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Tuberculosis among Healthcare Workers, United States, 2010-2016

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Abstract

Tuberculosis among Healthcare Workers, United States, 2010-2016
By Thitipong Mongkolrattanothai

Background: Occupational risk of tuberculosis (TB) remains a public health concern for healthcare workers (HCWs). We compare the characteristics between HCWs and other adults in the United States, and describe the measure of association between HCWs and exclusively pulmonary TB (PTB) as well as sputum culture conversion, by examining U.S. national TB surveillance data from 2010 to 2016.

Methods: TB cases reported from 50 states and the District of Columbia from 2010 through 2016 were analyzed. Demographic, clinical, and risk factors were compared between HCWs with TB and other adults with TB. Multivariable logistic regression models were used to assess the relationship between the main exposure variable, HCW/other adult, and main outcome variables, disease site and sputum conversion.

Results: Among 64,770 total TB cases involving patients 18 years of age or older reported from 2010 through 2016 to the National Tuberculosis Surveillance System, 2,460 (4%) were classified as HCWs, and 62,310 (96%) were classified as other adults. HCWs were less likely to have exclusively PTB (uOR, 0.70 [95% CI, 0.64-0.76]). Analyses of HCWs were also stratified by origin of birth. Among U.S.-born persons with TB, there was no significant difference between HCWs and other adults for PTB (uOR, 0.89 [95% CI, 0.74-1.07]; aOR, 1.09 [95% CI, 0.90-1.31]). Among non-U.S.-born persons, unadjusted and adjusted estimates show that HCWs were less likely than other adults to have exclusively PTB (uOR, 0.67 [95% CI, 0.61-0.74]; aOR, 0.76 [95% CI, 0.69-0.84]). HCWs were more likely to have a sputum culture conversion of < 60 days compared with other adults (uOR, 1.49 [95% CI, 1.26-1.77]; aOR, 1.24 [95% CI, 1.04-1.48]).

Conclusion: Although there may be occupational risks in healthcare settings, this study demonstrates that being a HCW was negatively associated with PTB. HCWs are more likely to convert their sputum culture to negative within 60 days compared with other adults. Other variables such as birth country status may be a more important risk factor for TB, even among HCWs.

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Background

Epidemiology of Tuberculosis

Tuberculosis (TB) is an airborne infectious disease caused by a group of closely related bacterial species termed *Mycobacterium tuberculosis* complex (1). The incidence, prevalence, and burden of TB vary by country. Nonetheless, globally, TB is a major public health concern that accounted for approximately 1.7 million deaths and 10.4 million new cases in 2016 (2). Furthermore, approximately 23% of the world population has latent TB infection (LTBI), an asymptomatic condition that is not infectious (3). Although antimicrobial drugs can be used to treat active TB disease and prevent LTBI from developing into active TB disease, there have been growing concerns of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB transmission (4–6). MDR and XDR TB have been associated with poor treatment outcomes (7,8)

In the United States, there has been a marked decrease in incidence of TB from 52.6 cases per 100,000 population in 1953 to 2.9 cases per 100,000 population in 2016 (1). The steady annual decrease in incidence was briefly interrupted from 1985 through 1992; the resurgence was associated with factors including infrastructure issues, increased immigration, congregate settings, and the human immunodeficiency virus (HIV) epidemic (9–11). Since 1993, the annual decrease has been greater than 0.2 cases per 100,000 persons. This decline slowed during 2013 to 2015 where case rates stagnated at approximately 3.0 cases per 100,000 population (12). The reported number of TB cases in 2016 demonstrated a 3.6% decrease from 2015 corresponding to a case rate of 2.9 per 100,000 persons (1).

The reported incidence of TB rates varies between states, with nine states having rates above the national average. Among these states, four states including California, Florida, New York, and Texas accounted for more than half of the total cases in the United States. The rates of TB are higher for many U.S.-affiliated Pacific Islands which range from 1.8 cases per 100,000 in American Samoa to 243.9 cases per 100,000 in the Republic of the Marshall Islands (1). Although drug resistance has become a concern for many countries, the percentage of TB cases that are drug resistant (including MDR and XDR TB) within the United States has remained stable for the past 20 years (1,4). A major risk factor for TB disease is travelling to or being born in countries with high rates of TB. In 2016, the rate of TB diagnosed in the U.S. among non-U.S.-born persons was 14.7 cases per 100,000 population compared to 1.1 cases per 100,000 population among U.S.-born persons; this corresponds to a case rate that is approximately 14 times higher for non-U.S.-born persons (1). Additional risk factors include diabetes, alcohol use, co-infection with HIV, drug use, being homeless, and being a resident of a correctional facility (2,13).

Epidemiology of TB in Healthcare Workers

TB poses a health risk to healthcare workers (HCWs) globally. Outbreaks of varying magnitudes of severity have been documented in healthcare settings as a result of patient-to-HCW transmission as well as HCW-to-patient transmission (14–16). Although risk is substantially higher in lower/middle-income endemic countries, many high-income countries have a significant number of healthcare-related transmissions (17,18). The extent of occupational risk of TB depends on department, patient population,

effectiveness of infection control measures, type of healthcare worker, and location of the facility (15,19,20).

The occupational risk of TB for HCWs was demonstrated during a series of outbreaks during the early 1990s where patient-to-HCW transmission of TB and MDR TB occurred (5,21,22). During 1995 to 2007, the estimated annual incidence of TB for HCWs in United States was similar to that of the overall national TB case rate, 3.8-4.6 and 4.4-5.1 cases per 100,000 population respectively; however, the incidence of TB among non-U.S.-born HCWs in the United States was 10 times higher than among U.S.-born HCWs (20). Studies have suggested that immigrants to the United States, especially those from TB-endemic countries, enter with no apparent health problems but have LTBI from prior TB disease exposure (23). A 2015 analysis of recent TB transmission estimated that over 80% of all TB cases in the United States originated from reactivation of LTBI (24). Reactivation of LTBI has been estimated to account for anywhere between 70% to 84% of TB cases in the non-U.S.-born population while the most recent national estimate from 2016 suggested that over 90% of TB among non-U.S.-born persons is caused by reactivation of LTBI (25–27).

Epidemiology of Pulmonary TB

The highest proportion of reported TB cases in the United States are pulmonary TB (PTB), followed by extrapulmonary TB (EPTB), and concurrent pulmonary-extrapulmonary TB, respectively (1). The proportion of EPTB cases increased from 15.7% in 1993 to 21.8% in 2010 while the proportion of PTB cases decreased from 84.3% in 1993 to 78.2% in 2010. That trend has marginally reversed in recent years; the percentage of PTB, and EPTB cases in 2016 were 79.7%, and 20.3%, respectively. In the

United States, the epidemiology of PTB is assumed to be similar to TB epidemiology due to most cases being diagnosed with PTB.

Sputum Culture Conversion

Sputum conversion is important as it is a measure of treatment success and infectiousness (28). Sputum culture conversion is measured as the amount of time that a culture obtained from an active TB case takes to become negative. Patients typically have a culture taken at the time of diagnosis and approximately after two months of intensive phase of treatment. A patient is considered as non-infectious after a sputum culture has become negative (29). Patients who fail to achieve a sputum conversion by two months may be more likely to have poor treatment outcomes (30–32).

Objective

HCWs may have differential risk factors for TB, especially occupational risk factors, when compared to the general population; therefore, epidemiology of TB for HCWs needs to be updated. The last published epidemiological data describing the epidemiology of TB among HCWs in the United States ranged from 1995-2007. The study found differences between HCW characteristics based on country of birth as well as association between HCWs and PTB/EPTB. However, the association has yet to be explored (20). Additionally, sputum culture conversion has not been studied in the context of public health epidemiology in the United States and is an important indicator. The objectives of this analysis were to 1) compare characteristics between HCWs and other adults, 2) compare characteristics between non-U.S.-born HCWs and U.S.-born HCWs, and 3) describe the measure of association between HCWs and PTB as well as

sputum conversion in the United States by examining U.S. national TB surveillance data from 2010 to 2016. Updates will reflect the changing epidemiology of TB in the United States including demographics and clinical characteristics for HCW and other adults.

Methods

TB Surveillance System

TB is a nationally notifiable disease and reporting is mandated for all 50 states and the District of Columbia. Data are collected by local and state health departments and submitted electronically to the Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination. Active TB cases are reported to the National Tuberculosis Surveillance System (NTSS) at the CDC through the Report of Verified Case of Tuberculosis (RVCT) (33). This standardized form includes demographic, clinical, laboratory, treatment, risk factors, and outcome characteristics reported for TB cases from all 50 states, the District of Columbia, and U.S. territories. The RVCT form was revised in 2009 to include additional variables such as nucleic acid amplification test results, interferon gamma release assay results, primary reason for TB disease evaluation, and additional TB risk factors (1).

Some states use a modified version of the RVCT form; the forms unique to these jurisdictions contain the same data contained in the RVCT form (33). Additional data and locally defined variables included in those forms are not sent to the CDC. The CDC provides technical assistance and funding to health departments for TB case reporting. However, health departments are responsible for developing procedures and policies for reviewing incomplete or incorrect data. Surveillance systems specific to each state vary in terms of structure, and organization. Subsequently, completeness and quality assurance of TB case reporting may vary according to each jurisdiction.

Measures

All variables included in the analysis except for recent transmission (RT) are defined in the RVCT Instruction Manual (33). TB cases were categorized by occupational status, site of disease, and sputum culture conversion. Occupational status was reported as HCW or other adults. HCWs were defined as any paid or unpaid persons who worked in a healthcare setting within 12 months prior to TB diagnosis. Other adults were those who did not meet the HCW criteria and included persons who were unemployed and retired. Site of disease was reported as PTB or EPTB and concurrent PTB/EPTB. PTB was defined as TB disease that occurs only in the lungs, typically with clinical symptoms (cough) and an abnormal chest x-ray. EPTB was defined as TB disease that occurs in places other than the lung including but not limited to the lymph nodes, pleura, brain, kidney, or bones. Sputum culture conversion was categorized as a sputum culture conversion of less than (<) 60 days or greater than and equal to (≥) 60 days. Sputum culture conversion was defined as the time from date of the first positive sputum culture to the date of documented sputum conversion and restricted to patients who were alive at diagnosis, had a confirmed positive sputum culture result at diagnosis, and documented sputum conversion.

Demographic information included sex, age, origin of birth, and race/ethnicity. Origin of birth was categorized as U.S.-born or non-U.S.-born. U.S.-born is defined as any persons born in any of the 50 states or the District of Columbia, or born outside of the United States to at least one parent who was a U.S. citizen. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Hispanic, Asian, Native American/Alaska Native/Hawaiian Native/Pacific Islander, or multiple races.

Clinical information included tuberculin skin test (TST) result at time of TB diagnosis, interferon gamma release assay (IGRA) result at time of TB diagnosis, culture result, initial drug resistance, and human immunodeficiency virus (HIV) result at time of diagnosis. TST results at time of diagnosis were categorized as positive, negative, or not performed/unknown. TST results were reported as positive if patients met the criteria for a positive TST result, and negative if patients did not meet the criteria. The criteria for a positive TST result was based on induration sizes of 5, 10, or 15 millimeters dependent on additional risk factors (or lack thereof) such as HIV status and age. IGRA results were categorized in the same manner as TST results. The criteria for a positive IGRA result was based on the presence of at least one positive blood test result. Culture results were categorized as positive for *Mycobacterium tuberculosis* for sputum only, tissues/other body fluids only, or sputum and tissues/other body fluids. Sputum-only culture result was defined as any positive spontaneous or induced sputum cultures collected before two weeks after receiving treatment. Tissues/other body fluids-only culture result was defined as any positive fluid or tissue culture (other than sputum) collected before two weeks after receiving treatment. Initial drug resistance was categorized as susceptible to isoniazid (INH) and rifampin (RIF), INH monoresistance, RIF monoresistance, MDR, or XDR. MDR was defined as any TB bacteria that is resistant to both INH and RIF. XDR was defined as any TB bacteria that meets the criteria for MDR, and has resistance to any fluoroquinolone and at least one of three injectable second-line drugs. Initial drug resistance was limited to results reported from conventional drug susceptibility tests (DST) and do not include rapid DST test results. HIV results were categorized as negative, positive, refused HIV testing, or unknown/indeterminate/not offered.

Documentation of an HIV test from a hospital, clinic, or private provider result was required for positive, negative, and indeterminate results.

Risk factors included previous diagnosis of TB, RT, excess alcohol use, drug use, incarceration at time of diagnosis, and residential status at a longterm care facility at time of diagnosis. Previous diagnosis of TB was categorized as recurrent or non-recurrent TB. Recurrent TB was categorized as any past verified report of TB, or prior completion of therapy for TB disease. RT was categorized in the same manner as previous diagnosis of TB, RT or non-RT. RT was defined using a plausible source case method based on *M. tuberculosis* genotyping, residential location, age, and timing of diagnosis relative to a given case. Details of the method are described elsewhere (34). Excess alcohol use within the past year was categorized as excess alcohol use or no excess alcohol use. There was no standard definition for excess alcohol use and this variable was assessed during interviews with the patient. Drug use within the past year was categorized as drug use or no drug use and also assessed during interviews with patients. Drug use included both injection and non-injection drug use. Injection drug use was defined as any use of hypodermic needles for the injection of drugs not prescribed by a health care provider and non-injection drug use was defined as any use of licensed, prescription, or illegal drugs that were not injected or prescribed by a health care provider. Incarceration at time of diagnosis was categorized as incarcerated or not incarcerated. Incarceration was defined as being an inmate of any correctional facility at the time of diagnosis. Similarly, residential status at a longterm care facility at time of diagnosis was categorized as resident or not a resident of a longterm care facility.

Treatment outcomes included method of TB treatment, and completion of TB treatment. Method of TB treatment was categorized as directly observed therapy (DOT), self-administered therapy (SAT), both DOT and SAT, or unknown/missing. DOT involved the direct visual observation of ingestion of medication by a health care provider or trained individuals while SAT involved no direct supervision. Completion of TB treatment was categorized as completed therapy, did not complete therapy, or unknow/missing.

Analyses

This study included TB cases reported from January 1, 2010 through December 31, 2016. Sputum culture conversion, method of TB treatment, and completion of treatment were assessed on follow-up, so only cases through 2014 were included for culture conversion, method of TB treatment, and completion of treatment analyses to allow for two years of case follow-up. Analyses excluded U.S. territories and were limited to reported cases from 50 states and the District of Columbia. Analyses were also limited to persons 18 years of age or older. Demographic, clinical, and risk factors were compared between HCWs with TB and other adults with TB using descriptive statistics and bivariate statistical analyses with unadjusted odds ratios (uOR) and 95% confidence interval (CI). Demographic, clinical, and risk factors analyses among HCWs with TB were also stratified based on origin of birth. Although disease site was analyzed in both non-stratified and stratified analyses, PTB was used as the referent group since EPTB and concurrent PTB/EPTB were not combined into one category.

Two separate multivariable logistic regression models were used to assess the relationship between the main exposure variable, HCW/other adult, and main outcome

variables, disease site and sputum conversion. Based on current available data and literature, sex, age, race/ethnicity, origin of birth, previous TB diagnosis, excess alcohol use, drug use, incarceration, RT, drug resistance, and HIV status were used as potential covariates to address possible confounding or effect modification (1). A determination to assess interaction of HCW by origin of birth for disease site was made in advance; prior analyses showed a greater percentage of EPTB among non-U.S.-born HCWs in the United States suggesting differences in disease site by origin of birth (1). Collinearity diagnostics and interaction assessment were conducted prior to model fitting. A backwards elimination variable selection process was used to derive the most descriptive multivariable model for each outcome. Results of the final models are presented as adjusted odds ratios (aOR) and 95% CI.

The original dataset included 72,751 reported cases of TB from 2010 through 2016. This number was reduced to 64,770 after excluding persons under 18 years of age, and cases reported from U.S. territories. The final model for disease site included 62,021 cases and the final model for sputum conversion included 21,841 cases after restricting the dataset based on availability of the covariate, and outcome data. The flowchart diagram for all data exclusions is shown on Figure 1.

All analyses were conducted using SAS, version 9.3 (SAS Institute, Cary, NC). Statistical significance was determined at alpha = 0.05.

Ethical Review

The protocol for this project was reviewed by both the Centers for Disease Control and Prevention Analytic Steering Committee and Emory University Institutional

Review Board. It was determined to be public health surveillance activity not requiring human subjects research review.

Results

HCWs with TB Compared with Other Adults with TB

Among 64,770 total TB cases involving patients 18 years of age or older reported from 2010 through 2016 to the NTSS, 2,460 (4%) were classified as HCWs, and 62,310 (96%) were classified as other adults (Table 1). For demographic characteristics, compared with other adults with TB, HCWs with TB were more likely to be women (uOR, 3.92 [95% CI, 3.59-4.28]), be non-U.S.-born (uOR, 1.45 [95% CI, 1.32-1.59]), be non-Hispanic black (uOR, 1.92 [95% CI, 1.67-2.20]), or be Asian (uOR, 1.80 [95% CI, 1.58-2.06]). For clinical characteristics, HCWs were more likely to have EPTB (uOR, 1.56 [95% CI, 1.43-1.71]), have concurrent PTB/EPTB (uOR, 1.16 [95% CI, 1.02-1.33]), have a positive TST result (uOR, 1.93 [95% CI, 1.62-2.31]), have a sputum conversion of < 60 days (uOR, 1.52 [95% CI, 1.31-1.77]), or have any drug-resistant TB (uOR, 1.32 [95% CI, 1.15-1.52]) than other adults. HIV test results, and IGRA results were not significantly different between HCWs and other adults. For risk factors, HCWs, compared with other adults, were less likely to be a RT case (uOR, 0.73 [95% CI, 0.62-0.87]), have previous diagnosis of TB (uOR, 0.68 [95% CI, 0.55-0.84]), have excess alcohol use within the past year (uOR, 0.23 [95% CI, 0.18-0.29]), or have drug use within the past year (uOR, 0.21 [95% CI, 0.16-0.29]). For treatment outcomes, compared to other adults, HCWs were more likely to be on SAT for TB (uOR, 2.31 [95% CI, 2.01-2.65]), be on both SAT and DOT (uOR, 1.32 [95% CI, 1.19-1.47]), or complete TB treatment (uOR, 3.29 [95% CI, 2.61-4.17]).

Non-U.S.-born HCWs with TB Compared with U.S.-born HCWs with TB

Among 2,460 TB cases classified as HCWs, 627 (25%) were born in the United States, and 1,833 (75%) were born outside of the United States (Table 2). For demographic characteristics, compared with U.S.-born HCWs, non-U.S.-born HCWs with TB were less likely to be women (uOR, 0.62 [95% CI, 0.50-0.76]). Age groups were not significantly different between U.S.-born and non-U.S.-born HCWs. For clinical characteristics, non-U.S.-born HCWs were more likely to have EPTB (uOR, 2.09 [95% CI, 1.66-2.62]), have concurrent PTB/EPTB (uOR, 1.58 [95% CI, 1.15-2.18]), have a positive TST result (uOR, 2.22 [95% CI, 1.55-3.17]), have a positive IGRA result (uOR, 1.73 [95% CI, 1.21-2.50]), have a sputum conversion of < 60 days (uOR, 1.71 [95% CI, 1.20-2.44]), or have any drug-resistant TB (uOR, 2.60 [95% CI, 1.71-3.95]) than U.S.-born HCWs. HIV test results were not significantly different between non-U.S.-born HCWs and U.S.-born HCWs. For risk factors, compared with U.S.-born HCWs, non-U.S.-born HCWs with TB were less likely to be a recent transmission case (uOR, 0.33 [95% CI, 0.23-0.46]), have excess alcohol use within the past year (uOR, 0.22 [95% CI, 0.14-0.35]), or have drug use within the past year (uOR, 0.09 [95% CI, 0.05-0.19]). Non-U.S.-born HCWs were more likely to have previous diagnosis of TB (uOR, 2.43 [95% CI, 1.28-4.60]) compared with U.S.-born HCWs. Residential status in a longterm care facility at diagnosis, method of TB treatment, and completion of TB treatment were not significantly different between U.S.-born and non-U.S.-born HCWs. There were no incarcerated U.S.-born HCWs reported to the NTSS during this time frame.

Disease Site for HCWs Compared with Other Adults

Unadjusted estimates show that HCWs with TB were less likely than other adults with TB to have PTB (uOR, 0.70 [95% CI, 0.64-0.76]). There was a statistically significant interaction by origin of birth on HCW status and disease site ($OR_{Mantel-Haenszel}$, 0.72, [95% CI, 0.66-0.78]; Breslow-Day Test for Homogeneity of Odds Ratios, $P = 0.0077$). For this reason, adjusted analyses for HCW and disease site are presented stratified on origin of birth (Table 3). The proportion of PTB among U.S.-born persons and non-U.S.-born persons were 75% and 67%, respectively. Among U.S.-born persons with TB, there was no significant difference between HCWs and other adults for PTB in both the unadjusted (uOR, 0.89 [95% CI, 0.74-1.07]) and adjusted (aOR, 1.09 [95% CI, 0.90-1.31]) models. Among non-U.S.-born persons, unadjusted estimates show that HCWs were less likely than other adults to have PTB (uOR, 0.67 [95% CI, 0.61-0.74]). After adjusting for potential confounders (sex, previous TB diagnosis, excess alcohol use, and RT), non-U.S.-born persons were still less likely than other adults to have PTB (aOR, 0.76 [95% CI, 0.69-0.84]). The Hosmer and Lemeshow goodness-of-fit test was not statistically significant (χ^2, 1.23; $P = 0.87$) which suggests the model fit the data. The final model for non-U.S.-born persons included sex, HIV status, excess alcohol use, and drug use as covariates. The Hosmer and Lemeshow goodness-of-fit test was not statistically significant (χ^2, 1.15; $P = 0.89$) which suggests the model fit the data.

Sputum Culture Conversion for HCWs Compared with Other Adults

Among persons with documented sputum conversion, unadjusted estimates show that HCWs were more likely to have a sputum conversion of < 60 days compared with other adults (uOR, 1.49 [95% CI, 1.26-1.77]). All assessed interaction terms were not

statistically significant. After adjusting for potential confounders (sex, race/ethnicity, origin of birth, initial drug resistance, excess alcohol use, and previous TB diagnosis), HCWs were still more likely to have a sputum conversion of < 60 days (aOR, 1.24 [95% CI, 1.04-1.48]) compared with other adults (Table 4). The Hosmer and Lemeshow goodness-of-fit test was not statistically significant (χ^2, 2.17; $P = 0.98$) which suggests the model was a good fit for the data.

Discussion

HCWs with TB differ from other adults with TB on multiple characteristics. Compared to other adults with TB, HCWs with TB were more likely to be women, be non-U.S.-born, have EPTB or concurrent PTB/EPTB, have a sputum conversion of < 60 days, have any drug-resistant TB, more likely to be on SAT or SAT and DOT, or complete TB treatment. After stratification on origin of birth, non-U.S.-born HCWs were less likely to be women, or a RT case compared with U.S.-born HCWs; non-U.S.-born HCWs were more likely to have EPTB, have concurrent PTB/EPTB, have a sputum conversion of < 60 days, have any drug-resistant TB, or have a previous TB diagnosis compared with U.S.-born HCWs. There was a statistically significant interaction between HCW status and disease site by origin of birth. Non-U.S.-born HCWs were less likely to have PTB compared with non-U.S.-born other adults. However, there was no significant difference between U.S.-born HCWs and other adults for PTB. HCWs were more likely to have a sputum conversion of < 60 days compared with other adults.

The last study that used NTSS data to examine TB among HCWs in the United States was conducted for years 1995 through 2007; the main findings showed that, compared to other adults, HCWs were more likely to be women, be non-U.S.-born, have EPTB, complete TB treatment, and have a reported HIV test result (20). Our findings concur with all associations found from this previous study except for HIV testing. Unlike previous studies, our study did not find a strong association between HCWs with TB and HIV status, compared with other adults with TB (20,35). This may be due to more complete reporting after revisions to the RVCT form were implemented in 2009. Another possibility is that monitoring and diagnostic testing for HIV co-morbidities has

increased in conjunction with an overall decrease in incidence of HIV in the United States (36). Accordingly, there was an increase in proportion of persons who reported a positive or negative HIV result. The percentage of persons from the previous study who did not have a reported HIV test result were 37% and 43% for HCWs and other adults, respectively (20). Our findings (Table 1) showed that the percentage of persons who did not have a reported HIV test result were 10% and 11% for HCWs and other adults, respectively.

The previous study found that non-U.S.-born HCWs who had TB were more likely to have INH monoresistant TB, have EPTB, and complete TB treatment compared to U.S.-born HCWs (20). Our study showed the same associations for non-U.S.-born HCWs and INH monoresistant TB as well as EPTB. However, our study did not find an association between non-U.S.-born HCWs and completion of TB treatment. The lack of association may simply be due differences in categorization of unknown/missing data; the previous study grouped patients who had unknown/missing data as did not complete TB treatment whereas our study divided completion of TB treatment into three distinct groups. This may also be due to a smaller sample size of HCWs in our study period or proportional differences in U.S.-born and non-U.S.-born HCWs. The proportion of U.S.-born HCWs and non-U.S.-born HCWs reported during 1995 to 2007 were 45% and 55%, respectively (20). From 2010 to 2016, these proportions have changed to 25% and 75% for U.S.-born HCWs and non-U.S.-born HCWs, respectively. Moreover, completion rates from 1995-2007 were 91% and 93% for U.S.-born HCWs and non-U.S.-born HCWs, respectively. Our study shows that completion rates for both U.S.-born and non-U.S.-born HCWs have improved to 94% and 96%, respectively.

To our knowledge, this is the first multivariable analysis study using national surveillance data to describe the associations between HCWs and PTB in the United States. Studies have found that EPTB cases mostly occurred among non-white racial/ethnic groups, particularly in black and Asian persons (10). Some studies have suggested that differences between PTB and EPTB in certain groups may be partially explained by immune-mediated or genetic predispositions (37). Other studies have described variations in circulating *M. tuberculosis* strains based on geographical differences (10). The largest number of TB cases in the United States are reported among Asian persons and most Asian persons with TB in the United States are non-U.S.-born (1). Consequently, it is not surprising that non-U.S.-born HCWs have a lower odds of PTB compared with non-U.S.-born other adults, but the same association is not present in U.S.-born persons.

Prior to this study, HCWs and sputum culture conversion have not been examined in the United States. Other studies conducted outside of the United States have shown sputum conversion to be a factor in predicting treatment outcomes (29,30). Based on the association between HCWs and sputum conversion, and TB therapy completion rates found in this study, this may suggest findings from previous studies to be true. Nonetheless, further investigation is needed to fully explain the association. Differences between sputum conversion may result from clinical characteristics including high initial sputum bacillary counts, drug resistance, miliary TB, and presence of bilateral radiologic lesions (38).

The main strength of our study is that it provides additional data on TB in HCWs using all nationally reported TB cases in the United States. Additionally, use of

multivariable models allows evaluation of the relative importance of HCW, as a predictor, in the presence or absence of potential confounders. Moreover, model fit statistics were not significant for any final models. This study also includes an update of existing demographic, clinical, risk factor, treatment outcome characteristics for TB among HCWs which was last reported for years 1995 through 2007 (20).

Limitations of the analysis included number of variables collected using RVCT. Risk factors included in the analysis are limited to variables collected in the public health surveillance dataset. Data on financial status, additional social and behavioral factors, additional clinical comorbidities, and LTBI information are not collected. Subsequently, this may not give a thorough picture of potential covariates that affect HCW and PTB or sputum culture conversion. Although the 2009 update to the NTSS was modified to include previous diagnosis of LTBI with incomplete treatment, only 1,637 (3%) cases were reported for 2010 through 2016. Many reports have suggested that reactivation of LTBI accounts for a significant number of TB cases among non-U.S.-born populations (25,27,39). For future studies, identification and reporting of LTBI progression for HCWs and other adults, especially those who are non-U.S.-born may be critical to accurately assess associations.

Another limitation is the number of unknow/missing data found in the dataset. Proportionally, the amount of unknow/missing data for HCWs and other adults for both treatment outcome and method of TB treatment were 7% and 10%, respectively, for 2010-2016 (Table 1). Approximately 8% of HIV status data in the NTSS for 2010 through 2016 is missing or unknown (Table 1). Reported data for HIV status in 2010 showed that approximately 22% of data were missing or unknown whereas there were

less than 5% unknown or missing reported data for years 2011 through 2016. This change can be explained by data reported by California; the state did not report HIV status from 2005 to 2010 (1). However, the percentage of total missing or unknown HIV status data is similar for HCWs (10%) and other adults (11%) so the impact on comparisons of HCWs and other adults is expected to be small. Completeness of TB reporting will provide more accurate reporting of results.

There are a host of risk factors for active TB disease, some of which may not have been explored extensively. PTB is the most prevalent form of TB, and occupational risk for HCWs has been demonstrated in several studies (18,20,40). Although there may be occupational risks in healthcare settings, this study demonstrates that being a HCW is not significantly associated with PTB only among U.S.-born persons. Rather, in accordance with numerous studies and reports, our findings suggest that being non-U.S.-born is an important risk factor for any TB disease in the United States, even among HCWs (1,20,26,41,42). Furthermore, this study shows that HCWs are more likely to be infectious for a shorter period of time after diagnosis, as evidence by culture conversion < 60 days and have better treatment outcomes compared with other adults. Even though the proportion of HCWs with TB is low compared with other adults with TB, vigilance should be maintained regarding the epidemiology of TB among HCWs. Ultimately, public health interventions in the United States should focus on control and prevention of TB among adults who are not HCWs, particularly those who were not born in the United States.

References

1. Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2016. Atlanta, GA: 2017.(https://www.cdc.gov/tb/statistics/reports/2016/pdfs/2016_Surveillance_FullReport.pdf)

2. World Health Organization. Global tuberculosis report 2017. 2017.(http://apps.who.int/iris/bitstream/handle/10665/259366/9789241565516-eng.pdf)

3. Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: A re-estimation using mathematical modelling. *PLoS Med*. 2016;13(10):e1002152.

4. Migliori GB, D'Arcy Richardson M, Sotgiu G, et al. Multidrug-resistant and extensively drug-resistant tuberculosis in the West. Europe and United States: epidemiology, surveillance, and control. *Clin. Chest Med.* 2009;30(4):637–65.

5. Dooley SW, Jarvis WR, Martone WJ, et al. Multidrug-resistant tuberculosis. *Ann. Intern. Med.* 1992;117(3):257–259.

6. Shah NS, Pratt R, Armstrong L, et al. Extensively drug-resistant tuberculosis in the United States, 1993-2007. *J. Am. Med. Assoc.* 2008;300(18):2153–60.

7. Johnston JC, Shahidi NC, Sadatsafavi M, et al. Treatment outcomes of multidrug-resistant tuberculosis: A systematic review and meta-analysis. *PLoS One*. 2009;4(9).

8. Cegielski JP, Kurbatova E, Van Der Walt M, et al. Multidrug-resistant tuberculosis

treatment outcomes in relation to treatment and initial versus acquired second-line drug resistance. *Clin. Infect. Dis.* 2015;62(4):418–430.

9. Centers for Disease Control and Prevention (CDC). Tuberculosis elimination revisisted: obstacles, opportunities, and renewed commitment - Advisory Council for the Elimination of Tuberculosis (ACET). *Morb. Mortal. Wkly. Rep.* 1999;48(RR-9):1–13.

10. Peto HM, Pratt RH, Harrington TA, et al. Epidemiology of extrapulmonary tuberculosis in the United States, 1993–2006. *Clin. Infect. Dis.* 2009;49(9):1350–1357.

11. Schneider E, Moore M, Castro KG. Epidemiology of tuberculosis in the United States. *Clin. Chest Med.* 2005;26(2):183–195.

12. Salinas JL, Mindra G, Haddad MB, et al. Leveling of Tuberculosis Incidence — United States, 2013–2015. *Morb. Mortal. Wkly. Rep.* 2016;65(11):273–278.

13. Narasimhan P, Wood J, MacIntyre CR, et al. Risk factors for tuberculosis. *Pulm. Med.* 2013;63(1):37–46.

14. Schepisi MS, Sotgiu G, Contini S, et al. Tuberculosis transmission from healthcare workers to patients and co-workers: A systematic literature review and meta-analysis. *PLoS One*. 2015;10(4).

15. Kilinc O, Ucan ES, Cakan MDA, et al. Risk of tuberculosis among healthcare workers: Can tuberculosis be considered as an occupational disease? *Respir. Med.* 2002;96(7):506–510.

16. Menzies D, Joshi R, Pai M. Risk of tuberculosis infection and disease associated with work in health care settings. *Inernational J. Tuberc. Lung Dis.* 2007;11(6):593–605.

17. Joshi R, Reingold AL, Menzies D, et al. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med.* 2006;3(12):e494.

18. Baussano I, Nunn P, Williams B, et al. Tuberculosis among health care workers. *Emerg. Infect. Dis.* 2011;17(3):488–494.

19. Behrman A, Buchta WG, Budnick LD, et al. Protecting health care workers from tuberculosis, 2013. *J. Occup. Environ. Med.* 2013;55(8):985–988.

20. Lambert LA, Pratt RH, Armstrong LR, et al. Tuberculosis among healthcare workers, United States, 1995-2007. *Infect. Control Hosp. Epidemiol.* 2012;33(11):1126–32.

21. Pearson ML, Jereb JA, Frieden TR, et al. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. A risk to patients and health care workers. *Ann. Intern. Med.* 1992;117(3):191–6.

22. Wenger PN, Otten J, Breeden A, et al. Control of nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis among healthcare workers and HIV-infected patients. *Lancet*. 1995;345(8944):235–240.

23. Wilson FA, Miller TL, Stimpson JP. Mycobacterium tuberculosis infection, immigration status, and diagnostic discordance: A comparison of tuberculin skin

test and quantiFERON®-TB gold in-tube test among immigrants to the U.S. *Public Health Rep.* 2016;131(2):303–310.

24. LoBue PA, Mermin JH. Latent tuberculosis infection: the final frontier of tuberculosis elimination in the USA. *Lancet Infect. Dis.* 2017;17(10):e327–e333.

25. Linas BP, Wong AY, Freedberg KA, et al. Priorities for screening and treatment of latent tuberculosis infection in the United States. *Am. J. Respir. Crit. Care Med.* 2011;184(5):590–601.

26. Ricks PM, Cain KP, Oeltmann JE, et al. Estimating the burden of tuberculosis among foreign-born persons acquired prior to entering the U.S., 2005-2009. *PLoS One*. 2011;6(11).

27. Tsang CA, Langer AJ, Navin TR, et al. Tuberculosis among foreign born persons diagnosed ≥10 years after arrival in the United States, 2010–2015. *Am. J. Transplant.* 2017;17(5):1414–1417.

28. World Health Organization. Treatment of tuberculosis guidelines. 2010.(http://apps.who.int/iris/bitstream/handle/10665/44165/9789241547833_eng)

29. Kayigamba FR, Bakker MI, Mugisha V, et al. Sputum completion and conversion rates after intensive phase of tuberculosis treatment: An assessment of the Rwandan control program. *BMC Res. Notes*. 2012;5.

30. Feng-zeng Z, Levy MH, Sumin W. Sputum microscopy results at two and three months predict outcome of tuberculosis treatment. *Int. J. Tuberc. Lung Dis.* 1997;1(6):570–572.

31. Bouti K, Aharmim M, Marc K, et al. Factors influencing sputum conversion among smear-positive pulmonary tuberculosis patients in Morocco. *ISRN Pulmonol.* 2013;2013:1–5.

32. Kuaban C, Bame R, Mouangue L, et al. Non conversion of sputum smears in new smear positive pulmonary tuberculosis patients in Yaoundé, Cameroon. *East Afr. Med. J.* 2009;86(5):219–225.

33. Centers for Disease Control and Prevention. Report of verified case of tuberculosis (RVCT): Instruction manual. 2009.(https://www.cdc.gov/tb/programs/rvct/InstructionManual.pdf)

34. France AM, Grant J, Kammerer JS, et al. A field-validated approach using surveillance and genotyping data to estimate tuberculosis attributable to recent transmission in the United States. *Am. J. Epidemiol.* 2015;182(9):799–807.

35. Tudor C, Van Der Walt ML, Margot B, et al. Occupational risk factors for tuberculosis among healthcare workers in KwaZulu-Natal, South Africa. *Clin. Infect. Dis.* 2016;62:S255–S261.

36. Hall HI, Song R, Tang T, et al. HIV trends in the United States: diagnoses and estimated incidence. *JMIR Public Heal. Surveill.* 2017;3(1):e8.

37. Fernando SL, Saunders BM, Sluyter R, et al. A polymorphism in the P2X7 gene increases susceptibility to extrapulmonary tuberculosis. *Am. J. Respir. Crit. Care Med.* 2007;175(4):360–366.

38. Fortún J, Martín-Dávila P, Molina A, et al. Sputum conversion among patients

with pulmonary tuberculosis: Are there implications for removal of respiratory isolation? *J. Antimicrob. Chemother.* 2007;59(4):794–798.

39. Kim L, Moonan PK, Yelk Woodruff RS, et al. Epidemiology of recurrent tuberculosis in the United States, 1993-2010. *Int. J. Tuberc. Lung Dis.* 2013;17(3):357–360.

40. Jones RM. Burden of occupationally acquired pulmonary tuberculosis among healthcare workers in the USA: A risk analysis. *Ann. Work Expo. Heal.* 2017;61(2):141–151.

41. Davidow AL, Katz D, Ghosh S, et al. Preventing infectious pulmonary tuberculosis among foreign-born residents of the United States. *Am. J. Public Health*. 2015;105(9):e81–e88.

42. Cain KP, Benoit SR, Winston CA, et al. Tuberculosis among foreign-born persons in the United States. *J. Am. Med. Assoc.* 2008;300(4):405–412.

Tables and Figures

Figure 1. Data restriction flow diagram for bivariate and multivariable analyses

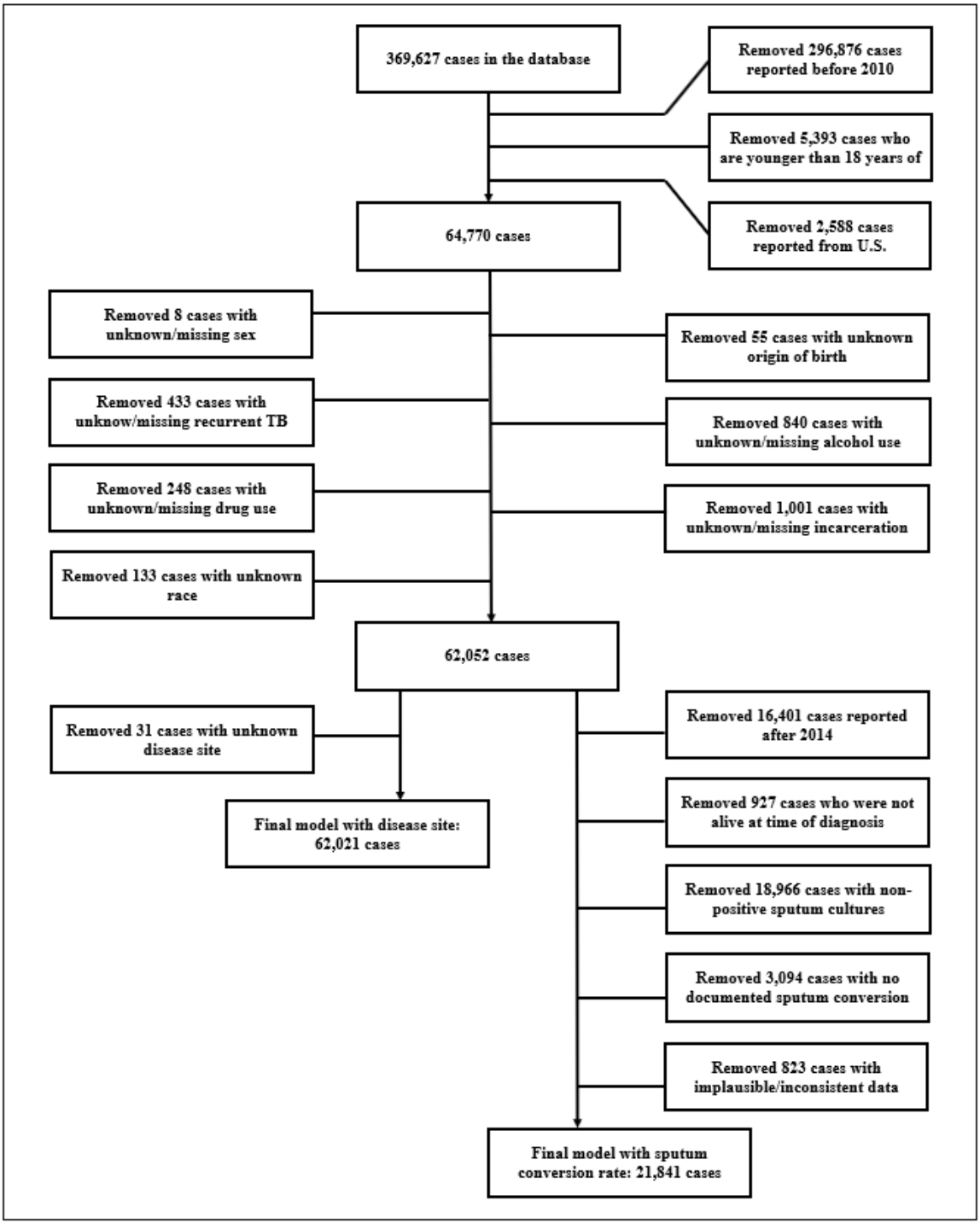

Table 1. Characteristics of United States patients with tuberculosis (TB) by healthcare worker (HCW) status, among individuals 18 years of age or older, January 2010 to December 2016

United States	Patients with TB (n = 64,770)		
Characteristic	HCWs (N = 2,460) n (%)	Other adults (N = 62,310) n (%)	OR (95% CI) [a]
Sex			
Male	742 (30)	39,158 (63)	Reference
Female	1,718 (70)	23,144 (37)	3.92 (3.59-4.28)
Mean/median age at diagnosis, years	42/41	50/50	-
Age at diagnosis range, years	18-95	18-109	-
Age group, years			
18-35	900 (37)	17,593 (28)	Reference
36-54	1,039 (42)	19,062 (31)	1.07 (0.97-1.17)
≥ 55	521 (21)	25,655 (41)	0.40 (0.36-0.44)
Origin of birth			
United States	627 (25)	20,638 (33)	Reference
Other [b]	1,833 (75)	41,617 (67)	1.45 (1.32-1.59)
Race/ethnicity			
White, non-Hispanic	283 (12)	9,460 (15)	Reference
Black, non-Hispanic	770 (31)	13,415 (22)	1.92 (1.67-2.20)
Hispanic	276 (11)	17,632 (28)	0.52 (0.44-0.62)
Asian	1,081 (44)	20,040 (32)	1.80 (1.58-2.06)
Native/Pacific Islander [c]	33 (1)	1,247 (2)	0.88 (0.61-1.27)
Multiple races	14 (1)	348 (1)	1.34 (0.78-2.32)
TST result at time of TB diagnosis			
Negative	144 (6)	6,011 (10)	Reference
Positive	974 (40)	21,044 (34)	1.93 (1.62-2.31)
Not performed/unknown	1,342 (55)	35,255 (57)	1.59 (1.34-1.89)
IGRA result at time of TB diagnosis			
Negative	151 (6)	3,993 (6)	Reference
Positive	955 (39)	21,756 (35)	1.16 (0.97-1.38)
Not performed/unknown	1,354 (55)	36,561 (59)	0.98 (0.83-1.16)
Culture positive for *Mycobacterium tuberculosis*			
Sputum only	865/1,901 (46)	26,817/49,644 (54)	Reference
Tissue/other bodily fluids only	686/1,901 (36)	13,823/49,644 (28)	1.54 (1.39-1.70)
Sputum and tissue/other bodily fluids	350/1,901 (18)	9,004/49,644 (18)	1.21 (1.06-1.37)
Sputum conversion [d]			
≥ 60 days	182/767 (24)	8,464/21,518 (32)	Reference
< 60 days	585/767 (76)	14,739/21,518 (69)	1.52 (1.31-1.77)
Site of disease			
Pulmonary TB only	1,512 (61)	43,353 (70)	Reference
Extrapulmonary TB only	692 (28)	12,686 (20)	1.56 (1.43-1.71)
Concurrent pulmonary and extrapulmonary TB	253 (10)	6,228 (10)	1.16 (1.02-1.33)
Initial drug resistance [e]			
Susceptible to Isoniazid and Rifampin	1,641/1,867 (88)	44,057/48,649 (91)	Reference
Resistance to any drug (total)	226/1,867 (12)	4,592/48,649 (9)	1.32 (1.15-1.52)
Isoniazid monoresistance	177/226 (78)	3,828/4,592 (83)	1.24 (1.06-1.45)
Rifampin monoresistance	3/226 (1)	137/4,592 (3)	-
Multidrug-resistance (MDR-TB)	46/226 (20)	611/4,592 (13)	2.02 (1.49-2.74)
Extensive drug-resistance (XDR-TB)	-	16/4,592 (< 1)	-
HIV test result reported at time of diagnosis			
HIV negative	1,985 (81)	49,361 (79)	Reference
HIV positive	138 (6)	3,754 (6)	0.91 (0.77-1.09)
Refused HIV testing	96 (4)	2,151 (3)	0.90 (0.73-1.11)
Unknown/indeterminate/not offered	241 (10)	7,044 (11)	0.85 (0.74-0.97)
Non-recurrent TB	2,373 (96)	59,110 (95)	Reference
Recurrent TB	87 (4)	3,200 (5)	0.68 (0.55-0.84)
Non-recent transmission	2,303 (94)	56,959 (91)	Reference
Recent transmission [f]	157 (6)	5,351 (9)	0.73 (0.62-0.87)
No excess alcohol use (within the past year)	2,384 (97)	54,824 (88)	Reference
Excess alcohol use (within the past year)	76 (3)	7,486 (12)	0.23 (0.18-0.29)
No drug use (within the past year)	2,415 (98)	57,336 (92)	Reference
Drug use (within the past year)	45 (2)	4,974 (8)	0.21 (0.16-0.29)
Not incarcerated at time of diagnosis	2,455 (100)	59,635 (96)	Reference
Incarceration at time of diagnosis	5 (< 1)	2,675 (4)	0.05 (0.02-0.11)
Method of TB treatment [g]			
Directly observed therapy (DOT)	910/1,803 (51)	26,704/43,902 (61)	Reference
Self-administered therapy (SAT)	291/1,803 (16)	3,698/43,902 (8)	2.31 (2.01-2.65)
Both DOT and SAT	570/1,803 (32)	12,659/43,902 (29)	1.32 (1.19-1.47)
Unknown/missing	32/1,803 (2)	841/43,902 (2)	1.12 (0.78-1.60)
Treatment outcome [g]			
Did not complete therapy	74/1,803 (4)	5,414/43,902 (12)	Reference
Completed therapy	1,721/1,803 (95)	38,216/43,902 (87)	3.29 (2.61-4.17)
Unknown/missing	8/1,803 (< 1)	272/43,902 (1)	2.15 (1.03-4.51)

NOTE. Data are no. (%) or proportion (%) of persons with TB, unless otherwise indicated. Sum of percentages may not equal 100% due to rounding. HIV, human immunodeficiency virus; TST, tuberculin skin test; IGRA, interferon gamma release assay.

[a] Unadjusted Odds Ratios of HCW vs other adults for the risk group, relative to the odds in the reference group.

[b] Birth outside of the United States.

[c] Native includes Native American, Alaska Native, and Native Hawaiian.

[d] Analysis was limited to those with a positive sputum culture result, documented sputum conversion, and alive at diagnosis.

[e] Analysis was limited to those with a positive culture result and an isolate that had drug resistance results reported.

[f] Recent transmission is based on a plausible-source case method that identifies cases based on the following five characteristics: *M. tuberculosis* genotype, an infectious form of TB disease, patient who is ≥ 10 years, diagnosis within 2 years before the given case, and residential location within 10 miles of a contact case.

[g] Analysis was limited to those who were alive at time of diagnosis, had documented initial treatment, and analyzed through 2014 to provide a 2-year complete reporting.

Table 2. Characteristics of United States patients with tuberculosis (TB) among non-U.S.-born and U.S.-born healthcare workers (HCW) 18 years of age or older, January 2010 to December 2016

United States	HCWs with TB (n = 2,460)		
Characteristic	Non-U.S.-born (N = 1,833) n (%)	U.S.-born (N = 627) n (%)	OR (95% CI) [a]
Sex			
Male	598 (33)	144 (23)	Reference
Female	1,235 (67)	483 (77)	0.62 (0.50-0.76)
Mean/median age at diagnosis, years	42/40	43/42	-
Age at diagnosis range, years	18-95	18-87	-
Age group, years			
18-35	668 (36)	232 (37)	Reference
36-54	803 (44)	236 (38)	1.18 (0.96-1.46)
≥ 55	362 (20)	159 (25)	0.79 (0.62-1.00)
Race/ethnicity			
White, non-Hispanic	68 (4)	215 (34)	Reference
Black, non-Hispanic	531 (29)	239 (38)	7.02 (5.14-9.60)
Hispanic	173 (9)	103 (16)	5.31 (3.68-7.66)
Asian	1,041 (57)	40 (6)	82.28 (54.21-125.89)
Native/Pacific Islander [b]	9 (< 1)	24 (4)	1.19 (0.53-2.67)
Multiple races	9 (< 1)	5 (1)	5.69 (1.84-17.56)
TST result at time of TB diagnosis			
Negative	78 (4)	66 (11)	Reference
Positive	705 (38)	269 (43)	2.22 (1.55-3.17)
Not performed/unknown	1,050 (57)	292 (46)	3.04 (2.14-4.33)
IGRA result at time of TB diagnosis			
Negative	97 (5)	54 (9)	Reference
Positive	723 (39)	232 (37)	1.73 (1.21-2.50)
Not performed/unknown	1,013 (55)	341 (54)	1.65 (1.16-2.36)
Culture positive for *Mycobacterium tuberculosis*			
Sputum only	629/1,438 (44)	236/463 (51)	Reference
Tissue/other bodily fluids only	562/1,438 (39)	124/463 (27)	1.70 (1.33-2.17)
Sputum and tissue/other bodily fluids	247/1,438 (17)	103/463 (22)	0.90 (0.68-1.18)
Sputum conversion [c]			
≥ 60 days	116/555 (19)	66/212 (30)	Reference
< 60 days	439/555 (81)	146/212 (70)	1.71 (1.20-2.44)
Site of disease			
Pulmonary TB only	1,058 (58)	454 (72)	Reference
Extrapulmonary TB only	574 (31)	118 (19)	2.09 (1.66-2.62)
Pulmonary and extrapulmonary TB	199 (11)	54 (9)	1.58 (1.15-2.18)
Initial drug resistance [d]			
Susceptible to Isoniazid and Rifampin	1,213/1,412 (86)	428/455 (94)	Reference
Resistance to any drug (total)	199/1,412 (14)	27/455 (6)	2.60 (1.71-3.95)
Isoniazid monoresistance	156/199 (78)	21/27(78)	2.62 (1.64-4.19)
Rifampin monoresistance	2/199 (1)	1/27 (4)	-
Multidrug-resistance (MDR-TB)	41/199 (21)	5/27 (19)	2.89 (1.14-7.37)
Extensive drug-resistance (XDR-TB)	-	-	-
HIV test result reported at time of diagnosis			
HIV negative	1,460 (80)	525 (84)	Reference
HIV positive	106 (6)	32 (5)	1.19 (0.79-1.79)
Refused HIV testing	71 (4)	25 (4)	1.02 (0.64-1.63)
Unknown/indeterminate/not offered	196 (11)	45 (7)	1.57 (1.12-2.20)
Non-recurrent TB	1,757 (96)	616 (98)	Reference
Recurrent TB	76 (4)	11 (2)	2.43 (1.71-3.95)
Non-recent transmission	1,745 (95)	558 (89)	Reference
Recent transmission [e]	88 (5)	69 (11)	0.33 (0.23-0.46)
No excess alcohol use (within the past year)	1,802 (98)	582 (93)	Reference
Excess alcohol use (within the past year)	31 (2)	45 (7)	0.22 (0.14-0.35)
No drug use (within the past year)	1,823 (99)	592 (94)	Reference
Drug use (within the past year)	10 (1)	35 (6)	0.09 (0.05-0.19)
Not incarcerated at time of diagnosis	1,828 (100)	627 (100)	-
Incarceration at time of diagnosis	5 (< 1)	-	
Method of TB treatment [f]			
Directly observed therapy (DOT)	656/1,338 (49)	254/465 (55)	Reference
Self-administered therapy (SAT)	224/1,338 (17)	67/465 (14)	1.29 (0.95-1.76)
Both DOT and SAT	434/1,338 (32)	136/465 (29)	1.24 (0.97-1.57)
Unknown/missing	24/1,338 (2)	8/465 (2)	1.16 (0.52-2.62)
Treatment outcome [f]			
Did not complete therapy	50/1,338 (4)	24/465 (5)	Reference
Completed therapy	1,284/1,338 (96)	437/465 (94)	1.41 (0.86-2.32)
Unknown/missing	4/1,338 (< 1)	4/465 (1)	-

NOTE. Data are no. (%) or proportion (%) of persons with TB, unless otherwise indicated. Sum of percentages may not equal 100% due to rounding. HIV, human immunodeficiency virus; TST, tuberculin skin test; IGRA, interferon gamma release assay.

[a] Unadjusted Odds Ratios of non-U.S.-born HCWs vs U.S.-born HCWs for the risk group, relative to the odds in the reference group.
[b] Native includes Native American, Alaska Native, and Native Hawaiian.
[c] Analysis was limited to those with a positive sputum culture result, documented sputum conversion, and alive at diagnosis.
[d] Analysis was limited to those with a positive culture result and an isolate that had drug resistance results reported.
[e] Recent transmission is based on a plausible-source case method that identifies cases based on the following five characteristics: *M. tuberculosis* genotype, an infectious form of TB disease, patient who is ≥ 10 years, diagnosis within 2 years before the given case, and residential location within 10 miles.
[f] Analysis was limited to those who were alive at time of diagnosis, had documented initial treatment, and analyzed through 2014 to provide a 2-year complete reporting.

Table 3. Multivariable analysis of the association between healthcare workers (HCW) and disease site: Stratified on origin of birth

U.S.-born	Disease site (n = 20,332)		Final Model			
Patient Characteristics	**PTB (N = 15,190) n (%)**	**EPTB [a] (N = 5,142) n (%)**	**aOR**	**Confidence Interval**		**p-value**
HCW						
Other adults	14,750 (97)	4,975 (97)	Reference			
HCWs	440 (3)	167 (3)	1.09	0.90	1.31	0.3821
Sex						
Male	10,407 (69)	3,138 (61)	Reference			
Female	4,783 (31)	2,004 (39)	0.75	0.70	0.80	< 0.0001
Previous TB diagnosis						
Non-recurrent TB	14,441 (95)	4,944 (96)	Reference			
Recurrent TB	749 (5)	198 (4)	1.25	1.07	1.47	0.0060
Drug use (within the past year)						
No drug use	12,232 (81)	4,506 (88)	Reference			
Drug use	2,958 (19)	636 (12)	1.57	1.43	1.72	< 0.0001
Recent transmission (RT) [b]						
non-RT	12,576 (83)	4,568 (89)	Reference			
RT	2,614 (17)	574 (11)	1.55	1.40	1.70	< 0.0001
Non-U.S.-born	**Disease site (n = 41,689)**		**Final Model**			
Patient Characteristics	**PTB (N = 27,733) n (%)**	**EPTB [a] (N = 13,956) n (%)**	**aOR**	**Confidence Interval**		**p-value**
HCW						
Other adults	26,700 (96)	13,197 (95)	Reference			
HCWs	1,033 (4)	759 (5)	0.76	0.69	0.84	< 0.0001
Sex						
Male	17,201 (62)	7,294 (52)	Reference			
Female	10,532 (38)	6,662 (48)	0.71	0.68	0.74	< 0.0001
HIV test result reported at time of diagnosis						
HIV negative	22,659 (82)	10,945 (78)	Reference			
HIV positive	986 (4)	927 (7)	0.48	0.44	0.53	< 0.0001
Refused HIV testing	961 (3)	500 (4)	0.98	0.88	1.09	< 0.0001
Unknown/indeterminate/not offered	3,127 (11)	1,584 (11)	0.98	0.91	1.04	< 0.0001
Excess alcohol use (within the past year)						
No excess alcohol use	25,620 (92)	13,388 (96)	Reference			
Excess alcohol use	2,113 (8)	568 (4)	1.62	1.46	1.79	< 0.0001
Drug use (within the past year)						
No drug use	26,767 (97)	13,692 (98)	Reference			
Drug use	966 (3)	264 (2)	1.48	1.28	1.71	< 0.0001

NOTE. Disease site is pulmonary TB (PTB), and extrapulmonary TB (EPTB) and concurrent PTB/EPTB. HIV, human immunodeficiency virus; TB, tuberculosis.

[a] EPTB includes EPTB only and concurrent PTB/EPTB

[b] Recent transmission is based on a plausible-source case method that identifies cases based on the following five characteristics: *M. tuberculosis* genotype, an infectious form of TB disease, patient who is ≥ 10 years, diagnosis within 2 years before the given case, and residential location within 10 miles.

Table 4. Multivariable analysis of the association between healthcare workers (HCW) and sputum culture conversion

	Sputum conversion (n = 21,841)		Final Model			
Patient Characteristics	**< 60 days (N = 15,025) n (%)**	**≥ 60 days (N = 6,816) n (%)**	**aOR**	**Confidence Interval**		**p-value**
HCW						
Other adults	14,447 (96)	6,638 (97)	Reference			
HCWs	578 (4)	178 (3)	1.24	1.04	1.48	0.0160
Sex						
Male	9,537 (63)	4824 (71)	Reference			
Female	5,488 (37)	1,992 (29)	1.26	1.18	1.34	< 0.0001
Race/ethnicity						
White, non-Hispanic	1,975 (13)	1,316 (19)	Reference			
Black, non-Hispanic	3,073 (20)	1,467 (22)	1.32	1.20	1.45	< 0.0001
Hispanic	4,460 (30)	2,133 (31)	1.17	1.05	1.29	0.0031
Asian	5,137 (34)	1,674 (25)	1.54	1.38	1.71	< 0.0001
Native/Pacific Islander [a]	279 (2)	180 (3)	1.08	0.88	1.32	0.4758
Multiple races	101 (1)	46 (1)	1.27	0.88	1.82	0.2076
Origin of birth						
United States	4,621 (31)	2,823 (41)	Reference			
Other [b]	10,404 (69)	3,993 (59)	1.29	1.19	1.40	< 0.0001
Initial drug resistance						
Susceptible to Isoniazid (INH) and Rifampin (RIF)	13,343 (90)	6,062 (90)	Reference			
INH monoresistance	1,299 (9)	509 (8)	1.08	0.96	1.20	0.1952
RIF monoresistance	38 (< 1)	28 (< 1)	0.59	0.36	0.97	0.0387
Multidrug-resistance (MDR-TB)	185 (1)	153 (2)	0.46	0.37	0.57	< 0.0001
Excess alcohol use (within the past year)						
No excess alcohol use	13,046 (87)	5,370 (79)	Reference			
Excess alcohol use	1,979 (13)	1,446 (21)	0.70	0.65	0.76	< 0.0001
Drug use (within the past year)						
No drug use	13,688 (91)	5,941 (87)	Reference			
Drug use	1,337 (9)	875 (13)	0.88	0.77	1.00	0.0529

NOTE. Sputum conversion is < 60 days and ≥ 60 days. TB, tuberculosis.
[a] Native includes Native American, Alaska Native, and Native Hawaiian.
[b] Birth outside of the United States.