286 (\$4324, \$15 602)	\$60 654 (\$34 723, \$96 080)
Follow-up	\$323 (\$101, \$404)	\$52 (\$26, \$131)
Hospitalization ¹		\$42 147 (\$35 539, \$57 526)
Overall²		\$123 183 (\$94 895, \$160 033)

¹Hospitalization costs could not be broken down by cost category as they are charged as daily per diems

²Contact investigation costs were not considered

B2. MORBIDITY TRENDS AND ASSOCIATED CHARACTERISTICS IN MULTI-DRUG RESISTANT AND EXTENSIVELY DRUG RESISTANT TUBERCULOSIS IN TEXAS, 2010-2017

Nguyen DT, Graviss EA. Houston Methodist Research Institute, Houston, TX, USA.

BACKGROUND

Multi-drug resistant tuberculosis (MDR-TB), including its more severe form, extensively drug resistant TB (XDR-TB), is a global public health challenge. MDR-TB requires lengthy and complex regimens with more toxic medications, yet has low adherence rates and high mortality even in developed countries. This population-based analysis aimed to analyze and determine the morbidity trends of MDR-TB and its associated characteristics in Texas using state-wide surveillance data.

DESIGN/METHODS

De-identified TB surveillance data reported from Texas between 01/2010 and 12/2017 were obtained from the CDC's TB Genotyping Information Management System. Comparisons were conducted between MDR/XDR-TB versus drug-susceptible or mono-resistant TB patients. Non-parametric testing was used for morbidity trends. One-to-one propensity score matching on age and gender between groups was also analyzed.

RESULTS

In 10,103 TB patients reported between 2010 and 2017, 70 (0.69%) MDR-TB (including 2 XDR-TB) patients were reported. Over the 7-year period, the MDR-TB proportion fluctuated between 0.41% and 1.21% with a peak in 2011 (1.21%) and an overall non-significant trend ($z=-1.01$, $p=0.31$). Propensity score matching analysis indicated that MDR-TB was more likely associated with foreign-birth, diabetes and cavitation on chest radiography. Compared with drug-susceptible and mono-resistant TB, MDR-TB had lower rates of treatment completion (6877/9508, 72.3%; 411/525, 78.3%, and 37/70, 52.9%, respectively, $p<0.001$). Age ≥ 45 years was associated with higher overall mortality in MDR-TB patients (4/6, 66.7% versus 15/64, 23.4%, $p=0.02$).

CONCLUSION

MDR-TB remains a challenge in Texas with significantly lower treatment completion rates. More effective strategies to improve treatment adherence are critical for managing MDR-TB disease.

Figure 1. Flowchart of the study population, propensity score matching

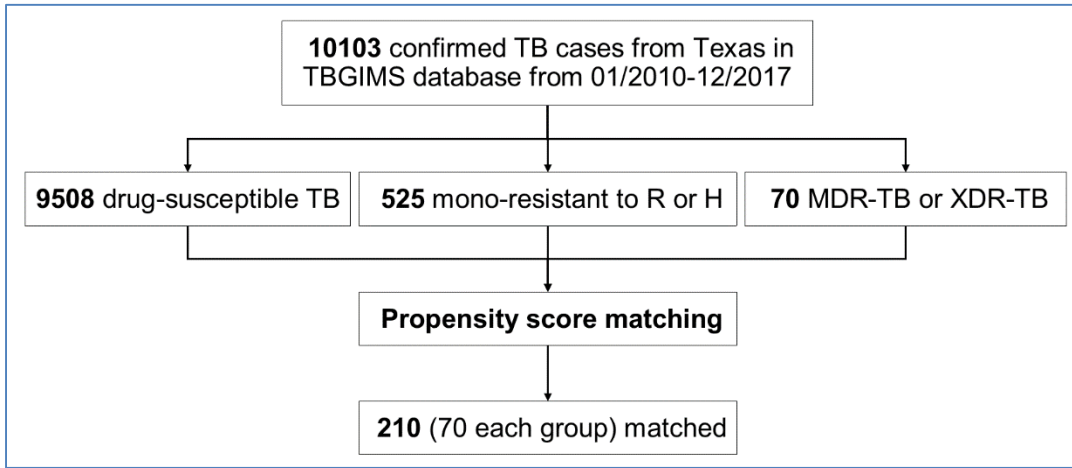


Figure 2. Trend of multi-drug resistant and extensively drug resistant tuberculosis morbidity in Texas, 2010-2017

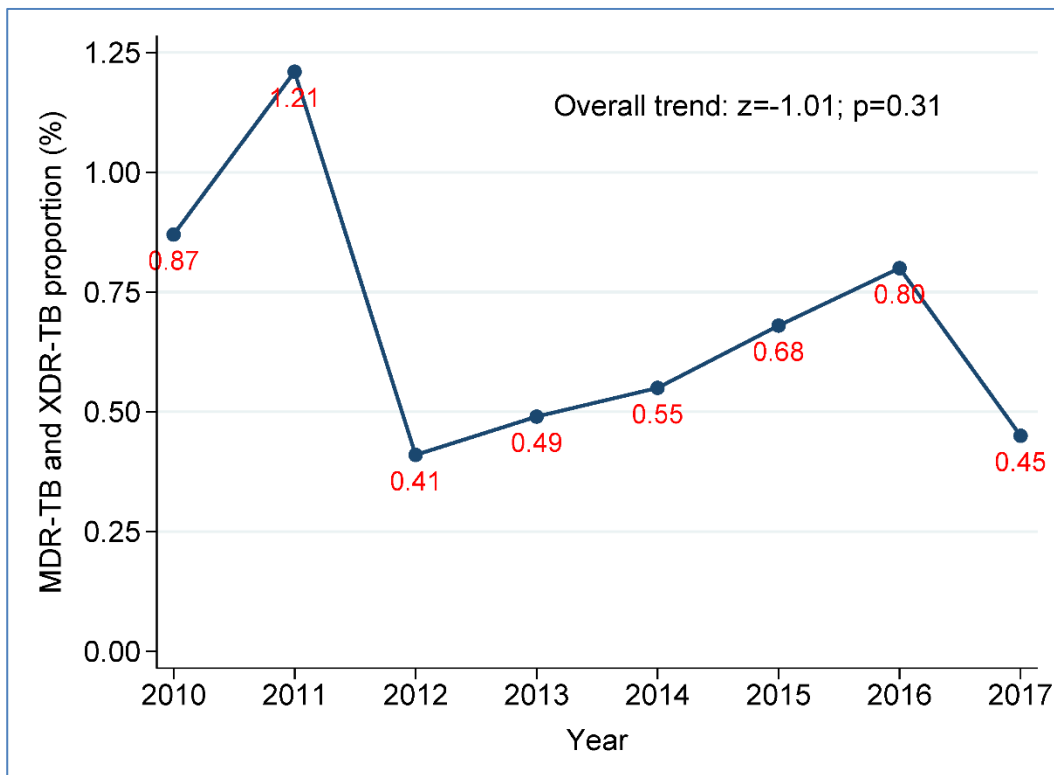


Table 1. Patient characteristics, drug-sensitive versus MDR-/XDR-TB, propensity score matching

	All (N=210)	Drug-sensitive [1] (n=70)	Monoresistant [2] (n=70)	MDR- or XDR-TB [3] (n=70)	Overall p-value	[1] vs. [2] p-value	[2] vs. [3] p-value	[1] vs. [3] p-value
Age (years)					1.00	1.00	1.000	1.00
0-4	3 (1.4)	1 (1.4)	1 (1.4)	1 (1.4%)				
5-14	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
15-24	30 (14.3)	10 (14.3)	10 (14.3)	10 (14.3%)				
25-44	120 (57.1)	40 (57.1)	40 (57.1)	40 (57.1%)				
45-64	48 (22.9)	16 (22.9)	16 (22.9)	16 (22.9%)				
≥65	9 (4.3)	3 (4.3)	3 (4.3)	3 (4.3%)				
Male gender	123 (58.6)	41 (58.6)	41 (58.6)	41 (58.6%)	1.00	1.00	1.00	1.00
White	20 (9.5)	9 (12.9)	8 (11.4)	3 (4.3%)	0.18	0.80	0.12	0.07
US-born	69 (34.8)	29 (41.4)	28 (40.0)	12 (20.7%)	0.03	0.86	0.02	0.01
Homeless	6 (2.9)	2 (2.9)	3 (4.3)	1 (1.4%)	0.60	0.65	0.31	0.56
Inmate of a correctional facility	25 (13.2)	14 (20.0)	7 (10.0)	4 (8.0%)	0.10	0.10	0.71	0.07
Resident of long-term care facility	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
IDU	5 (2.4)	1 (1.4)	1 (1.4)	3 (4.3%)	0.44	1.00	0.31	0.31
Non-IDU	19 (9.0)	7 (10.0)	6 (8.6)	6 (8.6%)	0.94	0.77	1.00	0.77
Excessive alcohol use	33 (15.7)	10 (14.3)	15 (21.4)	8 (11.4%)	0.25	0.27	0.11	0.61
Diabetes	29 (13.8)	4 (5.7)	12 (17.1)	13 (18.6%)	0.054	0.03	0.83	0.02
Organ transplant receiver	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
Chronic kidney failure	2 (1.0)	1 (1.4)	0 (0.0)	1 (1.4%)	0.60	0.32	0.32	1.00
Immunosuppression	6 (2.9)	2 (2.9)	2 (2.9)	2 (2.9%)	1.00	1.00	1.00	1.00
Pulmonary TB	183 (87.1)	55 (78.6)	66 (94.3)	62 (88.6%)	0.02	0.01	0.23	0.11
TB site, cervical lymph	7 (3.3)	4 (5.7)	1 (1.4)	2 (2.9%)	0.36	0.17	0.56	0.40
Miliary TB	4 (2.0)	1 (1.5)	0 (0.0)	3 (4.5%)	0.16	0.30	0.07	0.31
TB-CXR	180 (90.5)	55 (84.6)	65 (94.2)	60 (92.3%)	0.14	0.07	0.66	0.17
Miliary TB on CXR	4 (2.3)	1 (1.8)	0 (0.0)	3 (5.4%)	0.14	0.27	0.06	0.32
Cavitation on CXR	74 (41.1)	11 (20.0)	32 (49.2)	31 (51.7%)	<0.001	<0.001	0.79	<0.001
AFB smear (+)	112 (61.2)	24 (43.6)	43 (65.2)	45 (72.6%)	0.00	0.02	0.36	0.00
Culture (+)	150 (83.8)	29 (55.8)	62 (93.9)	59 (96.7%)	<0.001	<0.001	0.46	<0.001
Culture not converted (from + to -)	21 (10.0)	5 (7.1)	6 (8.6)	10 (14.3%)	0.33	0.75	0.29	0.17
Positive culture, NAA, or AFB smear	187 (89.0)	47 (67.1)	70 (100.0)	70 (100.0%)	<0.001	<0.001		<0.001
HIV status (+)	9 (4.3)	5 (7.1)	3 (4.3)	1 (1.4%)	0.47	0.76	0.42	0.20
MDR-TB or XDR-TB								
MDR-TB	68 (32.4)	0 (0.0)	0 (0.0)	68 (97.1%)	NA	NA	NA	NA
XDR-TB	2 (1.0)	0 (0.0)	0 (0.0)	2 (2.9%)	NA	NA	NA	NA
East Asian <i>Mtb</i> family	26 (15.4)	5 (12.5)	5 (7.5)	16 (25.8%)	0.01	0.39	0.01	0.10
TB treatment completed	152 (72.4)	52 (74.3)	63 (90.0)	37 (52.9%)	<0.001	0.02	<0.001	0.01
Died at diagnosis	3 (1.4)	1 (1.4)	1 (1.4)	1 (1.4%)	1.00	1.00	1.00	1.00
Died during TB treatment	12 (5.7%)	6 (8.6%)	1 (1.4%)	5 (7.1%)	0.16	0.053	0.10	0.75
Died, overall	15 (7.1)	7 (10.0)	2 (2.9)	6 (8.6%)	0.22	0.09	0.15	0.77

Note: Values are in number (%); CXR: chest radiograph; TB-CXR, abnormalities on CXR consistent with tuberculosis; MDR-TB, Multi-drug resistant TB; XDR-TB, Extensively drug-resistant TB; NAA, Nucleic Acid Amplification; IDU, injecting drug user

B3. **FLUOROQUINOLONES IN THE TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS: EXPERIENCE FROM THREE US TB TREATMENT CENTERS**

Al-Shaer MH¹, Alghamdi WA¹, An G², Alsultan A³, Alkabab Y⁴, Banu S⁵, De Miranda Silva C⁶, Hajihosseini A⁶, Kipiani M⁷, Maleki F⁶, Drusano G⁸, Schmidt S⁶, Heysell SK⁴, Kempker RR⁹, Cegielski P¹⁰, [CA Peloquin](#)¹.
¹Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL; ²Division of Pharmaceutics and Translational Therapeutics, College of Pharmacy, University of Iowa, Iowa City, IA, USA; ³Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia; ⁴Division of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, VA, USA; ⁵Infectious Disease Division, International Centre for Diarrhoeal Diseases Research, Dhaka, Bangladesh; ⁶Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL, USA; ⁷National Center for TB and Lung Diseases, Tbilisi, Georgia; ⁸Department of Medicine, Institute for Therapeutic Innovation, University of Florida, Orlando, FL; ⁹Division of Infectious Diseases, Department of Medicine, Emory University, Atlanta, GA; ¹⁰Pulmonary Infectious Disease Section, University of Texas Health Sciences Center, Tyler, TX, USA.

BACKGROUND

We present accumulated USA experience with fluoroquinolones (FQs) ciprofloxacin (CIP), ofloxacin (OFL), levofloxacin (LVX) and moxifloxacin (MOX) for multidrug-resistant tuberculosis (MDR-TB).

DESIGN/METHODS

3 US TB centers: A.G. Holley Hospital (AGH), Texas Center for Infectious Diseases (TCID), University of Texas Health Science, Tyler. MDR-TB patients (1984-2015) received FQ ≥ 28 days. Data: demographics, cultures, durations, and FQ serum concentrations. Time-to-event (TTE) analysis compared culture conversion. Population pharmacokinetic (PK) models generated maximum concentrations (C_{max}) and areas under the concentration-time curves (AUC₀₋₂₄). For the pharmacokinetic/ pharmacodynamic (PK/PD) analyses, epidemiological cut-off values (ECOFF) in liquid medium as minimum inhibitory concentration (MIC).

RESULTS

106 MDR-TB patients: median age was 39.5 years, weight 59.2 kg. 51 patients (48.1%) received CIP or OFL; 55 received LVX or MOX. TTE analysis: LVX/MOX showed faster time to culture conversion in MDR-TB patients vs. CIP/OFL (median 16 vs 40 weeks, log-rank $p=0.0577$). Median (range) LVX C_{max} and AUC₀₋₂₄ were 9.9 mg/L (6.4-16.1) and 118.8 mg.hr/L (76.7-287.6), while MOX were 4.0 mg/L (2.9-8.3) and 46.1 mg.hr/L (28.7-90.9). Patients who achieved free C_{max}/MIC >10 were 1 for LVX (4%) and 12 (46%) for MOX. For free AUC₀₋₂₄/MIC >100 : 8 (32%) for LVX and 19 (73%) for MOX.

CONCLUSION

In MDR-TB patients, LVX and MOX showed faster time to culture conversion vs. CIP and OFL. Higher percentage of patients achieved the PK/PD target with MOX compared to LVX, which may indicate that higher doses of LVX are needed.

B4. PHARMACOKINETIC-PHARMACODYNAMIC TARGET ATTAINMENT ANALYSIS OF CYCLOSERINE IN TB PATIENTS

Alghamdi WA¹, Alsultan A², Al-Shaer MH¹, An G³, Hajihosseini A⁴, Maleki F⁴, De Miranda Silva C⁴, Alkabab Y⁵, Banu S⁶, Kipiani M⁷, Drusano G⁸, Schmidt S⁴, Heysell SK⁵, Kempker RR⁹, Cegielski P¹⁰, [Peloquin CA](#)¹.

¹Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, USA; ²Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia; ³Division of Pharmaceutics and Translational Therapeutics, College of Pharmacy, University of Iowa, Iowa City, IA; ⁴Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL; ⁵Division of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, VA, USA; ⁶Infectious Disease Division, International Centre for Diarrhoeal Diseases Research, Dhaka, Bangladesh; ⁷National Center for TB and Lung Diseases, Tbilisi, Georgia; ⁸Department of Medicine, Institute for Therapeutic Innovation, University of Florida, Orlando, FL; ⁹Division of Infectious Diseases, Department of Medicine, Emory University, Atlanta, GA; ¹⁰Pulmonary Infectious Disease Section, University of Texas Health Sciences Center, Tyler, TX, USA.

BACKGROUND

There are limited pharmacokinetic/pharmacodynamic (PK/PD) data for cycloserine (CS) in TB patients. We estimated population PK parameters and performed Monte Carlo simulation and target attainment analyses to optimize dosing.

DESIGN/METHODS

Data: healthy subjects and TB patients from 6 sites: Georgia, Bangladesh, and four US sites. Software: Monolix (2018R1) and mlxR package (v3.3.0) in R. We simulated 1000 TB patients (steady state) for each tested regimen. PKPD targets of time above MIC $\geq 30\%$ and $\geq 64\%$, representing bactericidal activity and effective concentration at 80% potential maximum (EC₈₀ from Deshpande et al. and Gumbo). MICs studied (4 to 64 mg/L). Probability of target attainment (PTA) of at least 90% for the highest MIC was the PKPD breakpoint.

RESULTS

We analyzed 1069 CS plasma concentrations from 247 subjects (age 42 years, weight 61 kg, males 75%). Weight and creatinine clearance had significant effects on PK model volume and clearance parameters, respectively. PTA increased with dose across 250 mg, 500 mg, and 750 mg daily. Dividing the daily dose modestly increased the PTA. Dividing the dose reduced the C_{max} significantly. The 250 mg regimens failed to achieve PTA >90% for MIC >16 mg/L. The 500 mg TID regimen achieved the targets for MIC of 32 mg/L. The 500 TID regimen and higher doses produced C_{max} >55 mg/L, which may not be tolerable.

CONCLUSION

Although dividing the dose resulted in a slight increases in the PTA, it resulted in a significant decrease in C_{max}, which might reduce the adverse CNS effects.

B5. LOW-DOSE AMINOGLYCOSIDE DOSING IN THE TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB): A SINGLE CENTRE EXPERIENCE

Sabur NF¹, Brar MS², Wu L³, Brode SK⁴. ¹Department of Respiriology, St. Michael's Hospital and West Park Healthcare Centre; ²Department of Surgery, University of Toronto; ³West Park Healthcare Centre; ⁴Department of Respiriology, University Health Network, Toronto Western Hospital and West Park Healthcare Centre, Toronto, ON, Canada.

BACKGROUND

The WHO recommends intravenous amikacin for the treatment of MDR-TB at a dose of 15 mg/kg. However, higher doses are associated with significant toxicity. Since 2010, patients with MDR-TB treated at our institution have received amikacin at 8-10 mg/kg, with dose adjustment based on therapeutic drug monitoring. Here we describe our experience with low-dose amikacin for the treatment of MDR-TB.

DESIGN/METHODS

We conducted a retrospective cohort study of all patients with MDR-TB who received amikacin as part of their treatment regimen between 2010-2016. Patient demographics, clinical and microbiologic data, treatment regimens, adverse events and clinical outcomes were abstracted.

RESULTS

45 patients met inclusion criteria. 46% were female and 82% had pulmonary disease. The median starting dose of amikacin was 8.8 mg/kg (IQR 7.9, 10), and target therapeutic drug levels (peak of 25-35 mg/L) were achieved at a median of 12.5 days (IQR 5, 29). The median duration of amikacin treatment was 6.6 months (IQR 5.5, 8). The median time to sputum culture conversion was 1 month (IQR 1,2). 11% of patients experienced hearing loss based on audiometry testing (95% CI 4-24%); 24% had subjective hearing loss (95% CI 12-39%) and 33% subjective tinnitus (95% CI 19-49%). 26% of patients had a significant rise in serum creatinine (95% CI 13-43%), but only 8.6% had a GFR <60 at treatment completion. 79% of patients had a successful treatment outcome (95% CI 66-92%).

CONCLUSIONS/RECOMMENDATIONS

Low dose amikacin is effective in MDR-TB treatment, and although not without toxicity, it is associated with relatively low rates of hearing loss.

B6. **EVALUATING UTILIZATION OF LINE PROBE ASSAYS FOR DETECTION OF MULTIDRUG-RESISTANT TUBERCULOSIS IN TORONTO, CANADA**

Sabur NF¹, Brar MS², Brode SK³. ¹Department of Respiriology, St. Michael's Hospital and West Park Healthcare Centre; ²Department of Surgery, University of Toronto; ³Department of Respiriology, University Health Network, Toronto Western Hospital and West Park Healthcare Centre, Toronto, ON, Canada.

BACKGROUND

The gold standard diagnostic test for MDR-TB is culture-based drug susceptibility testing; however, results take several weeks to report. The *MTBDRplus* line probe assay (Hain Lifescience, Nehren, Germany) allows rapid detection of drug resistance and can identify multiple mutations on different chromosomal targets. The *MTBDRplus* test was introduced in Ontario in 2010, but must be specifically requested by the treating clinician. The purpose of this study was to audit the use of *MTBDRplus* testing among cases of MDR-TB treated at our institution, which treats most MDR-TB cases in Toronto.

DESIGN/METHODS

We conducted a retrospective cohort study of all patients with MDR-TB who were treated at our institution between 2010-2016. Patient demographics, clinical data, details of microbiologic testing and drug-susceptibility reporting, and clinical outcomes were abstracted.

RESULTS

Information on initial TB testing and treatment was obtained in 35 patients. 83% of patients had an *MTBDRplus* test requested. 51% of patients were female and 80% had pulmonary involvement. *MTBDRplus* testing was requested in all patients with a documented history of prior TB treatment, and in all those with a known MDR-TB contact. The median time from first positive TB test to appropriate treatment was significantly shorter in patients who underwent *MTBDRplus* testing compared to those who did not have *MTBDRplus* testing (21 days vs. 40 days; $p=0.02$). There was no difference in treatment outcomes between the two groups ($p=0.6$).

CONCLUSIONS/RECOMMENDATIONS

MTBDRplus testing is being performed in the majority of patients subsequently diagnosed with MDR-TB in Toronto. Use of *MTBDRplus* testing significantly reduces time to appropriate treatment.

B7. CASE MANAGEMENT FOR XDRTB: IMPLICATION AND CHALLENGES

Shaykevich E¹, Lardizabal A². ¹Middlesex County TB Control Center, Edison; ²Global Tuberculosis Institute, Rutgers, The State University of New Jersey, Newark, NJ, USA.

BACKGROUND

Extensively Drug-Resistant TB (XDR-TB) is a rare type of MDR-TB. Because XDR-TB is resistant to first- and second-line drugs, patients are left with treatment options that are less effective. XDR treatment usually begins in a hospital setting. However, it can be done in the community when Public Health nurses are prepared to case-manage complicated XDR TB clients with a culturally congruent, patient-centered care. Successful treatment outcomes depend on utilizing a team approach.

RESPONSE

We describe challenges to managing XDR TB patient in out-patient setting in Middlesex County, New Jersey. A foreign born, 58 y/o male diagnosed with bilateral, cavitary, smear positive lung disease. XDR TB treatment introduced and continued in community setting. Public Health Nurses manage patient for side-effects, monitor lab testing, assist with access to care for co-morbidities, and assure the adherence to TB treatment.

RESULTS

Barriers to managing XDR case in a community setting: Russian/Ukrainian speaking patient, un-insured with co-morbidities IDDM, Hepatitis C, no steady primary care physician.

Utilization of existing XDR treatment monitoring tools: Drug-gram and lab monitoring and developing language specific communication tool for symptom monitoring.

CONCLUSION

Public Health Nurses play a significant role in managing extensively drug-resistant TB in community setting. To be effective, the nurse must understand the disease, understand patient's cultural needs, monitor patient for possible side effects, advocate for patient, assist patient in navigating the health system, and support patient's adherence to TB treatment.

C. CLINICAL (TREATMENT AND DIAGNOSIS)

C1. DELAYED EMPYEMA IN TWO PATIENTS TREATED FOR PULMONARY TUBERCULOSIS

Grocholski S, Dirks J. University of Manitoba, Winnipeg, MB, Canada.

BACKGROUND

Development of an empyema during the treatment of pulmonary tuberculosis is rarely reported. Differential includes treatment failure, paradoxical upgrading reaction, and lupus-like reaction to isoniazid. Mechanisms of treatment failure include decreased pleural penetrance of anti-tuberculous chemotherapy, decreased gut absorption, and sub-optimal adherence. Two patients who developed tuberculous empyema after commencing appropriate treatment for pulmonary tuberculosis are presented.

INTERVENTION

Patient One developed pan-sensitive, smear negative, culture positive pulmonary tuberculosis with exudative effusion. Treatment included Rifampin, Isoniazid, Pyrazinamide, and Moxifloxacin, with step-down to Rifampin and Isoniazid at 8 weeks. Effusion resolved. A new exudative pleural effusion developed at 18 weeks of treatment. Fluid was smear positive, culture negative, and PCR positive. Levofloxacin and Amikacin were added to his regimen. He completed 16 months of treatment. Patient Two developed smear positive, culture positive, pan-sensitive disseminated TB. He presented with V Fib Arrest. Small bilateral effusions consistent with aggressive fluid resuscitation were present. Effusions resolved with improved volume status. Rifampin, Isoniazid, Pyrazinamide, and Moxifloxacin were prescribed. Regimen changed to Rifampin, Ethambutol, and Moxifloxacin after three weeks for hepatotoxicity. At 10 weeks, Rifampin and isoniazid were continued. Empyema developed at 31 weeks. Fluid was smear positive, culture negative, and PCR positive. Treatment was extended by 9 months.

RESULTS

Dissolution of effusion was prolonged with ongoing anti-tuberculous chemotherapy. No relapse has been detected to date.

CONCLUSION

The cause of culture negative effusion is difficult to ascertain. Possible causes include treatment failure, paradoxical upgrading reaction, and lupus-like reaction. In uncertainty, treatment failure requires directive management.

C2. A SYSTEMATIC REVIEW OF THE DIAGNOSTIC ACCURACY OF ARTIFICIAL INTELLIGENCE BASED COMPUTER PROGRAMS TO ANALYZE CHEST X-RAYS FOR PULMONARY TUBERCULOSIS

Harris M^{1,2,3}, Qi A^{2,3}, Torabi N⁴, Menzies D^{1,3,5}, Korobitsyn A⁶, Pai M^{1,3,5}, Nathavitharana RR⁷, Ahmad Khan F^{1,3,5}. ¹Department of Epidemiology and Biostatistics, McGill University; ²Department of Medicine, McGill University Health Centre; ³Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute & Research Institute of the McGill University Health Centre, Montreal, QC; ⁴St. Michael's Hospital, Li Ka Shing International Healthcare Education Centre, Toronto, ON; ⁵McGill International TB Centre, Montreal, QC, Canada; ⁶Laboratories, Diagnostics & Drug Resistance Global TB Programme WHO, Geneva, Switzerland; ⁷Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, MA, USA.

BACKGROUND

The need to improve tuberculosis (TB) diagnostic and screening services in high-burden countries is clear: in 2016, active TB was the leading cause of death due to an infectious agent, and only 69% of the 10.4 million people that developed this disease were detected by or notified to national TB programmes.

DESIGN/METHODS

We undertook a systematic review of the diagnostic accuracy of artificial intelligence-based software for identification of radiologic abnormalities (*computer-aided detection*, or CAD) compatible with pulmonary tuberculosis (PTB) on chest x-rays (CXR). We searched four databases for articles published between January 2005-November 2017. We summarized data on CAD type, study design, and measures of diagnostic accuracy. We assessed risk of bias with the QUADAS-2 method.

RESULTS

We included 42 of the 3978 articles reviewed: 32 studies Development studies and 10 Clinical studies. Meta-analyses were not performed due to differences in study design. Development studies were more likely to use CXR databases that had greater potential for bias as compared to Clinical studies. Areas under the receiver operating characteristic curve (AUC) were significantly higher: in Development studies (AUC: 0.87 [0.81-0.90]) versus Clinical studies (0.68 [0.65-0.75]; p-value 0.004); and with programs using deep learning versus (0.93 [0.90-0.97]) vs machine-learning (0.81 [0.69-0.88]; p=0.001) software.

CONCLUSION

We conclude that artificial intelligence based CAD programs are promising, but much of the work thus far is in the development rather than the clinical phase. This review provides concrete suggestions on what study design elements should be improved.

C3. **THE PROTOTYPICAL CASE OF SMEAR-POSITIVE AND SMEAR-NEGATIVE PULMONARY TUBERCULOSIS IN CANADA: A CLINICAL HEURISTIC TO AID DIAGNOSIS**

Heffernan C¹, Barrie J², Doroshenko A^{1,3}, Egedahl ML¹, Paulsen C¹, Senthilselvan A³, Long R^{1,3}. ¹Department of Medicine, and the Department of Radiology and Diagnostic Imaging; ²Faculty of Medicine and Dentistry; ³School of Public Health, University of Alberta, Edmonton, AB, Canada.

BACKGROUND

Although several studies have reported on the symptoms and radiographic presentation of pulmonary tuberculosis (PTB), most are not population-based and do not provide a comprehensive picture of disease presentation by smear status. From both public health and individual perspectives there is a need to generate a clear picture of the prototypical case, particularly the smear-positive (infectious) case; suspicion of disease being prerequisite to the submission of sputum for acid-fast bacilli smear and culture, and a timely diagnosis.

METHODS

This study reports on the clinical and radiographic presentation of PTB by smear status in Canada, a country that now reports more than 70% of its cases in the foreign-born. Our cohort is of 313 culture-positive cases; 151 smear-positive, and 162 smear-negative. We recorded information on seven defining clinical characteristics and the chest radiograph for each case. Thereafter, we used multinomial logistic regression to assess the contribution of clinical predictors on the outcomes: smear-positive case with a typical chest radiograph, smear-positive case with an atypical chest radiograph, and smear-negative with typical and atypical chest radiographs.

RESULTS

The prototypical infectious case of PTB is a young-middle aged, foreign-born or Indigenous adult (>14 years) of either sex with a duration of symptoms of two weeks or more, a normal or low hemoglobin with a normal or low leukocyte count, typical adult-type chest x-ray findings, and a history of having been prescribed a broad-spectrum prior to their diagnosis. This constellation of demographic, historical, and laboratory findings represent a clinical heuristic for making a timely diagnosis of PTB.

C4. **TUBERCULOSIS DISEASE IN RECIPIENTS OF ORGAN-TRANSPLANTATION, CALIFORNIA 2010-2017**

Katrak S^{1,2}, Westenhouse J¹, Barry P^{1,2}, Flood J¹. ¹Tuberculosis Control Branch, California Department of Public Health, Richmond; ²Division of Infectious Diseases, University of California, San Francisco, San Francisco, CA, USA.

Keywords: tuberculosis, organ transplantation, infections of immune-compromised

Corresponding author: Correspondence should be sent to Shereen Katrak, MD, MPH, at 850 Marina Bay Parkway, Building P, Richmond, California 94804, shereen.katrak@cdph.ca.gov

BACKGROUND

Tuberculosis (TB) disease in persons who have received organ transplantation causes high morbidity, but the epidemiology and clinical features of this problem remain poorly described.

METHODS

Using California TB registry data from 2010-2017, we describe clinical features of all TB cases occurring in patients who previously received organ transplantation. We compared TB cases with and without transplant, and examined mortality controlling for age.

RESULTS

During eight years of observation, the California TB Registry recorded 116 cases of post-transplant TB. A majority of patients with post-transplant TB were > 45 year old (84%), non-white (90%), and born outside of the United States (84%). Of 116 cases, 48 (41%) had pulmonary disease, while 68 (59%) had extra-pulmonary or both pulmonary and extra-pulmonary disease, compared to 69% and 31%, respectively, in non-transplant-associated TB ($p < .0001$). Common sites of extra-pulmonary disease in transplant patients included pleura (19%), cervical lymph nodes (12%), and bone (12%). Controlling for age, transplant cases were nearly twice as likely to die as non-transplant-associated TB cases (OR=1.92, CI=1.13, 3.25). Post-transplant TB did not increase over time (Cochran-Armitage trend test $p = .751$). Among 49 post-transplant TB cases with a positive TB skin test (TST) or interferon gamma release assay (IGRA), 12 (24%) had the test performed > 6 months prior to TB diagnosis.

CONCLUSION

Our findings suggest that post-transplant TB disease is more likely to be extra-pulmonary and result in death than non-transplant-associated TB, and that opportunities may exist for preventing TB disease through screening and treatment for LTBI in this population.

C5. **ASSESSMENT OF TUBERCULOSIS (TB) TREATMENT IMPLEMENTATION IN THE DEMOCRATIC PEOPLE’S REPUBLIC OF KOREA (DPRK): INTERVIEW-BASED INVESTIGATION**

Kim ES^{1,2}, Im AY¹, Lee SY¹, Shin HY¹. ¹Institute for Health and Unification Studies, Seoul National University School of Medicine, Seoul, South Korea; ²Rutgers New Jersey Medical School, Newark, NJ, USA.

BACKGROUND

The state of tuberculosis management in North Korea is poorly understood due to serious challenges in obtaining information. We assess North Korean implementation of TB treatment practices by comparing public TB reports with interviews of former North Korean TB patients.

METHODS

Public data was extracted from Global Fund’s DPRK TB Grant Performance Report (October-December 2013). Selected were interviews of 8 North Korean patients treated for TB between 2000-2014 in North Korea, carried out by the Korea Foundation for International Health and the Institute for Health and Unification Studies at Seoul National University School of Medicine.

RESULTS

Global Fund’s assessment of DOTS provision shows that, of all new smear positive TB cases registered, 90.3% were successfully treated (22,532/24,597), while only 1.84% were cases with drug resistant TB which started treatment but were lost to follow up at six months. Comparatively, interviews indicate none of the eight patients received inpatient or outpatient DOTS and 3/8 (37.5%) were lost to follow up. The interviewed patients’ average duration of treatment was 5.88 months, from a range of 4-12 months. Additionally, Global Fund’s report also indicates 100% of units reported no stock-outs of anti-TB medications. Comparatively, interviews showed only 4/8 (50%) patients received TB medication at a health facility, while 5/8 (62.5%) patients had to purchase all or part of it on the black market.

CONCLUSION

Our findings demonstrate a gap between performance markers and actual treatment reception in North Korea, highlighting the necessity of further needs-assessment and identification of drug-resistance mechanisms in the country.

C6. **ANALYSIS OF THE TIME INTERVAL FROM DIAGNOSIS TO TREATMENT INITIATION FOR CULTURE-POSITIVE, ACTIVE TUBERCULOSIS IN CANADA, 2011 – 2015**

He N^{1,2}, LaFreniere M². ¹University of Toronto, Toronto; ²Public Health Agency of Canada, Ottawa, ON, Canada.

BACKGROUND

Tuberculosis (TB) treatment delays (time from diagnosis to treatment initiation) can negatively influence disease outcomes and facilitate disease transmission. This analysis aimed to 1) provide a descriptive overview of demographic and clinical factors for TB cases with treatment delays of <7 days and ≥7 days in Canada, and 2) examine factors associated with treatment delays ≥7 days.

DESIGN/METHODS

All culture-positive active TB cases with a valid diagnosis date and treatment initiation date reported to the Canadian Tuberculosis Reporting System from 2011 – 2015 were included in this analysis. Multivariate logistic regression was used to investigate factors associated with treatment delays ≥7 days.

RESULTS

The analysis included 4,770 TB cases, of which 828 (17.4%) had a treatment delay ≥7 days. Those with a treatment delay ≥7 days were significantly more likely ($p < 0.05$) to have non-respiratory TB (OR 4.40; 95% CI 3.57 – 5.42), and to have a negative bacterial microscopy result (OR 1.86; 95% CI 1.53 – 2.24), and were less likely to be aged 15 – 24 years (OR 0.67; 95% CI 0.48 – 0.94), to be First Nations (OR 0.56; 95% CI 0.34 – 0.92), or Inuit (OR 0.43; 95% CI 0.22 – 0.86) compared to those with treatment delays of < 7 days.

CONCLUSION

In Canada, the majority of TB cases receive treatment within a week of diagnosis. Further understanding the factors associated with treatment delays may improve TB management in Canada.

C7. **INCIDENCE AND SIGNIFICANCE OF THROMBOEMBOLIC DISEASE IN CRITICALLY ILL PULMONARY TB PATIENTS**

Lau A¹, Sligl W¹, Barrie J², Long R¹. ¹Department of Medicine; ²Department of Radiology, University of Alberta, Edmonton, AB, Canada.

BACKGROUND

Pulmonary TB (PTB), even when advanced, does not usually cause serious respiratory impairment as ventilation and perfusion are reduced in parallel. We have been impressed by the frequency with which ventilator-dependent PTB patients are found to have pulmonary thromboemboli (PTE). Conceivably, the redistribution of pulmonary blood flow and PTE to intact lung in PTB contribute to respiratory failure and mortality. The aim of this study is to describe the incidence and significance of PTE in critically ill PTB patients.

METHODS

We reviewed clinical and laboratory records of all smear-positive PTB cases admitted to the general systems ICU of the University of Alberta Hospital, between 2006-2016. Thromboembolic events and outcomes are reported.

RESULTS

Of 240 adult (age >17 years) smear-positive PTB cases admitted to the University of Alberta Hospital, a total of 20 (8.3%) were admitted to the ICU. Computerized tomographic (CT) scans were performed in 10 cases and PTE was found in 5 (50%). One of these cases, and three others who had not undergone a CT had a deep venous thrombosis. Nine (45%) patients died during treatment (4 in ICU and 5 within 3 months of discharge from ICU). Mortality in patients with and without PTE, and with unknown PTE status were 2 (40%), 2 (40%), and 5 (50%), respectively.

CONCLUSION

TB is understood to cause a hypercoagulable state. The pathophysiologic defect in PTB would predict that PTE would cause serious gas exchange impairment. Our experience justifies this concern and supports the need to exclude thromboembolic events in ventilator-dependent PTB patients.

C8. TUBERCULOSIS TREATMENT OUTCOMES FROM THREE TB CENTERS IN THE US

Alghamdi WA¹, Al-Shaer MH¹, Hajihosseini A², Maleki F², Alsultan A³, An G⁴, De Miranda Silva C², Egelund E¹, Gomez M⁵, McKamey L⁶, Stambaugh J⁵, Tablante T¹, Zhao Y¹, Ashkin D⁵, Griffith DE⁷, Drusano G⁸, Schmidt S², Cegielski P⁷, Peloquin CA¹. ¹Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville; ²Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL, USA; ³Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia; ⁴Division of Pharmaceutics and Translational Therapeutics, College of Pharmacy, University of Iowa, Iowa City, IA; ⁵TB Control Section, Division of Disease Control and Health Protection, Florida Department of Health, Tallahassee, FL; ⁶Novant Health Presbyterian Medical Center, Charlotte, NC; ⁷Pulmonary Infectious Disease Section, University of Texas Health Sciences Center, Tyler, TX; ⁸Department of Medicine, Institute for Therapeutic Innovation, University of Florida, Orlando, FL, USA.

BACKGROUND

Three US TB centers accumulated decades of experience, including MDR-TB. We analyzed their experience.

DESIGN/METHODS

Data (1984-2015): A.G. Holley Hospital, Texas Center for Infectious Diseases (TCID), University of Texas Health Science, Tyler (TYLER). Data: demographics, comorbidities, drugs, cultures, and drug concentrations. Stratification: drug-susceptible (DS-TB); rifampin/multidrug-resistant (RR/MDR-TB). Drugs included if dosed ≥ 28 days. Outcomes: WHO definitions (primary analysis); Günther et al. (secondary analysis). Cured extended to ≥ 1 negative culture/smear after 2 months (DS-TB), and 6 months therapy (RR/MDR-TB) (no subsequent positive cultures). Favorable = cured; unfavorable outcomes = failed or dead. Individual bivariate and stepwise multiple logistic regressions performed.

RESULTS

356 patients: males (77%), mean (SD) age 47.0 (15.9) years, 41% had RR/MDR-TB, 19% diabetes, 17% HIV+. Outcomes: 250 patients (70%), others indeterminate. Site was significant covariate for DS-TB and RR/MDR-TB groups. DS-TB patients: favorable outcomes associated with length of stay, liver disease, and drug concentration monitoring, while age, recurrent TB, tobacco use, autoimmune disease, cancer, and complications associated with unfavorable outcomes. In multiple regression models, length of stay and liver disease (favorable) and recurrent TB, tobacco use and complications (unfavorable). Among TB drugs, injectables (unfavorable). For RR/MDR-TB patients, psychiatric disease (unfavorable, primary and secondary analyses). In multiple regression models, site (TCID favorable) and race (Black or Hispanic favorable). Fluoroquinolones favorable (primary), pyrazinamide and drug monitoring unfavorable (secondary).

CONCLUSION

TYLER included earliest cases (1980s) and older fluoroquinolones (ciprofloxacin and ofloxacin). Recurrent disease, tobacco abuse, and complications associated with difficult-to-treat cases. Fluoroquinolones associated with favorable outcomes in RR/MDR-TB patients.

D. SPECIAL POPULATION

D1. TUBERCULOSIS AMONG FIRST NATIONS IN NORTHERN MANITOBA, CANADA, 2008-2012: PROGRAM PERFORMANCE ON- AND OFF-RESERVE

Basham CA¹, Elias B², Fanning A³, Orr P². ¹University of British Columbia, Vancouver, BC; ²University of Manitoba, Winnipeg, MB; ³University of Alberta, Edmonton, AB, Canada.

BACKGROUND

In partnership with First Nations in Northern Manitoba, Canada, this project was undertaken in order to understand TB program performance in a region with persistently high TB incidence.

METHODS

A retrospective cohort of persons diagnosed with TB in Manitoba between January 1, 2008 - December 31, 2010, and their contacts, was extracted from Manitoba TB Registry. Performance measures based on US-CDC were analyzed. Adjusted probability ratios (aPR) and 95% confidence intervals (CIs) reported with comparisons between on/off-reserve First Nations, adjusted for age, sex, and treatment history.

RESULTS

$N = 149$ persons diagnosed with TB and $n = 3,397$ contacts. Comparisons off/on-reserve: Treatment completion (aPR = 1.03; 95%CI: 0.995 – 1.07); early detection (aPR = 0.87; 95%CI: 0.57, 1.33); HIV testing and reporting (aPR = 0.42 ; 95%CI: 0.21 – 0.83); pediatric TB (age<15y) (aPR = 1.20; 95%CI: 0.47 – 3.06); re-treatment for TB (aPR = 0.93; 95%CI: 0.89 – 0.97); contact elicitation (aPR = 0.94; 95%CI: 0.84 – 1.05); contact assessment (aPR = 0.69; 95%CI: 0.50 – 0.94). Pediatric (ages < 15y) TB incidence in northern Manitoba is 55.6 per 100,000.

CONCLUSION

First Nations Chiefs have called for the implementation, in a transparent and accountable manner, of TB performance measures in their communities. This study found TB program performance varies depending on residence in a reserve or non-reserve community. Action in collaboration with First Nation is urgently needed to address TB program performance in terms of contact investigation and HIV testing/reporting for First Nations off-reserve and to address high pediatric TB rate in northern Manitoba.

D2. **THE HISTORY OF TUBERCULOSIS IN NORTHERN ALBERTA AND SASKATCHEWAN BEFORE AND AFTER TREATY 8**

Cole J, Janvier D, Sparling L, Piche D, Nokohoo M, Heffernan C, Hackett P, Grant M, Long R. Tuberculosis Program Evaluation and Research Unit, University of Alberta, Edmonton, AB, Canada.

BACKGROUND

Treaty 8, signed in 1899, is fundamental to how the Federal government approaches delivery of healthcare to First Nations communities today, with implications for tuberculosis (TB) elimination strategies. This study explores the history of tuberculosis in the Athabasca and Clearwater River districts (Northern Alberta, and Saskatchewan, respectively) during the treaty making process. Both districts currently experience high rates of TB among Indigenous peoples. The view of this project is that policies of the past have created environments that sustain epidemic TB in these areas.

DESIGN/METHODS

My research uses quantitative and qualitative analysis of late 19th century Department of Indian Affairs correspondence regarding relief for the sick and destitute in the Clearwater River and Athabasca districts before treaty 8. These documents record the incidence of tuberculosis in this region, as well as approaches to TB control.

RESULTS

Indeed, the history of Tuberculosis in treaty 8 territory is distinct from the more southern regions of Canada. Those who worked towards improving health in the Clearwater River and Athabasca districts often faced geographical challenges. Access to medical intervention was limited. Furthermore, the proximity of policy makers from affected communities led to misunderstandings of community needs.

CONCLUSION

The history of TB prevention and control is relevant today, because similar challenges continue impact the process of TB elimination within these communities. Deconstructing the historical events that have contributed to persistent TB is central to reconciliation with Indigenous peoples in Canada, and may be a pathway to partnerships that make present-day clinical interventions more successful.

D3. **TB AND HOMELESSNESS, GEORGETOWN GUYANA, 2015-2017**

Ghanshiam E, Mohanlall J, Khan D, D'Oliveira-Henery L. National Tuberculosis Programme, Ministry of Public Health, Guyana.

BACKGROUND

According to World Health Organization homeless people are at increased risk of TB, have higher default rates and worse treatment outcomes than the general public. TB rates among the homeless can be up to 20 times higher than the general population. In Guyana, 2 % of all TB cases registered at the Georgetown Chest Clinic, 2014-2017 were among the Homeless population.

METHODS

A retrospective study was done on 24 homeless TB cases registered at the Georgetown Chest Clinic (GCC), 2015-2017. Data was collected from the Basic Management Unit at GCC and analysed using MS Excel 2007. Factors analysed includes age, sex, race, HIV status, bacteriologically confirmed cases and treatment outcome.

RESULTS

Male represents 95.8% the cases. 41.7% were between 50-59 years of age, 33.3% between 40-49 years and 12.5% were between 30-39 years and 60 -69 years. There were no cases below the age of 20 years. 62.5% were newly registered cases while 25% were previously Lost To Follow Up (LTFU) and 12.5% relapses. 45.8% successfully completed treatment and 41.7% were LTFU. 12.5% died while receiving treatment. 37.5% represents Indo Guyanese, 33.3% Afro Guyanese. 83.3% had an HIV test of which 16.7% were HIV Positive and another 16.7% had an unknown HIV status. 70 % were bacteriologically confirmed of which 58.8% successfully complete treatment and 41.2% were LTFU.

CONCLUSION

Ending TB means Ending Poverty. It is recommended that the Ministry of Public Health strengthens its collaboration with other Ministries and NGOs to make this possible.

D4. **SHIFTING PERSPECTIVES - A NEW APPROACH TO KNOWLEDGE TRANSLATION AND EXCHANGE FOR TB ELIMINATION IN INDIGENOUS COMMUNITIES**

Balakumar S¹, [Haworth-Brockman M](#)¹, Stout R². ¹National Collaborating Centre for Infectious Diseases, Winnipeg, MB; ²National Collaborating Centre for Aboriginal Health, Prince George, BC, Canada.

BACKGROUND

In Canada, TB elimination strategies for Indigenous Peoples have largely been dictated by non-Indigenous interests and western-colonial knowledge structures. To achieve TB elimination in Indigenous communities and close the health gap described in the TRC Calls to Action, Indigenous community self-determination must be actualized. De-colonizing the knowledge translation systems involved in TB elimination requires shifting the perspectives of knowledge keepers embedded throughout these systems. All stakeholders must not only engage with Indigenous Peoples, but prioritize their voices.

INTERVENTION/RESPONSE

With leadership and direction from AFN, ITK, MNC, NCCAH, and other Indigenous stakeholders, the National Collaborating Centre for Infectious Diseases hosted a knowledge exchange forum entitled, *Towards TB Elimination in Northern Indigenous Communities* in 2018. Prior to the event, provincial/territorial TB program consultations were conducted to assess their current approaches, needs, and knowledge gaps. Much of the forum was dedicated towards engaging with Indigenous community members with previous experience living with TB, or working with TB programs.

RESULTS

Over 100 in-person and virtual participants attended. These included Indigenous community knowledge holders from 9 Canadian provinces/territories, and individuals working in different sectors, roles and levels of TB policy and programming. Participants included clinicians, researchers, program managers, and community representatives. Of those who completed evaluations, 100% indicated gaining valuable knowledge at the event, and 90% identified opportunities to collaborate or coordinate action. Output from the meeting informed national discussions, and at least 12 instances of measurable impact were captured.

CONCLUSION

Transforming traditional approaches to knowledge translation for TB elimination in Indigenous communities is necessary, achievable, and impactful.

D5. SOCIAL DETERMINANTS OF HEALTH AMONG RESIDENTIAL AREAS WITH A HIGH TUBERCULOSIS INCIDENCE IN A REMOTE INUIT COMMUNITY

Kilabuk E, Momoli F, Mallick R, Van Dyk D, Pease C, Zwerling A, Edmunds Potvin A, Alvarez GG. Ottawa Hospital Research Institute, University of Ottawa Divisions of Respiriology and Infectious Diseases; Department of Medicine, The Ottawa Hospital, Ottawa, ON, Canada; Nunavut Department of Health; Nunavut Tunngavik Inc, Iqaluit, Nunavut; Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada.

Funding: Public Health Agency of Canada, The National Lung Health Framework

BACKGROUND

Tuberculosis (TB) remains a significant health burden among Inuit in Canada. Social determinants of health play a key role in TB infection, disease and ongoing transmission in this population. The objective of this research was to estimate the prevalence of social determinants of Inuit health (SDH) as they relate to latent TB infection (LTBI) among people living in residential areas at high risk for TB in Iqaluit, Nunavut.

METHODS

In-person home surveys were conducted among those who lived in predetermined residential areas at high risk for TB identified in a door to door TB prevention campaign in Iqaluit, Nunavut in 2011. Risk ratios for SDH and LTBI were estimated, and multiple imputation was used to address missing data.

RESULTS

261 participants completed the questionnaire. Most participants identified as Inuit (82%). Unadjusted risk ratios demonstrated that age, education, smoking tobacco, crowded housing conditions and Inuit ethnicity were associated with LTBI. After adjusting for other SDH, multivariable analysis showed an association between LTBI with increasing age (RR 1.07, 1.04-1.11, 95% CI), crowded housing (RR 1.48, 1.10-2.00, 95% CI), and ethnicity (RR 2.76, 1.33-5.73, 95% CI) after imputing missing data.

CONCLUSION

Among high risk residential areas for TB in a remote arctic region of Canada, crowded housing and Inuit ethnicity were associated with latent TB infection after adjusting for other social determinants of health. In addition to strong screening and treatment programs, alleviating the chronic housing shortage will be a key element in the elimination of TB in the Canadian Inuit Nunangat.

D6. **APPLYING RETROSPECTIVE SOCIAL NETWORK ANALYSIS TO AN ONGOING TUBERCULOSIS OUTBREAK IN A FIRST NATIONS COMMUNITY IN SASKATCHEWAN**

Klaver B^{1,2}, Hourigan S¹, Akinjobi G¹, Nelson S¹, Ndubuka N¹. ¹Northern Inter-Tribal Health Authority, Prince Albert, SK; ²Public Health Agency of Canada, Ottawa, ON, Canada.

BACKGROUND AND REASON FOR IMPLEMENTATION OR PROBLEM BEING ADRESSED

In June 2014, a tuberculosis (TB) outbreak was declared in a First Nations on-reserve community in Northern Saskatchewan. By 2016, the outbreak had been transmitted to a neighbouring community. At this point contact investigations began to miss contacts, resulting in isolated clusters of cases that had identical TB fingerprints to the outbreak cases. We conducted a retrospective social network analysis to reveal unknown relationships between the cases and to uncover transmission pathways.

INTERVENTION OR RESPONSE

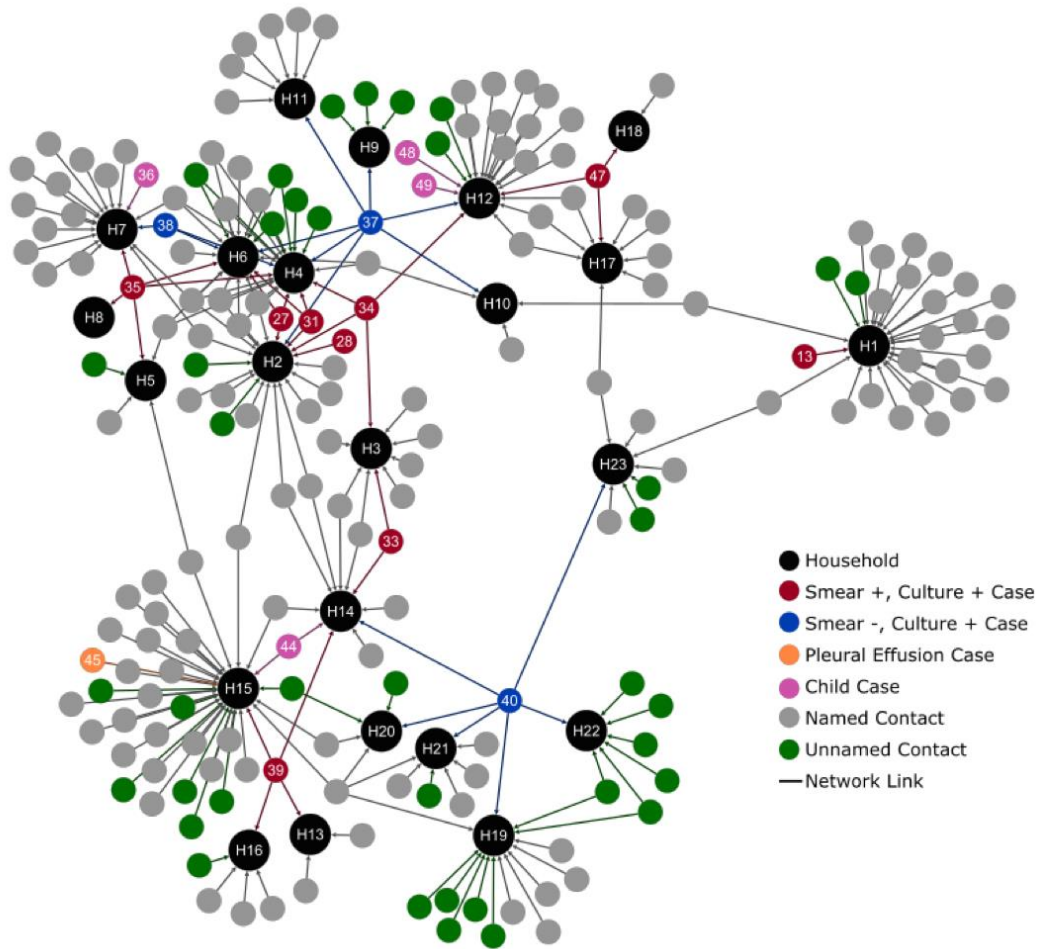
A community TB champion was able to identify the locations where 6 isolated outbreak cases lived or visited regularly, as well as other people that lived at or visited these locations. A social network map was created, which connected outbreak cases, named contacts, and unnamed contacts to households.

RESULTS AND LESSONS LEARNED

A total of 23 households and 215 people were identified between 2014 and June of 2018, of which 38 individuals were unnamed contacts. Through the social network analysis, all 6 previously isolated cases were linked by household to a smear positive outbreak case, which indicated probable transmission events. Additionally, there were 20 unnamed contacts connected by household to a smear positive case suggesting possible exposure and latent tuberculosis infection.

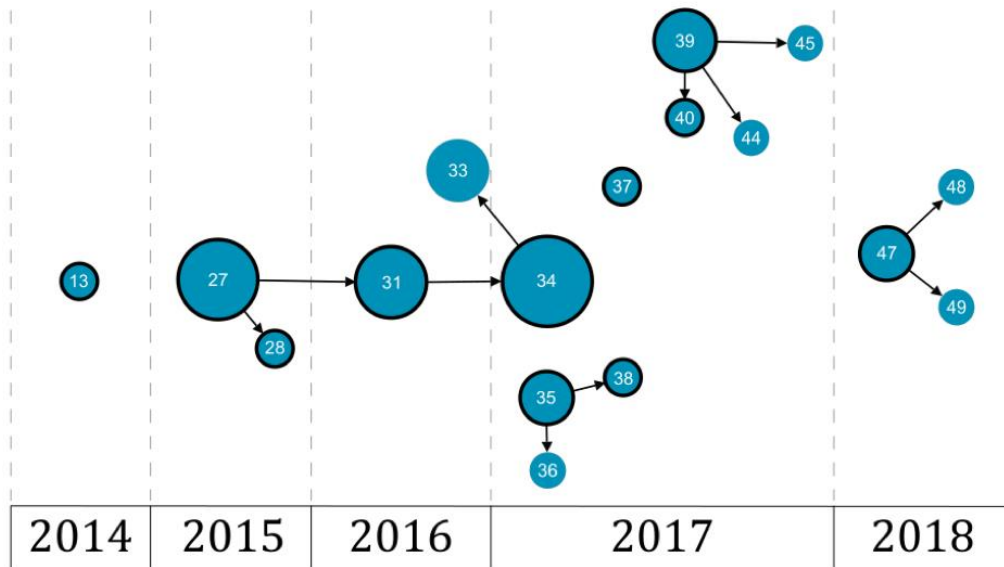
CONCLUSIONS AND KEY RECOMMENDATIONS

Using a retrospective social network analysis all previously isolated cases now have probable transmission pathways that were unidentified with traditional contact investigation. Furthermore, 20 unnamed contacts require follow-up assessments. Future TB outbreak management strategies should utilize social network analysis in real-time, in complement to traditional contact investigation and TB fingerprint analysis, to identify missed contacts that may have been infected.



- Household
- Smear +, Culture + Case
- Smear -, Culture + Case
- Pleural Effusion Case
- Child Case
- Named Contact
- Unnamed Contact
- Network Link

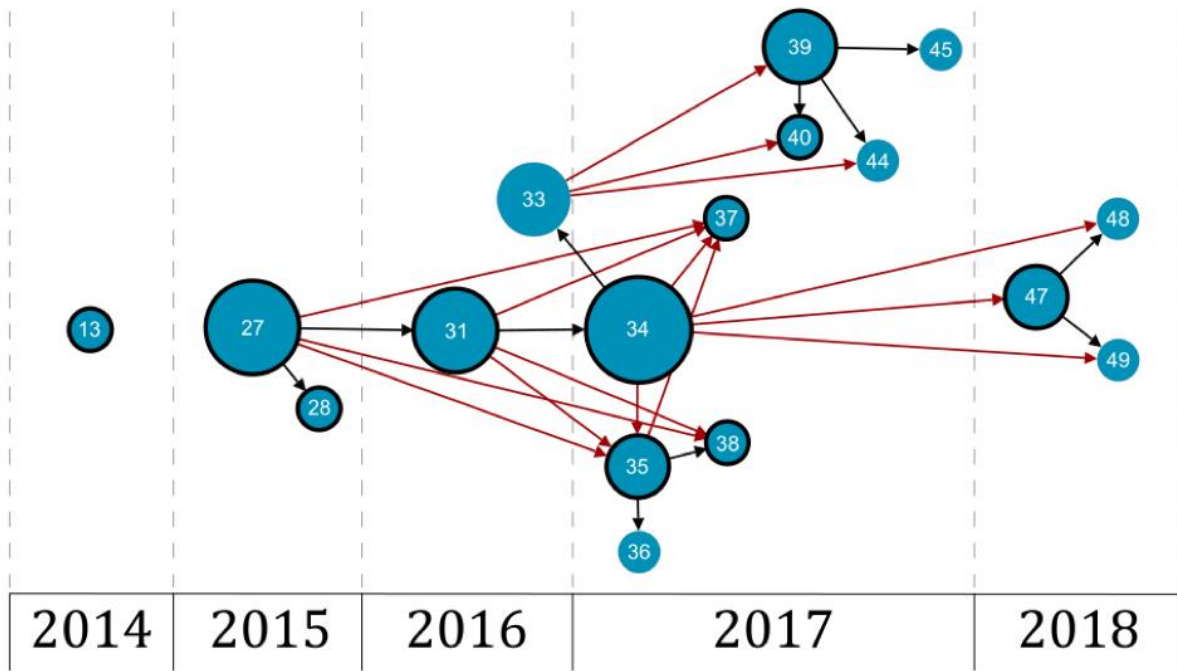
- Case
- TB Fingerprint Linked
- Contact Trace Linked



*Staggering represents sequence of diagnosis - but the distance between staggers does not reflect actual time.

*Size of node represents the number of transmission events stemming from the node (larger = more transmission).

- Case
- TB Fingerprint Linked
- Contact Trace Linked
- Social Network Linked



*Staggering represents sequence of diagnosis - but the distance between staggers does not reflect actual time.

*Size of node represents the number of transmission events stemming from the node (larger = more transmission).

D7. A PRELIMINARY STUDY OF RECURRENCE OF TUBERCULOSIS AMONG INUIT IN NUNAVUT

Kulleperuma K, Aglukark O, Travers K, Pim C, Patterson M, Kim B. Department of Health, Government of Nunavut, Iqaluit, NU, Canada.

BACKGROUND

The tuberculosis (TB) incidence among Inuit is the highest across all origin groups in Canada, over 290 times higher than the Canadian born non-indigenous. The average crude incidence of TB among Inuit in Nunavut between 2005 and 2017 is 184.2 per 100,000 individuals. TB recurrence is observed among reported TB cases but not fully described. Understanding the mechanism of TB recurrence can inform designing effective interventions in order to eliminate TB among Inuit in Canada. To this end, a preliminary study is conducted to estimate the rate of TB recurrence among the Inuit population in Nunavut.

METHODS

A retrospective cohort of all clinically or bacteriologically confirmed active TB cases reported to the Nunavut Department of Health between 2005 and 2010 was followed by calculating follow-up time in years until a recurrence, death or the end of study in Dec 2017.

RESULTS

A total of 319 TB cases were enrolled for a median follow-up period of 8 years. Among these cases, 9% had a recurrent episode of TB corresponding to a recurrence rate of 1.0 (95% CI 0.7 to 1.5) per 100 person-years.

CONCLUSION

The rate of TB recurrence among Inuit in Nunavut is 6 times higher than the incidence of new TB cases suggesting TB recurrence is a considerable contributor to the ongoing TB situation in Nunavut.

D8. TOWARDS RECONCILIATION: TRANSFORMING TUBERCULOSIS EPIDEMIOLOGY GOVERNANCE FOR INDIGENOUS PEOPLES IN BRITISH COLUMBIA, CANADA

Leung JW^{1,2}, Wolf I², Behn Smith D³, McDonald S², MacNaughton A², Adams E², Swinkels H², Cook VJ^{1,4}, Wong J¹. ¹British Columbia Centre for Disease Control, Coast Salish Territory; ²First Nations Health Authority, Coast Salish Territory, Vancouver; ³Office of the Provincial Health Officer, Ministry of Health, Coast Salish Territory, Victoria; ⁴Division of Respiratory Medicine, Faculty of Medicine, University of British Columbia, Coast Salish Territory, Vancouver, BC, Canada.

BACKGROUND

Indigenous Peoples in the area now known as British Columbia (BC) have a long history of healing systems that promote health and wellness, and they were unaffected by tuberculosis (TB) prior to contact with Europeans. Efforts toward TB elimination cannot be separated from actions toward reconciliation and decolonization, and the Truth and Reconciliation Commission of Canada's (TRC) Calls to Action provide important guidance for this work. A partnership between First Nations Health Authority (FNHA), BC Centre for Disease Control (BCCDC), and Office of the Provincial Health Officer aims to operationalize these principles in transforming the governance of TB epidemiology for Indigenous Peoples.

INTERVENTION/RESPONSE

A working group was formed to uphold principles of Indigenous data governance relating to data analysis, interpretation, and reporting to ensure cultural safety and benefit to Indigenous communities. A dedicated epidemiologist is co-located with FNHA and BCCDC to enhance equity and tailor reporting activities to the unique contexts of Indigenous communities. The epidemiologist's role was expanded to include involvement with FNHA education activities and field investigations, facilitating mutual learning and development of culturally-informed approaches to knowledge exchange.

RESULTS

Towards implementing TRC Calls to Actions 18 and 19, this partnership ensures efforts toward TB elimination and reconciliation with Indigenous Peoples are not isolated endeavors, but a shared responsibility and integrated within provincial processes. This collaborative model provides an example of meaningful engagement, shared decision-making, and progress towards effective Indigenous data governance.

CONCLUSION

Reconciliation requires innovative changes in processes, structures, and relationships, and BC's experiences can provide salient lessons for other programs.

D9. **COMORBIDITY: TUBERCULOSIS, DIABETES MELLITUS AND HIV, EPIDEMIOLOGICAL ANALYSIS IN THE STATE OF MÉXICO**

Mendoza Damián F, Vázquez Medina K, Díaz Garduño JI, Widrobo García L, Ramírez Hernández MDG, Jiménez Estrada JM, Velázquez Quiroz IR. Laboratorio Estatal de Salud Pública, Instituto de Salud del Estado de México, Toluca, Mexico.

BACKGROUND

Data from 2016 indicate approximately 10.4% of the Mexican population is diabetic¹ and 14,000 Mexicans were newly infected with HIV². The dual burden of TB and diabetes mellitus (DM) or TB and HIV/AIDS has become a major public health concern.

METHODS

Between 2014-2017, 3575 samples with suspected TB were tested, the prevalence of TB-DM was 8% (285) and TB-HIV/AIDS was 2% (73).

RESULTS

From DM patients: 27% were confirmed positive for TB; global prevalence was 4.1% (IQR 1.8%-6.2%). 20% show resistance to streptomycin, rifampin, isoniazid or pyrazinamide, while 1.3% show resistance to ethambutol. 6.8% of patients with HIV/AIDS were positive for Tuberculosis. 100% showed resistance to pyrazinamide, 40% showed resistance to isoniazid or rifampicin, 20% to streptomycin and no resistance to ethambutol was found in comorbidity with HIV.

CONCLUSIONS

Increasing TB-DM cases implies reorientation and integration of the health workforce and services to simultaneously address this double burden of disease by the limitation of dual screening for tuberculosis in patients with diabetes mellitus, and vice versa.

1 - http://www.who.int/diabetes/country-profiles/mex_en.pdf?ua=1

2 - <http://cfs.hivci.org/country-factsheet.html>

D10. IDENTIFICATION OF RESPIRATORY VIRUSES IN HIV-POSITIVE PATIENTS WITH PNEUMONIA AND IMPACT OF THESE ON PULMONARY FUNCTION AT 12 MONTHS: A COHORT STUDY

Rodriguez I¹, Rueda ZV², Cabrera R², Marin², Lopez L², Rodiño J², Aguilar Y¹, Keynan Y³, Herrera M¹, Velez L¹. ¹Universidad de Antioquia; ²Universidad Pontificia Bolivariana, Medellin, Antioquia, Colombia; ³University of Manitoba, Winnipeg, MB, Canada.

BACKGROUND

This study aimed to determine the presence of RV in bronchoalveolar lavage (BAL) samples and induced sputum and to correlate them with pulmonary function (PF) over time.

METHODS

Adults of 18 years or older, hospitalized in Medellin, Colombia between November 2015 and 2017, with diagnosis of pneumonia and/or HIV were recruited. They were excluded if they received antibiotics for >72 hours, severe immunosuppression, or severe lung disease. Three groups were recruited (HIV+/pneumonia+, HIV+/pneumonia-, and HIV-/pneumonia+) and followed for 12 months. We used multiplex RT-PCR to detect 16 respiratory viruses (RV), microbiological, and spirometric studies.

RESULTS

The 71% were men and median of 39 years old (IQR 27-51). The presence of at least one RV was identified in 51.9%, 45.1% and 57.1% of the groups, respectively. The most frequent virus was rhinovirus (24/65, 37%). At admission, 30.4% of patients with HIV+/pneumonia+, 16.6% of HIV+/pneumonia-, and 50% of HIV-/pneumonia+ had airflow limitation, with change in FEV1 in both groups with pneumonia (HIV+= 1.80L, IQR 1.03-2.78; and HIV-= 1.38L, IQR 0.70-1.68) compared to HIV+/pneumonia- which had FEV1 of 3.21L (IRQ 2.46-3.82). At follow-up at 1, 6 and 12 months, FEV1 improved significantly in the two groups with pneumonia and remained stable in the HIV+/pneumonia- group, regardless of the presence of RV.

CONCLUSION

RV are frequent in HIV+ patients, often coexisting with other pathogens. The PF was affected at admission in patients with pneumonia, improved significantly in the first months after infection. The presence of VR does not seem to affect PF consistently.

D11. **RECENT TUBERCULOSIS TRANSMISSION AND MORTALITY DURING TUBERCULOSIS TREATMENT AMONG PERSONS LIVING WITH HIV, UNITED STATES, 2011–2016**

Schmit KM, Shah N, Kammerer S, Marks SM, Bamrah Morris S. Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

Persons living with HIV are more likely to have tuberculosis (TB) disease attributed to recent transmission (RT) and to die during TB treatment than persons without HIV. We examined RT and mortality among HIV/TB patients.

DESIGN/METHODS

Using National TB Surveillance System data during 2011–2016, we used a plausible-source method to determine cases attributed to RT. We restricted analyses of mortality to cases reported during 2011–2014 to allow 2 years for reporting TB treatment outcome. We calculated multivariable adjusted odds ratios (aOR) with 99% confidence intervals (CI) to estimate associations between patient characteristics and RT or mortality.

RESULTS

TB disease was attributed to RT in 491 (20%) of 2,415 HIV/TB patients. RT was more likely among blacks (aOR:1.8, CI:1.1,3.0), and those reporting homelessness (aOR:2.5, CI:1.8,3.6) or substance use (aOR:1.5, CI:1.1,2.1) in the year prior to TB diagnosis; RT was less likely among non-U.S.-born persons (aOR:0.2, CI:0.1,0.3). Among 2,343 HIV/TB patients, 195 (8%) died during TB treatment. Age 45–64 years (aOR:2.2, CI:1.4,3.5) or ≥65 years (aOR:5.3, CI:2.4,11.6), and having a non-HIV immunosuppressive condition (aOR:3.4, CI:1.8,6.2) were associated with death; directly observed treatment (DOT) for TB was protective (aOR:0.5, CI:0.2,1.0).

CONCLUSIONS

Populations likely to have TB disease attributed to RT could be prioritized for public health interventions that decrease TB transmission. Improved adherence to treatment through DOT might result in less mortality, but additional interventions are needed to reduce mortality among older HIV/TB patients and those with medical risk factors for TB.

D12. **IMPACT OF PULMONARY TUBERCULOSIS AND/OR *PNEUMOCYSTIS JIROVECI* PNEUMONIA IN LUNG FUNCTION IN PATIENTS WITH HIV**

Tamayo L¹, Rodríguez I², Marín D¹, Cabrera R¹, López L¹, Rodiño J¹, Aguilar Y³, Keynan Y⁴, Vélez L³, Herrera M³, Rueda Z¹. ¹Universidad Pontificia Bolivariana; ²Hospital Universitario San Vicente Fundación; ³Universidad de Antioquia, Medellín, Antioquia, Colombia; ⁴University of Manitoba, Winnipeg, MB, Canada.

BACKGROUND

To determine the association of *Pneumocystis Jirovecii* pneumonia and/or *M. tuberculosis* with the presence of obstructive or restrictive pulmonary disease in patients with HIV, since it is currently one of the main causes of morbidity and mortality not only due to the decline in lung function but also because of the increase in cardiovascular risk.

DESIGN/METHODS

Prospective cohort study with two groups: HIV infected individuals presenting with community-acquired pneumonia (CAP) and without CAP. The exposure was *Pneumocystis jirovecii* pneumonia (PjP) and/or pulmonary tuberculosis (TB), and the primary endpoint was pulmonary dysfunction according to ATS guidelines. We did Ziehl Neelsen stain, mycobacteria culture and PCR to detect tuberculosis and modified toluidine blue o stain, methenamine silver for the diagnosis of *P. jirovecii* in bronchoalveolar lavage. All patients were assessed with spirometry at baseline, 1, 6, 12 months.

RESULTS

TB and PjP had higher mortality within the first six months after pneumonia onset compared to other patients that had other microorganisms diagnosed. At the baseline, TB and HIV coinfecting patients had higher restrictive pattern (Forced vital capacity <0.8) compared to other bugs or other HIV without pneumonia patients (TB/PjP: 76.9%, Others: 53.3%, None: 40%). During follow-up for a year, the FEV-1 <0.7, FVC<0.8 and FEV-1/FVC ratio were the same for TB and/or PjP, or without a previous episode of pneumonia.

CONCLUSION

Lung function is affected during pneumonia onset episode with TB and/or PjP, but during follow-up for a year, the lung function test in both groups are the same.

D13. IMPLEMENTATION OF A SHELTER CARD SYSTEM IN DUVAL COUNTY, FLORIDA – ONE STEP TOWARD ENDING TB

Washington T¹, Privett T², Meeks D², Rolle P¹. ¹Florida Department of Health in Duval County, Jacksonville; ²Florida Department of Health, Division of Disease Control and Health Protection, Bureau of Communicable Diseases, TB Control Section, Tallahassee, FL, USA.

BACKGROUND

From 2004-2011, Duval County experienced an extensive TB outbreak among the homeless population. In response to this outbreak, and with the goal of preventing future outbreaks, DOH-Duval partnered with local homeless shelters to implement a “shelter card” system.

INTERVENTION/RESPONSE

DOH-Duval’s shelter card system requires that clients seeking entry to homeless shelters present a “shelter card” indicating that they have had annual testing and bimonthly TB assessments by DOH-Duval. Test results are closely monitored by DOH-Duval staff and clients diagnosed with LTBI are encouraged to begin 3HP (Isoniazid and Rifapentine combination). In addition, frequent education sessions are provided to shelter staff to maintain close working relationships and to ensure compliance.

RESULTS

Data collected from clients being screened and subsequently treated through DOH-Duval shelter card system between 2014 and 2017 reveal that 7,174 clients were screened, 142 clients were started on LTBI therapy, and the yearly completion rate ranged from 36.7% to 60%. These completion rates are noteworthy considering the transient nature and additional challenges presented in testing and treating homeless clients.

CONCLUSION

DOH-Duval’s shelter card system serves as a model for screening homeless populations and could be easily replicated in other county health departments. The shelter card system has proven to be an exceptional surveillance initiative that is effective at identifying and eliminating transmission of TB disease in local homeless shelters and at reducing the risk of progression to active disease through successful treatment of LTBI. Moving forward, DOH-Duval remains committed to increasing LTBI treatment completion rates in all clients, especially the homeless.

D14. CIRCLE EXPLORATION OF TB

McMullin K¹, Gordon J², Montgomery J³, Hill J⁴, Duan Q⁵, Stickley S⁵, Dillon J⁶, Evans A⁵, Rea E⁷, Khan I⁸, Sharma M⁹, Jamieson F¹⁰, Hoepfner V¹¹, Patterson M¹², Puchalksi-Ritchie L¹³, Goodridge D¹¹, Cooper R¹⁴, Long R¹⁴, Bebe S⁵, Wobeser W⁵. ¹Gabriel Dumont Institute of Native Studies and Applied Research and University of Saskatchewan, Saskatoon, SK; ²Sioux Lookout First Nations Health Authority, Sioux Lookout, ON; ³Anishinaabe Territory, ON; ⁴Indigenous Initiatives, Queen's University; ⁵Department of Molecular and Biomedical Sciences, Queen's University; ⁶Department of Biochemistry, Microbiology and Immunology - College of Medicine and the Vaccine and Infectious Disease Organization - International Vaccine Centre - (VIDO InterVac), University of Saskatchewan, Saskatoon, SK; ⁷Toronto Public Health, Toronto, ON; ⁸First Nations and Inuit Health, Regina, SK; ⁹National Microbiology Laboratory, Winnipeg, MB; ¹⁰Public Health Ontario and University of Toronto, Toronto, ON; ¹¹Department of Medicine, University of Saskatchewan, Saskatoon, SK; ¹²Nunavut Health, Iqaluit, NU; ¹³Li Ka Shing Knowledge Institute and University of Toronto, Toronto, ON; ¹⁴Alberta Tuberculosis Control Program and University of Alberta, Edmonton, AB, Canada.

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 a best public health policy for recurrent TB in Canada.

METHOD

In September 2018 the team gathered to begin the knowledge exchange and develop a work plan. The gathering was held in the territory of the Haudenosaunee and Anishinaabek. A sharing circle which was open to the public was held and guided by Elders, Clanswomen and a Indigenous community engagement coordinator. The sharing circle was videotaped and is being prepared for public sharing.

RESULTS

Themes that arose during the sharing circle included the critical and negative contribution of stigma at all levels of the TB disease cascade, from prevention to diagnosis, management and appropriate policy development. Bureaucratic barriers to information sharing and knowledge exchange were also highlighted.

CONCLUSION

The sharing circle was an effective and efficient way to gain a common understanding and supported reciprocal learning which will be used to inform the development of best public health practice.

E. LABORATORY

E1. A MULTINATIONAL ASSOCIATION OF SUSCEPTIBILITY TESTING TO GENOTYPIC MECHANISMS OF RESISTANCE TO INH IN *M. TUBERCULOSIS*

Barnes AA¹, Ramirez-Busby SM¹, Hoffner S^{1,2}, Valafar F^{1#}. ¹Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden.

#Corresponding Author: faramarz@sdsu.edu; This work has been supported by National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Mycobacterium tuberculosis is the causative agent of tuberculosis (TB). Multi-drug resistant TB (MDR) strains (resistant to at least rifampicin [RIF] and isoniazid [INH]) are the most effective first-line drugs in treating TB. Increased rates of treatment failures and resistance levels are of major concern. Often, RIF is tested as a proxy for MDR, which misses INH-mono-resistant cases that could evolve into MDR. Mutations in *katG*, *inhA*, and *fabG1* should be included in MDR testing as they are known to confer INH-resistance. We associated these mutations with the resistance phenotype across 4441 genomes to assess their sensitivity and specificity.

METHODS

We aligned sequencing data for 4441 genomes downloaded from NCBI to H37Rv. A direct association was performed on resistance-conferring mutations in *katG*, *inhA*, *fabG1* to phenotypic drug susceptibility testing (BACTEC MGIT960, CC 0.1 mg/L). We tabulated the frequency of each mutation's susceptibility profile and calculated sensitivity and specificity.

RESULTS

1375 of 1508 INH-resistant (INHR) isolates (91.2% sensitivity) contain at least one known INH^R-conferring mutation. However, 222 INH-susceptible also had a resistance-conferring mutation (specificity 92.5%). *KatG* mutations were overrepresented in resistant isolates (1239 INH^R, 82.2%). Mutations in *fabG1* and *inhA* explained the resistance of 10.3% of INH^R isolates.

CONCLUSIONS

Sensitivity and specificity were in-line with previous reports; however, 209 were resistant without a known mutation. This suggests alternate mechanisms of resistance, possibly outside *katG*, *inhA*, and *fabG1*. As expected, *katG* mutations were most prevalent among resistant isolates, however, including *inhA* and *fabG1* mutations increases sensitivity to 91.2%, suggesting they should be considered when diagnosing INH^R.

E2. DETECTION OF XDR-TB USING HIGH-PRECISION PCR

Bleicher Z¹, Rice J¹, Wangh L*¹, de Vos M², Streicher E², van Helden P², Warren R², Kreiswirth B³, Kurepina N³. ¹Brandeis University, Waltham, MA, USA; ²DST/NRF Centre of Excellence in Biomedical Tuberculosis Research/MRC Centre for Molecular and Cellular Biology, Division of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa; ³Public Health Research Institute Center, UMDNJ, New Jersey Medical School, Newark, NJ, USA.

*Address correspondence to: wangh@brandeis.edu. Supported by NIH Grant # R01 A1099532.

BACKGROUND

There is a pressing need for accurate, sensitive, fast, affordable diagnostic tests for XDR-TB.

DESIGN/METHODS

An assay to distinguish all prevalent mutations in 7 different genes (*rpoB*, *inhA promoter*, *katG*, *rrs*, *eis promoter*, *gyrA* & *gyrB*) that confer resistance to rifampicin, isoniazid, kanamycin, amikacin and fluoroquinolones has been developed. All 7 targets are efficiently amplified in a single closed-tube reaction using individual pairs of asymmetric primers. The resulting abundant single-stranded DNA products are detected in four colors. The probes hybridize and melt off their targets within defined temperature ranges in a sequence-specific manner. Up to 48 12.5µL reaction tubes can be run at the same time in an available portable PCR device. Each reaction contains 10,000 human genomes, total time per run is under 1 hour.

RESULTS

Replicate samples containing *Mycobacterium tuberculosis* DNA down to the level of single genomes are highly reproducible. Mutations in the 7 target genes, known to confer resistance, were detected by significant changes in the melt profiles. No template controls are completely negative. Each run of 48 samples takes 59 minutes.

CONCLUSIONS

This assay holds promise for detection of XDR-TB in sputum of HIV positive patients, as well as in oral, blood, and urine samples containing low levels of TB. Because of its sensitivity, precision, and low cost (50 cents per test) it can also be used to detect low frequency drug resistance within samples that appear to be susceptible, and thus to avoid selection of drug resistance.

E3. **EPIGENETIC LOCI OF POTENTIAL PHENOTYPIC CONSEQUENCE ACROSS 93 *M. TUBERCULOSIS* CLINICAL ISOLATES IDENTIFIED THROUGH BAYESIAN ANALYSIS OF SINGLE MOLECULE SEQUENCING KINETICS**

Conkle-Gutierrez D¹, Modlin S¹, Kim C¹, Hoffner S^{1,2}, Valafar F^{1#}. ¹Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Originally, bacterial DNA methylation (DNAm) was considered to function exclusively as part of the bacterial immune system. However, in other bacteria orphan methyltransferases (endonuclease activity absent) serve as regulatory switches at specific hypomethylated sites. *M. tuberculosis* possesses two orphan methyltransferases, which have been shown to affect gene expression. We searched for frequently hypomethylated methyltransferase motif sites across 93 clinical isolates, to find potential sites where DNAm could affect phenotype.

DESIGN/METHODS

We de novo assembled the genomes of 93 clinical *M. tuberculosis* isolates sequenced with Single Molecule Real-Time (SMRT) sequencing. Bayesian classification from SMRT kinetics data determined the methylation status of bases within known methyltransferase target motifs. Hypomethylated motif sites were assigned identifiers based on their relative position to the nearest CDS.

RESULTS

Fifty of the 93 isolates had an active MamA methyltransferase. In these isolates, 0.312% of motif sites were hypomethylated, while seven were unmethylated in at least 20 isolates (cumulative binomial probability of $1.484e^{-39}$). Similarly, among the 70 isolates with active methyltransferase HsdM, 13 motif sites were hypomethylated in at least 20 isolates. In contrast, MamB had no target motifs hypomethylated in more than 4 isolates.

CONCLUSION

As expected, MamB motif sites were not consistently hypomethylated, because MamB has a partner restriction endonuclease, which would cleave any unmethylated MamB motif sites. In contrast, orphan methyltransferase sites showed site-specific patterns of hypomethylation across multiple isolates. This conserved, site-specific signal identifies loci where DNAm status potentially influences phenotypes such as antibiotic resistance, drug tolerance, or virulence.

E4. **CHEAP MULTIPLEX PCR ASSAY FOR MTB AND MNTB EARLY DIAGNOSIS FROM DIRECT SAMPLES**

Vázquez K, Mendoza F, [Díaz JJ](#), Widrobo L, Ramírez MDG, Jiménez JM, Velázquez IR. Laboratorio Estatal De Salud Pública, Instituto De Salud Del Estado De México, Toluca, México.

BACKGROUND

Early diagnosis is a key tool in the fight against tuberculosis, although there are many commercial options that have proven great value and diagnostic contribution but not all institutions are able to afford the cost of specific equipment and consumables. Supported by the basic infrastructure of a laboratory that performs conventional molecular tests (thermal cycler, electrophoresis chamber, transilluminator).

METHODS

We evaluate the performance of a multiplex PCR for the detection and discrimination of MTB and NTM from clinical samples, also evaluating 3 extraction methods (columns -2 different trademarks-, magnetic beads, heat) and 3 different Taq-DNA-Polymerases. We compared the performance of this test against the results of: GeneXpert, culture (liquid and solid medium) and smear microscopy.

RESULTS

The results indicates that this Multiplex PCR allows the identification of whether MTB or NTM is present in the sample. No differences were observed between the different extraction methods, nor between the use of different taq-DNA-polymerases. When comparing the results with the other diagnostic techniques: specificity 100%, sensitivity 98%, positive predictive value: 100%, negative predictive value: 98.9%, concordance index between tests: 98.9%, Kappa index: 0.95.

CONCLUSIONS

The average cost per test is around \$ 9 USD (lowest \$3.5 USD). Results emission in liquid samples: 3 hours from the beginning of the process and for solid samples (biopsies): 36 hours due to the enzymatic digestion process of the tissue.

E5. **STRONG ASSOCIATION OF MUTATIONS KNOWN TO CONFER RESISTANCE TO THREE INJECTABLE DRUGS IN A MULTINATIONAL ANALYSIS**

Kim C¹, Conkle-Gutierrez D¹, Ramirez-Busby S¹, Hoffner S^{1,2}, Rigouts L³, Valafar F^{1#}. ¹Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden; ³Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

The WHO recommends treating multidrug resistant tuberculosis with second-line drugs, including injectables, but injectable resistance continues rising globally. Mutations in *rrs* and the *eis* promoter regions confer resistance to injectables. We queried for mutations within these genomic regions in over 1000 clinical isolates and identified their association strength with phenotypic drug resistance.

DESIGNS/METHODS

We downloaded 1184 genomes of *M. tuberculosis* isolated from patients in Russia, Belarus, Belgium, India, Moldova, Philippines, South Africa, and Sweden. A direct association between mutations in *rrs* and *eis* promoter to phenotypic drug susceptibility testing (BACTECT MGIT960) for injectables amikacin (AMK) (1.0mg/L), capreomycin (CAP) (2.5mg/L), and kanamycin (KAN) (2.5mg/L) was performed.

RESULTS

A total of 326 of 1171, 325 of 1167, and 270 of 504 isolates were AMK, CAP, and KAN resistant, respectively. Sensitivity for *rrs* and/or the *eis* promoter mutations for predicting resistance to AMK, CAP, and KAN were 81%, 76.9%, and 91.9% respectively. The specificity was 100%, 98.5%, and 99.2%, respectively. A1401G in *rrs* was the most frequent variant and was indicative of resistance for all three injectables, separately and in cross-resistance cases. Mutations in the *eis* promoter were indicative of KAN resistance.

CONCLUSION

Sensitivities for AMK and CAP were lower than expected, possibly due to alternative mechanisms of resistance. The *rrs* mutation A1401G was strongly associated with resistance to all three drugs. We observed a strong correlation between mutations in *eis* promoter and KAN resistance in isolates from areas within and surrounding Russia, supporting the hypothesis of a geographic specific resistance mechanism.

E6. **MIRU-HEURISTICS FOR EVALUATION OF REPEATS AND THEIR ORDINAL (MIRUHERO):
MIRU ANALYSIS ON GENOMIC SEQUENCING DATA**

Machhi V, Fink L, Valafar F#. Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

MIRU-VNTR and spoligotyping techniques are regularly used by public health agencies for lineage typing of the *Mycobacterium Tuberculosis* Complex (MTBC). While these techniques can be performed in a laboratory, Whole Genome Sequencing (WGS) data is available for many isolates. To enable rapid lineage typing of growing MTBC WGS data we developed MiruHero, a software capable of reliable extraction of MIRU-VNTR and spoligo from WGS, eliminating the need for additional laboratory work.

DESIGN/METHODS

MiruHero BLASTs MIRU-VNTR sequences against a de novo assembled genome. Sequences with 97% identity of the subject sequence are recorded and sequential matches for each MIRU region are tabulated. Additionally, the program uses BLAST to search for spacer oligonucleotides (>94% identity) and returns octal format.

RESULTS

We verified the accuracy of MiruHero on 94 assemblies with experimental MIRU-VNTR and spoligotyping available on NCBI results were 97.3% concordant with experimental typing. The 2.7% discordance was manually investigated and revealed a missing spacer oligonucleotide in the experimental data that was identified using MiruHero.

MiruHero's MIRU-12 analysis of 88 MTBC genomes was concordant with 89.6% of laboratory-generated MIRU typing. The program detected two copies of a repeat region while laboratory MIRU typing only detected one in MIRU24.

CONCLUSION

MiruHero is an easy-to-use and downloadable stand-alone program for determining MIRU-VNTR and spoligotype in mycobacterial genomes. This method, compared to conventional PCR-based typing, can better resolve differences in MIRU and spoligo patterns among MTBC strains. Unlike TB-INSIGHT, MiruHero does not require the use of web-servers, maintaining privacy, and can accurately replace laboratory-generated MIRU and spoligotyping.

E7. **ACCURACY OF XPERT MTB/RIF FOR TUBERCULOSIS DIAGNOSIS AND RIFAMPICIN RESISTANCE IN CUBA**

Martínez MR, Sardiñas M, García G, Mederos LM, Díaz R. National Reference Laboratory in Tuberculosis, "Pedro Kouri" Institute, Havana, Cuba.

BACKGROUND

The sensitivity of diagnosis and cases detection by rapid tests is essential for Tuberculosis (TB) elimination. The aim of this study was to evaluate the performance of Xpert MTB/RIF in pulmonary and extrapulmonary samples.

MATERIALS/METHODS

963 clinical samples will be studied with indication of Xpert MTB RIF from July/ 2014 to September/ 2017. One milliliter that is made to perform the Xpert MTB / RIF and the rest is processed for direct exam and culture, according to the laboratory's procedures.

RESULTS

By Xpert were TB positive in 171 (17,7%) cases, of them 81 (47,4%) HIV +. TB was identified in 10 extrapulmonary samples (1 CSF, 4 tissue biopsies, 3 secretions and 2 in pleural fluid). Twelve cases with rifampicin resistance were detected (of them 5 HIV positive, 2 in fallow treatment patients and 2 previously treated). There was a very good correlation between the Xpert results and the conventional tests.

CONCLUSIONS

The Xpert improving the detection of cases and shortening the time of TB diagnosis to less than 2 hours and reduce the delay in the initiation of treatment, especially in patients AFB negative and HIV patients. To know the pattern of rifampicin resistance permit initiate the treatment with 2nd line drugs in the diagnosis cases and changes de treatment in patients with previous treatment.

E8. **WGS SNP PHYLOGENY OF *MYCOBACTERIUM TUBERCULOSIS* REVEALS DISCORDANCE IN SPOLIGOTYPING AND MIRU-VNTR**

Mitchell S¹, Ramirez-Busby SM¹, Hoffner S^{1,2}, Valafar F^{1#}. ¹Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Identification of lineage for *Mycobacterium tuberculosis* can help in contact tracing, understanding of transmission dynamics, and improving the effectiveness of treatment programs. The current techniques for lineage genotyping include mycobacterial interspersed repetitive units – variable tandem repeats (MIRU-VNTR), spoligotyping and SNP-typing. However, these methods can produce discordant or inconclusive results. To investigate this, we reconstructed the whole genome phylogeny of 4568 isolates and used it to determine the lineage of each isolate. We then compared the results to lineage classification of MIRU-VNTR and spoligotyping.

METHODS

The lineage typing through MIRU-VNTR and spoligotyping patterns was performed using a custom software called MiruHero. Genomes were labeled ‘discordant’ when the lineage typing of the methods disagreed. We then created a phylogeny from 4568 WGS of *M. tuberculosis* as follows. Raw reads were alignment variant calling was performed with respect to H37Rv. A multisequence FASTA file was created by concatenating the SNP calls in each genome. The tree was created using RAxML v8.2.10.

RESULTS

There were 111 isolates that were identified by MiruHero as discordant between spoligotyping and MIRU-VNTR. The WGS SNP method identified 255,017 polymorphic positions, and lineage typed all isolates spanning across all 7 lineages. The clustering on the phylogenetic tree was largely agreeable with MIRU-VNTR and spoligotyping. The discordant isolates grouped within lineages that were different from the results of either method.

CONCLUSIONS

WGS phylogeny was able to resolve the discordance created by MIRU-VNTR and spoligotyping, confirming that a WGS SNP phylogenetic approach can potentially provide a greater resolution than traditional methods.

E9. **AN UPDATED FUNCTIONAL ANNOTATION OF MYCOBACTERIUM TUBERCULOSIS REFERENCE STRAIN H37RV**

Modlin S, Gunasekaran D, Zlotnicki A, Elghraoui A, Kuo N, Chan C, Valafar F[#]. Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA.

[#]Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Most experimental work and nearly all genome assemblies of *M. tuberculosis* use reference strain H37Rv. TubercuList remains the primary *M. tuberculosis* gene annotation resource, despite being several years outdated. We updated the H37Rv reference annotation through systematic manual literature curation and stringent annotation transfer based on protein structural similarity.

METHODS

We identified 1,725 ambiguously annotated coding regions (CDSs) from TubercuList, then (1) systematically curated functional annotations from literature and (2) systematically named gene products according to similarity between proteins structures modeled using I-TASSER and solved protein structures from Protein Data Bank. Thresholds for functional assignment were determined through positive control set of proteins of known function.

RESULTS

We added function to 995 (57%) ambiguously annotated CDSs. Processes implicated in long-term persistence and obligate pathogenesis in genotoxic host microenvironments were overrepresented in our annotations, including lipid metabolism, polyketide biosynthesis, and membrane efflux. Our structural similarity approach circumvented challenges in identifying pathogenic effectors: (1) lack of known homologs, (2) low sequence similarity with analogs, and (3) difficulty replicating the host environment. Through this approach we ascribed function to dozens of PE/PPE family proteins, sixteen potential efflux proteins, and numerous putative effector proteins that mimic host protein structures and may manipulate host transcription, vesicular trafficking, immune cell fate, and pathogen-derived cargo localization.

CONCLUSIONS

By manually curating experimental characterizations from literature and inferring function from shared protein structure, we provide the most comprehensive *M. tuberculosis* genome annotation and new insight into *M. tuberculosis* metabolism, pathogenicity, antibiotic-resistance, virulence, and host-interaction.

E10. **REPRODUCIBILITY OF MINIMAL INHIBITORY CONCENTRATION VALUES FOR TWELVE ANTI-TUBERCULOSIS DRUGS USING THE SENSITITRE™ MYCOTB PLATFORM**

Morlock GP, Burns SP, Willby M, Posey JE. Laboratory Branch, Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA.

BACKGROUND

Drug susceptibility testing of *Mycobacterium tuberculosis* has traditionally involved culturing an isolate in media containing a single “critical concentration” of antibiotic. As the understanding of the molecular basis of *M. tuberculosis* drug resistance increases, there is a developing interest in using Minimal Inhibitory Concentration (MIC) testing to correlate specific mutations with levels of phenotypic resistance.

METHODS

The Sensititre™ MYCOTB platform is a broth microdilution system that includes twelve antibiotics. Ninety-one multidrug-resistant (MDR) or extensively drug-resistant (XDR) *M. tuberculosis* isolates were tested using this system. Each isolate was tested twice and visually read after 21 and 28 days of incubation. This resulted in four independent MIC readings for each isolate. Reproducibility was assessed by calculating the percentage of the replicates that had MIC values that were; identical or one, two and three (or greater) doubling dilution(s) different.

RESULTS

The percentage of test replicates with identical MIC values were as follows (percent): Rifampin (99.7), Isoniazid (91.3), Kanamycin (90.8), Amikacin (83.5), Ofloxacin (82.9), Moxifloxacin (82.9), Ethambutol (81.2) Cycloserine (74.0), Streptomycin (70.2), Para-aminosalicylic acid (68.2), Ethionamide, (59.2) and Rifabutin (59.0).

CONCLUSION

These results demonstrate variable reproducibility of MIC values amongst the twelve antibiotics. This variability might be partially mitigated by establishing interpretation guidelines, especially for those drugs in which trailing endpoints are frequently observed. The study isolates are also being sequenced in order to compare polymorphisms in known, and putative, drug resistance-associated loci with the MIC data. This analysis will be used to evaluate the accuracy of the MIC values.

E11. **LONG –READ SEQUENCING KINETICS REVEAL *MYCOBACTERIUM TUBERCULOSIS* CLINICAL ISOLATES SHARE EPIGENETIC PATTERNS DISTINCT FROM REFERENCE STRAIN H37RV**

Morrissey C¹, Modlin S¹, Conkle-Gutierrez D¹, Kim C¹, Mitchell S¹, Hoffner S², Valafar F^{1#}. ¹Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden.

#Corresponding Author: faramarz@sdsu.edu; This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

DNA methylation (DNAm) mediates processes integral to bacterial physiology, evolution, and adaptation, yet is scarcely explored in *M. tuberculosis* clinical strains. Single-molecule real time sequencing (SMRT-sequencing) permits finished *de novo* genome assembly and genome-wide DNAm detection with single-base resolution. We analyzed SMRT-sequencing kinetics to survey the landscape of epigenetic variation in *M. tuberculosis* clinical strains.

DESIGN/METHODS

We assessed how the DNA methylome of *M. tuberculosis* differs in accord with DNA methyltransferase (MTase) genotypes in 93 SMRT-sequenced (PacBio) mostly M/XDR *M. tuberculosis* clinical isolates and reference strains and built reference DNA methylomes for 26 MTase genotypes across the known *M. tuberculosis* MTases.

RESULTS

Sequencing kinetics showed that MTase genotype correlates reliably and strongly with DNAm patterns. Remarkably, H37Rv's methylome is dissimilar to most clinical strains and accounts for more differences than SNPs, even in the most phylogenetically distant isolates. *M. tuberculosis* harbors over 5,400 DNAm motifs, affecting over half of annotated coding sequences, yet differences due to DNAm are nearly unacknowledged in the literature. Of our sequenced isolates, under 5% have an MTase activity profile matching H37Rv and over one-third have an opposite profile.

CONCLUSION

DNAm has marked phenotypic consequences in diverse prokaryotes and affects transcription in *M. tuberculosis*. Our findings implicate a larger role for DNAm in *M. tuberculosis* physiology than currently appreciated and highlight a dire need for reference isolates with methylomes similar to clinical strains'. This work underscores the value of SMRT-sequencing for capturing the full spectrum of clinical strain variation and a need for standard comparative epigenomics methods for prokaryotes.

E12. GENOME-SCALE METABOLIC MODELING IN *M. TUBERCULOSIS*: UPDATING THE TOTAL NUMBER OF METABOLIC GENES FOR A MORE COMPLETE PICTURE

Onorato M, Gunasekaran D, Modlin S, Valafar F. Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA.

BACKGROUND

In silico metabolic models represent metabolic capabilities of an organism and incorporate biophysical constraints to simulate organismal functions including gene essentiality, growth rates, and metabolic fluxes. These simulation results have been verified experimentally for dozens of microbes. Currently, models for *M. tuberculosis* (*Mtb*) simulate *in vivo* and *in vitro* capabilities with modest predictive power, and a more complete metabolic model would enable more accurate simulations.

METHODS

We created a new *Mtb* metabolic model by incorporating previously unannotated metabolic genes (recently annotated by our lab) into the most up-to-date model, iEK1011. This entailed i) standardizing metabolite and reaction nomenclature between models, ii) reconciling annotation and metabolic pathway differences according to published experimental evidence, and iii) adding nearly one hundred previously unannotated functional genes (and corresponding metabolic enzymes) to the model using COBRApy, a Python package.

RESULTS

We tested our model by systematically performing single gene deletion simulations, which enabled us to predict gene essentiality for *Mtb* growth. Growth was predicted in the following simulated media: Middlebrook m7H10, Griffin, deJesus, Lowenstein-Jensen, and 'physiological' (*in vivo*). We compared our results to experimental data to determine percentages for all true and false positives and negatives, and then compared these percentages to those published for model iEK1011.

CONCLUSION

For our next model iteration, we plan to annotate more of the *Mtb* genome and add functional genes to the model, connect more of the metabolic network by linking metabolites and filling gaps, and eventually incorporate macromolecular expression data, such as transcriptomics and proteomics.

E13. **IDENTIFICATION OF PUTATIVE COMPENSATORY MUTATIONS IN RPOA/C SUGGESTS CONTRIBUTION TO THE FIXATION OF RIF RESISTANCE IN *M. TUBERCULOSIS***

Ramirez-Busby SM¹, Hoffner S^{1,2}, Elmaraachli W³, Valafar F^{1#}. ¹Laboratory for Pathogenesis of Clinical Drug Resistance and Persistence, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA; ²Karolinska Institute, Stockholm, Sweden; ³Division of Pulmonary, Critical Care, and Sleep Medicine, University of California, San Diego, San Diego, CA, USA.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Rifampicin (RIF) is an important first-line drug used to treat tuberculosis (TB). Without RIF the standard treatment duration could increase by one or more years. The rise in the prevalence of RIF resistance is largely attributed to fixation of resistance alleles in the RRDR within *rpoB*. Although mutations in the RRDR are known to have a fitness cost, compensation has been shown to alleviate this effect. We performed a large-scale association study on over 4000 whole-genome sequences of clinical *M. tuberculosis* isolates to determine the prevalence of compensatory mutations.

METHODS

We analyzed 4305 WGS of *M. tuberculosis* available on NCBI and identified the genotypic (RRDR)-phenotypic (BACTECT MGIT960) association as well as the association of a mutant RRDR to known compensatory mutations. We further sought to identify putative compensatory mutations based on a novel association method.

RESULTS

The sensitivity and specificity of a mutant RRDR for RIF resistance were 88.1% and 99.5%, respectively. Only 19% of RIF-resistant isolates had a previously reported compensatory mutation in *rpoC* or *rpoA*. We identified 118 *rpoC* and 18 *rpoA* novel mutations that co-occurred with a mutant RRDR and were considered putatively compensating.

CONCLUSION

The sensitivity was lower than expected, suggesting heterogeneity or an alternative mechanism of resistance. A low frequency of known compensatory mutations suggests that there may be other mutations compensating for the deleterious effect of a mutant RRDR. One such novel variant in *rpoC* was highly associated with a mutant RRDR and the East-Asian lineage, suggesting a lineage-specific mechanism of compensation.

E14. **“HOLE” GENOME SEQUENCING: ILLUMINA BLIND SPOTS IN THE *M. TUBERCULOSIS* H37RV GENOME**

Robinhold C, Shmaya T, Modlin S, Valafar F#. LPCDRP, Bioinformatics and Medical Informatics Research Center, San Diego State University, San Diego, CA, USA.

#Corresponding Author: faramarz@sdsu.edu. This work has been supported by grants from National Institute of Allergy and Infectious Diseases (NIAID) grant R01AI05185.

BACKGROUND

Illumina short-read sequencing has become the favored sequencing technology for *M. tuberculosis*. However, certain GC-rich, palindromic, and highly repetitive regions suffer from uncertain base calling due to low coverage, amplification bias, and ambiguous read mapping. Researchers frequently assume that excluding PE/PPE genes entirely addresses this problem. In this project we show that the problem is not limited to PE/PPE genes. We provide a list of “blind spots” in the *M. tuberculosis* genome that cannot be reliably sequenced by Illumina.

DESIGN/METHODS

We used 542 publicly available Illumina-sequenced *M. tuberculosis* isolates to determine which positions in the H37Rv reference strain were blind spots. Our pipeline to identify low coverage positions consisted of trimming reads using Trimmomatic, aligning reads to the reference strain using BWA, and creating an mpileup file using SAMtools. Positions with low depth that appeared in a statistically significant number of isolates were considered “blind spots.”

RESULTS

We identified 139,858 individual blind spot positions (3.17% of the H37Rv genome). High GC content, repeat regions, and/or palindromes explained 70.7% of the blind spots. We identified 13 significant motifs that appeared in the unexplained blind spots. Blind spot regions fell within 332 different genes, only 88 (26.5%) of which were PE/PPE genes.

CONCLUSION

Many blind spots fall within genes that are important for virulence and drug resistance. The list of positions we identified provides an important resource to the TB research community, allowing for an informed interpretation of genomic data, which will prove valuable for genome-wide association studies, phylogenomic studies, and in characterizing hypothetical genes.

E15. **MOLECULAR CHARACTERIZATION AND DRUG SUSCEPTIBILITY OF *MYCOBACTERIUM TUBERCULOSIS* FROM EASTERN SUDAN**

Shuaib YA^{1,2,3}, Merker M¹, Khalil EA⁴, Schaible U¹, Wieler LH^{3,5}, Bakheit MA⁶, Mohamed-Noor SE², Abdalla MA², Richter E^{1,7}, Kranzer K¹, Niemann S¹. ¹Research Center Borstel, Borstel, Germany; ²College of Veterinary Medicine, Sudan University of Science and Technology, Khartoum, Sudan; ³Institute of Microbiology and Epizootics, Freie Universität Berlin, Berlin, Germany; ⁴Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan; ⁵Robert Koch Institute, Berlin, Germany; ⁶Faculty of Veterinary Medicine, University of Khartoum, Khartoum, Sudan; ⁷Labor Limbach, Heidelberg, Germany

BACKGROUND

Tuberculosis (TB) is endemic in Eastern Sudan with an incidence of 275 per 100000 population. Data on genetic diversity of *Mycobacterium tuberculosis* and Multi drug resistant (MDR) are missing in this area. Therefore, in this study we focused on investigating drug susceptibility and population structure of *M. tuberculosis* in Eastern Sudan.

METHODS

A total number of 383 sputum samples were collected from Kassala, Port Sudan, and El-Gadarif hospitals from June to October 2014 and from January to July 2016. The samples were decontaminated and cultured into MGIT and onto Löwenstein-Jensen and Stonebrink slants for mycobacterial growth. Real-time PCR was conducted to verify the sensitivity of TB diagnosis using light microscopy in the study area. In addition, line probe assay, ITS gene sequencing, spoligotyping, MIRU-VNTR typing and whole generation sequencing (WGS) were also conducted.

RESULTS

Culture of the specimens revealed growth of mycobacteria from 51.2% (196/383) of all samples. The majority of the isolates (n=171) were *M. tuberculosis* while the rest were either *M. intracellulare* (n=14) or mixtures of *M. tuberculosis* and *M. intracellulare* (n=11). Any drug resistance was detected in 22.6% (39/177) of all of the *M. tuberculosis* isolates while MDR was detected in 10.2% (18/177). The use of molecular techniques showed that 73.4% of the isolates belong to lineage 3 (Delhi/CAS).

CONCLUSION

There was an evidence of MDR transmission and acquisition. Lineage 3 (Delhi/CAS) isolates are responsible for causing the majority of TB cases.

Keywords: Genotype, DST, tuberculosis, human, Sudan

E16. DEVELOPMENT OF A MYCOBACTERIOLOGY FALSE-POSITIVE INVESTIGATION TOOLKIT WITH AN ONLINE CASE STUDIES MODULE

Youngblood ME, Stafford C, Yakrus M, Oyegun E, Domaaal R, Starks A, Dalton T, Gaynor AM, Ancona N, Johnston SP. Centers for Disease Control and Prevention, Atlanta, GA; Association of Public Health Laboratories (APHL), Silver Spring, MD, USA.

BACKGROUND

False-positive results in the mycobacteriology laboratory can be caused by the transfer of bacilli from one specimen to another specimen not containing bacilli. In 1997, CDC and Association of State and Territorial Public Health Laboratory Directors (now known as APHL) developed a videotape and study booklet titled “Recognition and Prevention of False-Positive Test Results in Mycobacteriology – A Laboratory Training Program.” The program was designed to help mycobacteriology laboratorians recognize and prevent false-positive test results but has not been updated in recent years.

INTERVENTION/RESPONSE

To update the training material for false-positive investigations, a project was initiated for to address the needs of mycobacteriology laboratory personnel and tuberculosis (TB) control program staff. The toolkit will include job aids, posters, and templates aimed at preventing and monitoring for potential false-positives. Documents will provide guidance and laboratory best practices for performing a false-positive investigation. In collaboration with APHL, an interactive online training module is under development and consists of five case studies (pre-analytical, analytical, and post-analytical examples) to guide participants through potential false-positive investigations.

RESULTS

The toolkit and online training module will be available in 2019. Module usage will be monitored quarterly. Materials will be shared with laboratorians attending the National Conference on Laboratory Aspects of Tuberculosis in April 2019.

CONCLUSION

Mycobacteriology laboratory personnel and TB control program staff will have updated resources available to help prevent, identify, and investigate potential false-positive results. This toolkit will allow mycobacteriology laboratories to tailor false-positive investigation policies to help identify the most likely cause of erroneous test results.