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Prospects for Tuberculosis Elimination in the United States: Results of a Transmission Dynamic Model

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Abstract

We estimated long-term tuberculosis (TB) trends in the US population and assessed prospects for TB elimination. We used a detailed simulation model allowing for changes in TB transmission, immigration, and other TB risk determinants. Five hypothetical scenarios were evaluated from 2017 to 2100: 1) maintain current TB prevention and treatment activities (base case); 2) provision of latent TB infection testing and treatment for new legal immigrants; 3) increased uptake of latent TB infection screening and treatment among high-risk populations, including a 3-month isoniazid-rifapentine regimen; 4) improved TB case detection; and 5) improved TB treatment quality. Under the base case, we estimate that by 2050, TB incidence will decline to 14 cases per million, a 52% (95% posterior interval (PI): 35, 67) reduction from 2016, and 82% (95% posterior interval: 78, 86) of incident TB will be among persons born outside of the United States. Intensified TB control could reduce incidence by 77% (95% posterior interval: 66, 85) by 2050. We predict TB may be eliminated in US-born but not non-US-born persons by 2100. Results were sensitive to numbers of people entering the United States with latent or active TB, and were robust to alternative interpretations of epidemiologic evidence. TB elimination in the United States remains a distant goal; however, strengthening TB prevention and treatment could produce important health benefits.

Keywords

antitubercular agents; immigration; latent tuberculosis; tuberculosis; pulmonary

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The number of tuberculosis (TB) cases in the United States has declined over the past 7 decades, from more than 500 per million in 1953 to 30 per million in 2015 (1), and elimination has long been a goal of national TB policy (2). In 1989, a target date of 2010 was established for elimination, defined as annual incidence of fewer than 1 case per million (3). By 2010, TB rates remained 30–40 times higher, with progress delayed by a resurgence during 1989–1994 (4). TB elimination remains a prominent goal (5) with substantial potential for health and economic benefits (6). The US context contrasts with the global situation, where average TB incidence is 50 times higher than in the United States and only declining at 1%–2% per year (7), despite aggressive policy goals (8).

In recent years, declines in reported TB cases in the United States have flattened (9). Most notified TB (66%) now occurs among non-US-born persons, among whom the incidence of TB is much higher. This is particularly true for recent migrants, but due to elevated latent TB infection (LTBI) prevalence, even long-term non-US-born residents face higher TB risks (10). LTBI can cause disease many years after infection. Multidrug resistant TB (MDR-TB) currently represents a stable fraction of US TB cases, yet even modest increases in drug resistance would have important clinical and public health implications.

Although TB elimination is a major policy objective, it is unclear when this might be achieved and how declines in TB incidence can be accelerated. We estimated future US TB epidemiology under various scenarios to reevaluate prospects for TB elimination in light of current evidence, describe potential impacts of enhanced prevention and control efforts, and understand factors driving future TB-associated morbidity and death.

METHODS

Study model

We developed a deterministic compartmental model of TB epidemiology, building on 2 published transmission models (11, 12). In our model, a core TB dimension captures TB transmission, natural history, and treatment (Figure 1A). Additional dimensions represent 1) drug-resistance patterns, 2) prior treatment, 3) the consequences of human immunodeficiency virus (HIV) on TB epidemiology, 4) heterogeneity in TB risks among US-born and non-US-born populations, and 5) age-based differences in disease mechanisms and risk factor prevalence (Figure 1B–F). The full state space of the model results from the crossing of the 6 dimensions. At any point in time, the US population is represented in the model as a distribution across the 6 dimensions. The resulting model is complex, with many distinct compartments and processes. Although additional complexity can make understanding model behavior challenging, the various mechanisms represented in the model allowed us to extrapolate future outcomes based on current evidence, and test the sensitivity of results to changes in major epidemiologic determinants. We used the model to simulate historical (1950–2015) and current and future (2016–2100) demography and epidemiology for the US population. Simulating a long historical period allowed us to compare results to empirical data for model calibration and validation.

Data inputs

The National TB Surveillance System includes reported TB cases diagnosed in the United States (1). We extracted TB case numbers (available from 1953), stratified by age, nativity (US born or non-US born), recent immigration (for non-US-born individuals), HIV status, recent history of homelessness, prior treatment, and TB drug resistance (stratifications available from 1993), and used these data to describe current and historical disease trends by subgroup.

We estimated LTBI prevalence using data from the 2010–2011 National Health and Nutrition Examination Survey, the most recent year for which LTBI estimates were provided (13). We reanalyzed National Health and Nutrition Examination Survey data using published methods (10) to estimate interferon- γ release assay positivity by age group and nativity, as a marker of LTBI prevalence. We developed a time series of immigration by age and country of origin using data from the Office of Immigration Statistics (14) and the American Community Survey (15). We compiled evidence on other TB determinants, including HIV prevalence and antiretroviral therapy coverage, TB treatment discontinuation, and LTBI treatment uptake, from administrative data sources.

Future immigration forecasts were based on US Census Bureau projections (16), such that by 2100, 24% (95% posterior interval (PI): 19, 31) of the US population would be non-US-born. TB in arriving migrant cohorts was projected to decline at 2% per year for each sender country (17). TB drug resistance among arriving migrants was held constant, and HIV incidence was assumed to decline at 2% per year (18). For time-varying inputs, we allowed uncertainty in long-term trends and short-term fluctuations. Web Materials (available at <https://academic.oup.com/aje>) provide additional description of demographic and epidemiologic processes (Web Appendix 1, Web Figures 1–6) and routine interventions (Web Appendix 2, Web Figures 7–8) represented in the analysis. The model was programmed in R and C++ (Web Appendix 3).

We used a Bayesian evidence synthesis (19) to combine data sources and calibrate the model to a wide range of relevant evidence (Web Appendix 4). Using a large sample of simulated epidemic trajectories consistent with available evidence, we calculated mean estimates for outcomes of interest and reported uncertainty via equal-tailed 95% posterior intervals (20, 21).

Modeled scenarios

We projected future TB outcomes assuming continuation of current prevention and treatment activities (22), implying steady coverage and effectiveness of services provided for LTBI and active TB. We compared this base case with 4 hypothetical scenarios describing different approaches for strengthening TB prevention and control, including 1) provision of LTBI screening and treatment of LTBI (TLTBI) for all new legal immigrants and refugees entering the United States, excluding undocumented migrants or short-term visitors (TLTBI for new immigrants scenario); 2) increased uptake of LTBI screening and treatment among high-risk populations, doubling treatment uptake within each risk group compared with current levels, and increasing the fraction cured among individuals initiating LTBI treatment, via a 3-month

isoniazid-rifapentine drug regimen (improved TLTBI in United States scenario); 3) improved TB case detection, such that the duration of untreated active disease (i.e., time from TB incidence to treatment initiation) is reduced by 50% (better case-detection scenario); and 4) improved TB treatment quality, such that treatment default, failure rates, and the fraction of individuals receiving an incorrect drug regimen are reduced by 50% from current levels (better TB treatment scenario). A fifth scenario combined each of these individual changes (all improvements scenario). We assumed changes implied by these scenarios would be introduced over 5 years starting in 2017. Additional details on the specification of these modeled scenarios are provided in Web Appendix 5.

Sensitivity analyses

We allowed for uncertainty in many epidemiologic drivers and conducted sensitivity analysis to determine the role of these factors. First, we identified factors with the greatest influence over model results, using partial rank correlation coefficients (23).

Second, we examined alternative assumptions about future trends in key epidemiologic determinants. Two alternative scenarios compared 1) no transmission within the United States after 2016 (no transmission after 2016 scenario), and 2) no TB or LTBI among arriving migrants after 2016, without adjusting immigration volume (no TB or LTBI in new migrants after 2016 scenario). Although both scenarios are impossible, they demonstrate the relative significance of the 2 mechanisms generating new *Mycobacterium tuberculosis* infections. The following 5 additional scenarios were used to investigate the implications of possible future trends: 1) weakening of US prevention efforts, with the annual rate of TLTBI among target groups halved between 2016 and 2021 (reduced TB prevention efforts scenario); 2) increasing MDR-TB among arriving migrants to plateau at 19% and 55% of all *M. tuberculosis* infections among treatment-naïve and previously treated individuals, respectively, by 2050 (rising MDR-TB in new migrants scenario; these values represent the current highest MDR-TB rates for any individual geographic region) (24); 3) leveling of immigration volume at 2016 levels (future immigration at 2016 levels scenario); 4) improved global TB control, with TB burden among future migrants dropping by 3% per year, double the current rate (improving global TB control scenario); and 5) increasing LTBI reactivation risks resulting from increasing diabetes prevalence (25, 26), such that population-average LTBI reactivation risks increase by 40% by 2050 (rising reactivation risks scenario).

Finally, we tested the robustness of results to different assumptions about current TB epidemiology. To do so, we 1) recalibrated the model to produce a lower share of non-US-born cases attributable to recent transmission, matching the estimate of 7.5% reported by Yuen et al. (27); 2) adopted a lower estimate for current LTBI prevalence, based on a more stringent positivity criterion for National Health and Nutrition Examination Survey LTBI data (10); and 3) revised the model to assume the eventual leveling of temporal declines in LTBI reactivation risk after *M. tuberculosis* infection, as assumed by earlier TB models (12, 28).

Outcomes

Our primary outcome was TB incidence (defined as annual notified TB cases per million) for the total population and key subgroups. Secondary outcomes included annual *M. tuberculosis* infection risk per million, LTBI prevalence, MDR-TB prevalence among TB cases, and annual TB-attributable mortality per million. We estimated outcomes to 2100 and report detailed results for 2016, 2025, 2050, and 2100.

RESULTS

Model fit and current epidemiology

In Figure 2, we compare model estimates to data used for model fitting. The model reproduces time trends in TB incidence and the distribution of incidence within subgroups, as well as interferon- γ release assay positivity by age and nativity, and TB mortality. Model fit to other evidence sources is shown in Web Appendix 6 and Web Figures 9–13. Model estimates for total TB cases in 2016 (9,341 (95% posterior interval: 8,433, 10,320)) were within 1% of recently reported values for the same year (9,272) (29). Similarly, the estimated number of deaths among individuals with TB for 2015 ($n = 970$ (95% posterior interval: 793, 1,166)) was within 4% of the reported value for the same year ($n = 938$) (30). Neither the 2016 data for TB cases nor the 2015 data for TB deaths was used in model fitting. The model was judged to be consistent with available evidence, and the array of simulated epidemic trajectories (solid lines in Figure 2) was used to make inferences about current epidemiology and project future outcomes.

We estimate that 22,000 (95% posterior interval: 18,000, 25,000) incident *M. tuberculosis* infections were acquired in 2016, including reinfection among those with existing LTBI. In comparison, in the same year, 244,000 (95% posterior interval: 213,000, 280,000) individuals with existing LTBI immigrated to the United States. These 2 sources of LTBI declined over time, with the fraction attributable to domestic transmission declining more rapidly, from 13% (95% posterior interval: 11, 15) in 2000 to 8.1% (95% posterior interval: 6.8, 9.8) in 2016. Although most of these “new” LTBI cases arise from immigration, many latent infections will have been acquired early in life, years before immigration, with a subsequent risk of progression much lower than in a newly infected individual. Web Figure 14 shows recent time trends estimated for the annual rate of TB infection, stratified by nativity. For non-US-born individuals, rates were estimated to have fallen from 254 (95% posterior interval: 217, 297) per million in 2000 to 135 (95% posterior interval: 116, 157) per million in 2016. For US-born individuals, rates were estimated to have fallen from 140 (95% posterior interval: 116, 171) per million in 2000 to 59 (95% posterior interval: 49, 71) per million in 2016. Over the same period, infection risks in the general population were estimated to have fallen from 153 (95% posterior interval: 129, 182) to 70 (95% posterior interval: 60, 82) per million.

We estimated that in 2016, only 27% (95% posterior interval: 24, 31) of TB cases were caused by recent transmission (i.e., infections acquired within 24 months). This fraction varied by subgroup and was highest among the very young (71% (95% posterior interval: 67, 76) in children 0–4 years old; 49% (95% posterior interval: 44, 54) in children 5–15

years old), homeless populations (65% (95% posterior interval: 60, 70)), and individuals with HIV (41% (95% posterior interval: 34, 49)), and was lowest among the upper age groups (13% (95% posterior interval: 11, 15) in those age 65 years or older; 8.7% (95% posterior interval: 7.5, 10) in those age 85 years or older). TB among US-born populations was twice as likely to be due to recent transmission than TB among non-US-born populations (34% (95% posterior interval: 29, 38) vs. 18% (15, 21); risk ratio = 1.9 (95% posterior interval: 1.6, 2.2)). Web Figure 14 provides outcomes by subgroup. These results align closely with empirical estimates published in 2012 and based on genotyping data; recent transmission accounted for 33% and 16% of TB cases among US-born and non-US-born persons, respectively (31). Lower values were found in more recent analyses of these data (incorporating a wider range of empirical evidence), with 27% and 7.5% of TB cases attributable to recent transmission among US-born and non-US-born persons, respectively (27). In sensitivity analyses, we investigated the influence of these differences on epidemiologic projections.

Base-case epidemiologic projections

Figure 3 shows base-case projections of TB incidence by nativity, and Table 1 lists results for other outcomes. TB cases among the US-born population are projected to decline to 3.1 (95% posterior interval: 2.4, 4.1) per million by 2050, a 74% (95% posterior interval: 68, 79) reduction compared with 2016. TB cases among non-US-born residents are projected to decline to 56 (95% posterior interval: 36, 80) per million by 2050, a 60% (95% posterior interval: 46, 74) reduction compared with 2016. By 2050, an estimated 82% (95% posterior interval: 78, 86) of reported TB cases will be non-US-born individuals. Projected declines in TB incidence between 2016 and 2050 were more uncertain in younger than in older age groups: 43% (95% posterior interval: 12, 70) for individuals younger than 25 years old and 62% for those age 65 years and older. In the base-case scenario, the TB elimination goal of fewer than 1 case per million would not be attained before 2100. Whereas case rates in the US-born population may reach this target—with 37% of simulations showing fewer than 1 case per million for the US-born population by 2100—overall rates in the entire population are projected to be 7 times higher than the target rate, and an estimated 87% (95% posterior interval: 81, 90) of TB cases in 2100 will be diagnosed in the non-US-born population.

Other clinical outcomes are projected to follow trends similar to TB incidence, with TB infection risks, LTBI prevalence, and TB mortality all estimated to decline over the long term at a faster pace among US-born compared with non-US-born persons (Table 2). Between 2016 and 2050, MDR-TB incidence is projected to decline in absolute terms from 0.43 (95% posterior interval: 0.37, 0.50) permillion in 2016 to 0.27 (95% posterior interval: 0.12, 0.46) per million in 2050. This implies a modest increase in MDR-TB as a fraction of diagnosed TB cases, from 1.5% (95% posterior interval: 1.3, 1.7) in 2016 to 1.9% (95% posterior interval: 1.2, 2.7) in 2050.

Although active TB is successfully identified and treated in most people in whom the disease has developed, we estimate that in 2016 there were 16,000 (95% posterior interval: 13,000, 21,000) life-years lost due to TB-related death, in addition to 9,600 (95% posterior interval: 8,600, 11,000) life-years spent with active TB (including time spent receiving TB

treatment). For 2050, we project these values will drop to 9,500 (95% posterior interval: 6,200, 14,000) life-years lost due to TB-related death, and 5,800 (95% posterior interval: 3,800, 8,300) life-years spent with active disease.

Modeled scenarios for intensified TB prevention and control

Figure 4 shows time trends in major outcomes for each modeled scenario compared with the base case, from 2016 to 2050. Apart from the combination scenario, the better case detection scenario is projected to produce the greatest reduction in the number of new infections per million in the general population. However, this reduction in transmission has little effect on overall LTBI prevalence trends because transmission is only a minor contributor to future LTBI burden compared with prevalent LTBI among current US residents and individuals with LTBI immigrating to the United States. The modeled scenarios having the greatest impact on overall LTBI prevalence are those that expand LTBI treatment (i.e., the TLTBI for new immigrants and improved TLTBI in United States scenarios). These scenarios also have the greatest impact on overall TB incidence. For TB mortality, the better case detection and the expanded LTBI treatment scenarios are projected to have similar impact by 2050. The scenario for better TB treatment is projected to have little impact on these outcomes but does have the potential to reduce MDR-TB as a fraction of diagnosed TB cases. In contrast, this outcome is projected to increase modestly under the other scenarios, due to increased selection pressure promoting drug-resistant strains. Web Figure 15 shows results stratified by nativity. Results are listed in Web Tables 1–3 for each modeled scenario in 2025, 2050, and 2100, as well as the percentage changes compared with the base case. An interactive webtool (32) is available for exploring these results in greater detail.

Sensitivity analyses

We used partial rank correlation coefficients to identify factors with the greatest influence on *M. tuberculosis* infections, TB cases, and TB deaths per million in 2050 (Web Figure 16), with the magnitude of each coefficient indicating relative sensitivity of results to a particular factor. Future immigration volume and TB burden among migrants were important determinants of all 3 outcomes under the base-case scenario. Access to LTBI treatment also was an important determinant.

We modeled additional scenarios to understand the importance of local transmission relative to LTBI introduced through ongoing migration to the United States (i.e., the no transmission after 2016 vs. no TB or LTBI in new migrants after 2016 scenarios). Although the first of these scenarios showed improved TB outcomes compared with the base case, incidence in 2100 was still 6 times higher than the elimination goal. Projected incidence declines were substantially greater in the scenario with no TB or LTBI among future migrants, with incidence dropping to 0.63 (95% posterior interval: 0.19, 1.5) per million by 2100, meeting the elimination goal. These results confirm the central importance of prevalent LTBI among current and future migrants (as compared to transmission in the United States) as a driver of long-term US TB trends. Web Figure 17 and Web Table 4 provide additional results for these scenarios.

Several additional scenarios described differences in the trajectory of key epidemiologic determinants (i.e., reduced TB prevention efforts, rising MDR-TB in new migrants, future immigration at 2016 levels, improving global TB control, rising reactivation risks). Of these scenarios, improving global TB control and rising reactivation risks have the greatest impact on 2050 TB incidence, with estimated rates 25% (95% posterior interval: 15, 35) below and 26% (95% posterior interval: 9.3, 44) above the base case, respectively (additional results shown in Web Figure 18 and Web Table 5).

Finally, we tested the robustness of results to different assumptions about current TB epidemiology. Recalibrating the model to assume that 7.5% of non-US-born cases arise from recent transmission (27) reduced *M. tuberculosis* transmission in 2050 by 28% for the general population and 50% among the non-US-born population, compared with the main analysis. However, this change produced only minor (approximately 2%) changes in projected TB cases and associated deaths. Recalibrating the model to match lower estimates for current LTBI prevalence (10) produced estimates of *M. tuberculosis* transmission in 2050 that were 12% higher, and TB incidence and mortality 16% higher, compared with the main analysis. Changing the model to assume that temporal declines in LTBI reactivation risks eventually plateau led to much slower reductions in TB incidence and TB-related death, which were 32% and 57% higher, respectively, in 2050 as compared with the base case. This difference was greatest for the US-born population, in which TB incidence and TB-related death were 91% and 142% higher, respectively, in 2050. Estimates of incremental reductions in TB cases produced by the intervention scenarios were robust to these different assumptions (Web Figure 19).

DISCUSSION

Projections of long-term TB outcomes, such as the time to elimination, are highly uncertain because future trends in key epidemiologic determinants are difficult to anticipate. Given this uncertainty, the conclusions drawn from long-term projections are necessarily qualitative. Across all sensitivity analyses and modeled scenarios we examined, TB incidence in the general population did not fall below 1 case per million before the end of this century, suggesting that without major unanticipated changes in current trends, policy attention, or TB control tools, it will be many years until elimination is achieved. Despite this, the modeled scenarios examined in this analysis suggest more aggressive prevention and treatment could yield substantial reductions in TB burden. Taken together, we project they would reduce TB incidence by 51% in 2050 compared with the base-case projection, or 77% compared with current levels.

According to our results, LTBI and active TB among current and future migrants are the dominant drivers of future TB trends in the United States. This finding is a consequence of historical trends in US TB epidemiology compared with trends in sender countries. Having experienced a long period of low TB transmission, LTBI prevalence in US-born populations is much lower than among those born abroad (particularly in younger birth cohorts), and low TB transmission in the United States means that LTBI reactivation is the major source of new TB cases. Immigration flows represent the major driver of LTBI prevalence; thus, they likewise determine the course of the epidemic.

Although drug resistance threatens the effectiveness of TB treatment, it does not appear to be a major concern in these projections. However, the base-case scenario assumes there would not be major increases in drug resistance among arriving migrants nor changes in the fitness or resistance profile of existing resistant strains. Deviations from these assumptions could create additional challenges to reaching elimination targets. In addition, most scenarios examined in this analysis assumed ongoing funding and effectiveness of US TB prevention and control services, whereas a resurgence in TB and drug-resistant TB is possible if investments in TB control were reduced, evidenced by the spike in TB and MDR-TB cases during 1989–1994, after reduced TB funding in the 1970s (4).

Our analyses extend prior work forecasting future TB outcomes in the United States. Our results are generally consistent with estimates reported by Hill et al. (12), who fit a mechanistic TB model to the 2000–2008 time series of TB in US-born and non-US-born persons, yet they are significantly more pessimistic about the timing of TB elimination in the US-born population. In the Hill et al. analysis (12), TB elimination in the US-born population is predicted for the year 2063 (95% posterior interval: 2,039, 2,096) with current control efforts, whereas our base-case scenario suggests a less than 50% probability that this outcome will be achieved by 2100. The cause of this difference is unclear; however, it is likely due to different assumptions about how quickly reactivation risk declines after infection (faster in the Hill et al. analysis (12)), and mixing between non-US-born and US-born populations (lower in the Hill et al. analysis (12)). In recent projections for 4 states with high TB burden in the United States, Shrestha et al. (33) forecast stagnating incidence declines, with the annual percentage decline in TB incidence falling from 5.2%–8.8% for 1993–2013 to 1.5%–3.3% for 2015–2025. We estimate values of 5.9% (95% posterior interval: 5.2, 6.6) and 2.7% (95% posterior interval: 2.0, 3.5) for the same periods.

Long-term projections of disease trends must be interpreted carefully. The results of our analyses are contingent on future trends estimated for key epidemiologic drivers, which, themselves, are hard to predict. For example, changes in the political forces that shape immigration policy influence immigration trends and therefore are an important upstream determinant of US TB outcomes. Projections are also sensitive to policy changes affecting access to care for the 42 million non-US-born individuals currently living in the United States and other high-risk groups, yet it is very difficult to forecast how and how quickly these political factors will change. Similarly, it is likely that new TB prevention and control technologies will become available, such as better diagnostics of reactivation risk for individuals with LTBI, shorter effective treatment regimens for active TB disease and LTBI, or an effective TB vaccine. We do not know when these new technologies will become available, how effective they will be, or the TB control strategies they might enable. The alternative scenarios also demonstrated how small changes in the pace of global TB control, or the population distribution of TB risk factors, can have substantial cumulative effects on US TB burden in the future.

Studies of infectious disease eradication commonly adopt stochastic models to examine when the epidemic will end via interruption of transmission (34). Because we used a deterministic model, we were unable to examine these questions. However, there is little possibility that stochastic interruption of transmission will affect the timing of TB

elimination. In our analysis, most incident TB cases result from LTBI reactivation rather than recent transmission, consistent with molecular epidemiology studies (27, 35). Moreover, most new LTBI cases are projected to arise from migrants entering the country with an existing infection, rather than via transmission within the United States. The consequence of these factors is that the stochastic nature of TB transmission will have little impact on future TB epidemiology. As an extreme demonstration of this, the total removal of TB transmission from 2016 onward (examined in sensitivity analyses) is only estimated to reduce TB incidence in 2025, 2050, and 2100 by approximately 20% compared with the base case.

The sensitivity of future projections to immigration trends derives from a long history of successful domestic TB control. Given this historical success, the incremental benefit of more aggressive, local TB control appears modest when compared with other factors outside the scope of US domestic public health policies. Although this study did not investigate options for reducing TB burden abroad, strengthening TB control in major sender countries represents an additional approach that could benefit TB control in the United States and improve outcomes for populations at risk of TB in these countries. As differentials in TB epidemiology between the United States and sender countries become larger, this will increase the relative impact of efforts to address high rates of TB infection and TB among persons born abroad, and the need to address that risk before, during, and after immigration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

HIV	human immunodeficiency virus
LTBI	latent tuberculosis infection
MDR-TB	multidrug resistant tuberculosis
TB	tuberculosis

TLTBI treatment of latent tuberculosis infection

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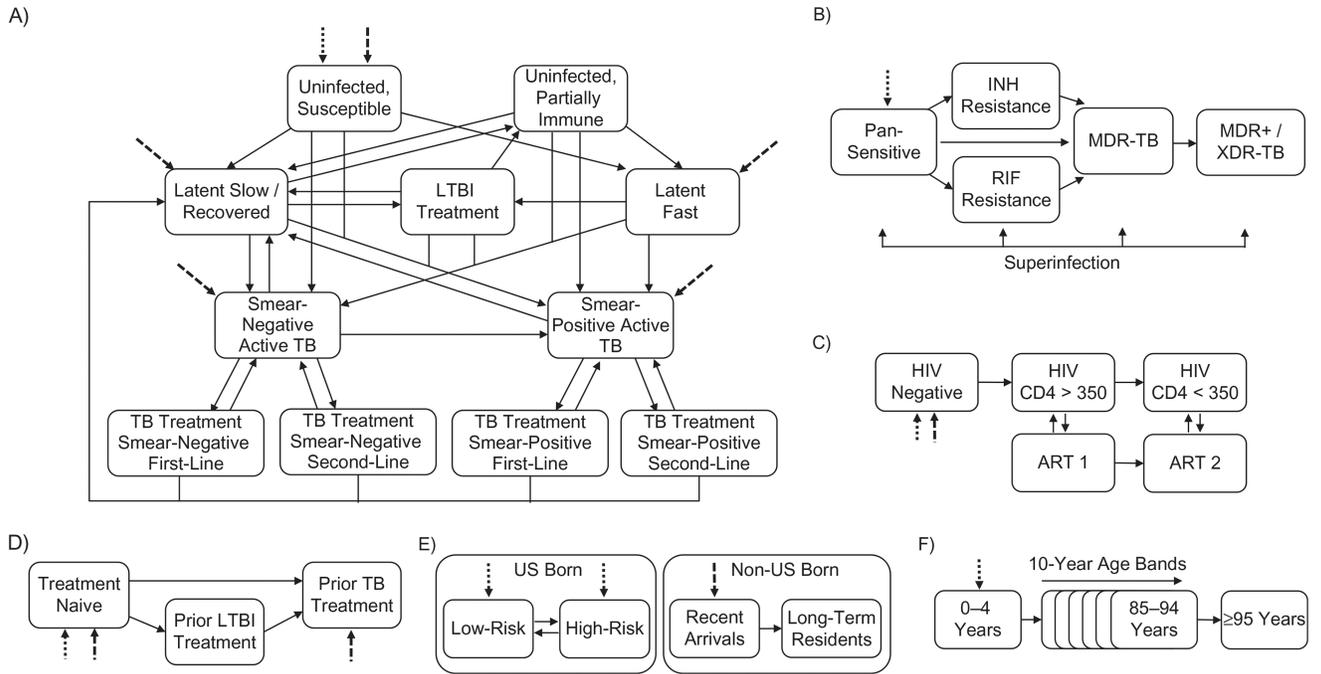


Figure 1. Schematic of tuberculosis simulation model. The schematic shows compartments within each dimension of the model. A) Core TB dimension. B) TB drug-resistance dimension. C) HIV dimension. D) TB treatment history dimension. E) Risk group dimension. F) Age group dimension. Arrows identify entries to the model and possible transitions between compartments. Solid arrows indicate state transitions, dotted arrows indicate model entry for US-born individuals, and dashed arrows indicate model entry for non-US-born individuals. Non-US-born individuals enter distributed across all drug-resistance and age compartments (not shown). Exits due to death are not shown. ART, antiretroviral therapy; CD4, CD4 cell count per cubic millimeter of blood; INH, isoniazid; LTBI, latent tuberculosis infection; MDR-TB, multidrug-resistant tuberculosis; RIF, rifampicin; TB, tuberculosis; XDR-TB, extremely drug-resistant tuberculosis.

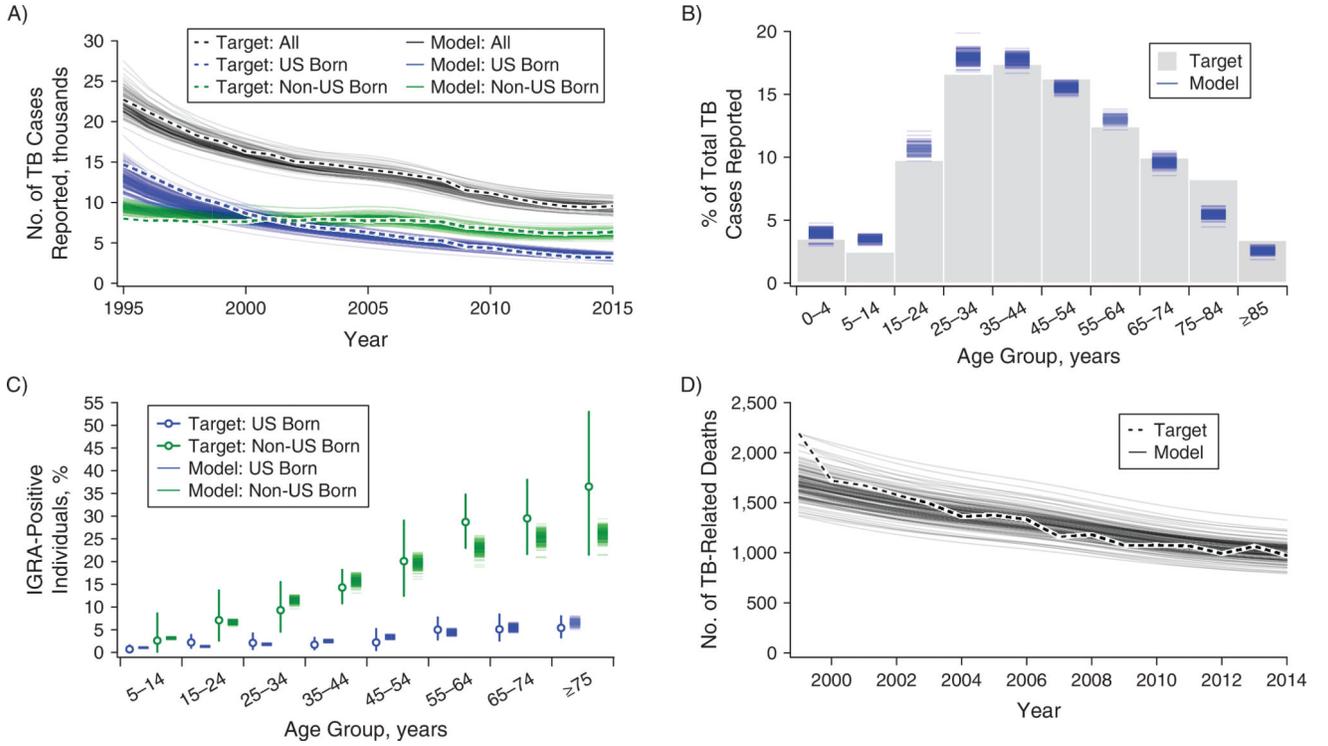


Figure 2. Comparison of model estimates and data describing recent TB outcomes: TB cases, drug-resistance patterns, LTBI prevalence, and death due to TB. Figure panels present data and estimates for 1995 to the most recent year available. Model results are plotted for 100 calibrated parameter sets to represent uncertainty in modeled results. TB case data were drawn from the routine TB case reporting system. The calibration target for human immunodeficiency virus–positive TB cases was adjusted to allow for incomplete reporting in early years. Calibration targets for LTBI prevalence estimates were derived from IGRA results from the National Health and Nutrition Examination Survey 2011–2012 (13). The calibration target for TB-related deaths represents reports of TB (*International Statistical Classification of Diseases and Related Health Problems, 10th Revision*, codes A16–19) included in multiple cause of death reports. IGRA, interferon- γ release assay; INH, isoniazid; LTBI, latent tuberculosis infection; MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

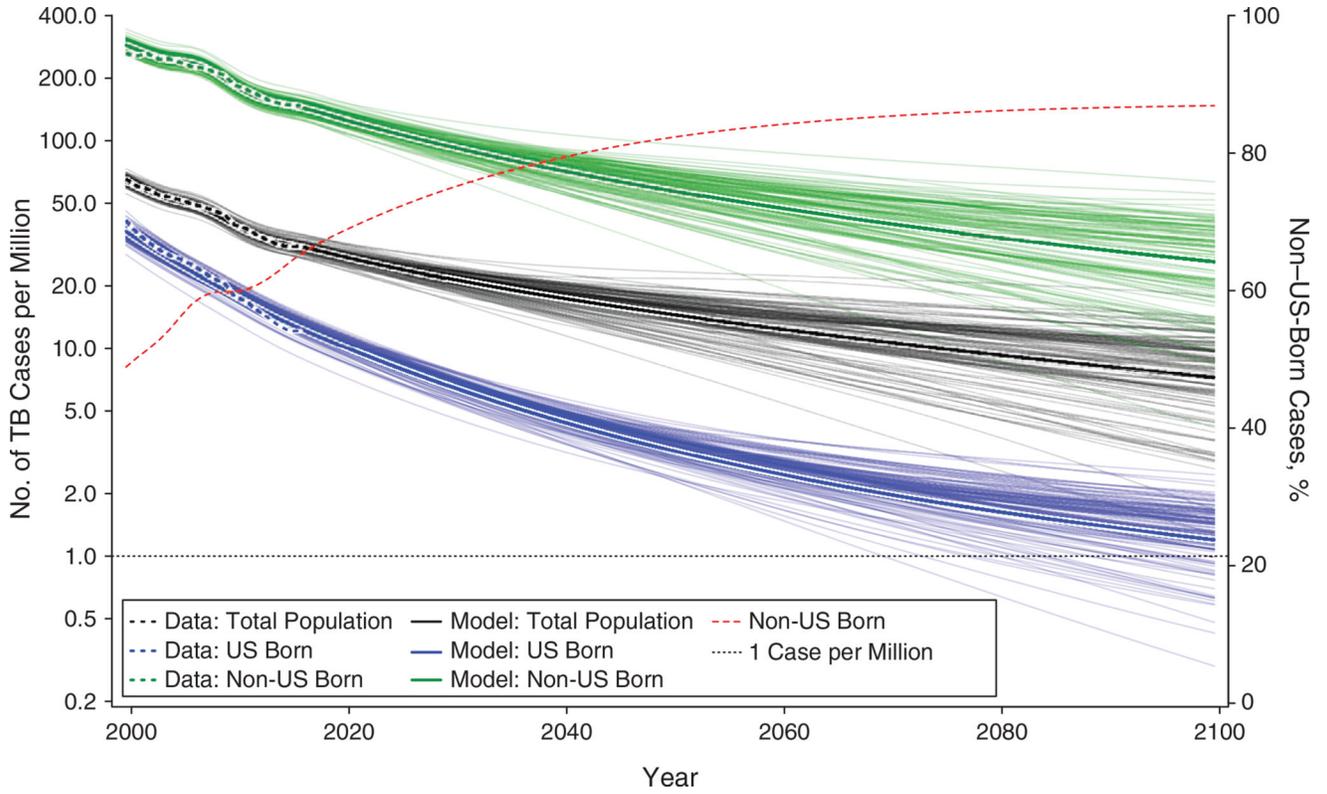


Figure 3. Historical and projected trends in TB cases in the United States with current prevention and treatment activities, stratified by nativity, 2000–2100. Bold solid lines represent the best estimate projection (posterior mean from Bayesian evidence synthesis) for a given population group and projection year. Faint solid lines represent results from 100 individual, calibrated parameter sets, representing uncertainty in modeled results. Dashed line represents the fraction of TB cases in each year among non-US-born persons. Horizontal dotted line represents the US TB elimination target (<1 annual TB cases per million). TB, tuberculosis.

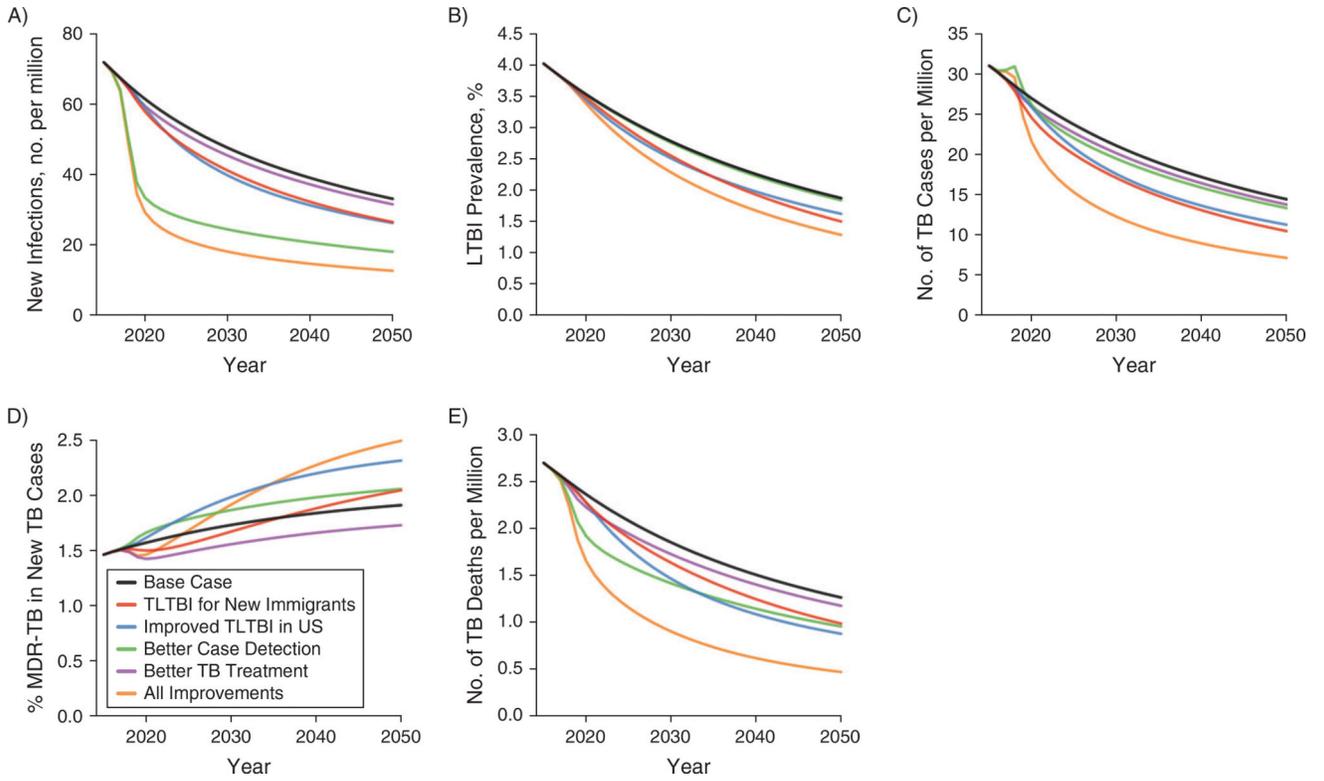


Figure 4. Projected trends in tuberculosis outcomes under modeled scenarios, 2015–2050. Lines represent best estimate projection (posterior mean from Bayesian evidence synthesis) for a given population group, scenario, and projection year. A) New *M. tuberculosis* infections per million. B) LTBI prevalence. C) Number of reported TB cases per million. D) Prevalence of MDR-TB among new TB cases. E) Number of TB deaths per million. LTBI, latent tuberculosis infection; MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis; TLTI, treatment of latent tuberculosis infection.

Table 1

Modeled Estimates of Tuberculosis Epidemiologic Outcomes for the Total, US-Born, and Non-US-Born Populations in 2016, 2025, 2050, and 2100

Population and Year	Outcomes														
	New Infections per Million ^a			LTBI Prevalence, %			TB Cases per Million			MDR-TB in Incident TB, %			TB Deaths per Million		
	Point Estimate ^b	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	
Total															
2016	69.7	59.6, 81.8	3.92	3.47, 4.40	30.2	27.3, 33.4	1.49	1.31, 1.71	2.63	2.04, 3.29					
2025	53.6	44.6, 64.1	3.12	2.77, 3.51	23.7	20.6, 27.0	1.66	1.41, 1.94	2.08	1.61, 2.63					
2050	33.0	21.4, 47.3	1.87	1.40, 2.37	14.4	9.7, 20.4	1.91	1.19, 2.73	1.26	0.88, 1.74					
2100	17.4	5.5, 35.9	0.92	0.29, 1.88	7.3	2.4, 15.2	2.08	0.55, 4.51	0.68	0.24, 1.33					
US born															
2016	58.8	48.7, 71.2	1.80	1.46, 2.18	11.9	10.2, 13.9	0.86	0.61, 1.21	1.24	0.96, 1.57					
2025	43.1	35.1, 53.0	1.23	0.99, 1.49	7.7	6.5, 9.1	0.94	0.67, 1.33	0.83	0.64, 1.06					
2050	24.1	16.5, 33.9	0.43	0.36, 0.52	3.1	2.4, 4.1	1.01	0.70, 1.45	0.33	0.24, 0.44					
2100	11.7	4.2, 23.4	0.08	0.06, 0.11	1.2	0.5, 2.3	0.91	0.44, 1.73	0.11	0.05, 0.21					
Non-US born															
2016	135	117, 157	16.6	15.0, 18.3	141	124, 162	1.80	1.60, 2.04	11.0	8.37, 14.1					
2025	107	85.7, 129	12.7	11.5, 14.1	105	89.0, 124	1.92	1.64, 2.24	8.43	6.34, 10.9					
2050	66.4	36.8, 102	7.24	5.11, 9.26	56.4	36.3, 80.4	2.10	1.27, 3.03	4.76	3.24, 6.67					
2100	35.0	9.2, 79.4	3.54	1.00, 7.21	26.1	8.2, 52.3	2.25	0.56, 4.92	2.46	0.84, 4.68					

Abbreviations: LTBI, latent TB infection; MDR-TB, multidrug-resistant TB; PI, posterior interval.

^aNew infections represent incident *Mycobacterium tuberculosis* infections acquired through transmission, excluding prevalent cases of LTBI among arriving migrants.

^bPoint estimate represents posterior mean from Bayesian evidence synthesis.

Table 2

Modeled Estimates of Tuberculosis Epidemiologic Outcomes for the Total, US-Born, and Non-US-Born Populations in 2025, 2050, and 2100 as a Percentage of Their 2016 Value

Population and Year	Outcomes											
	New Infections per Million ^a		LTBI Prevalence		TB Cases per Million		MDR-TB in Incident TB		TB Deaths per Million			
	Point Estimate ^b	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI	Point Estimate	95% PI		
Total												
2025	77	71, 82	80	77, 82	78	72, 84	111	102, 121	79	75, 83		
2050	47	32, 66	48	37, 59	48	33, 65	128	83, 180	48	37, 61		
2100	25	8, 52	24	7, 48	24	8, 49	140	38, 302	26	9, 49		
US born												
2025	73	69, 78	68	67, 70	65	62, 68	110	106, 113	67	64, 70		
2050	41	30, 55	24	23, 26	26	21, 33	118	102, 138	26	22, 31		
2100	20	7, 39	4	3, 6	10	4, 19	107	55, 198	9	4, 16		
Non-US born												
2025	79	69, 87	77	73, 80	75	68, 80	107	96, 116	77	72, 81		
2050	49	28, 72	44	31, 55	40	27, 55	116	73, 164	43	33, 54		
2100	26	7, 58	21	6, 43	19	6, 37	125	32, 269	22	8, 41		

Abbreviations: LTBI, latent TB infection; MDR-TB, multidrug-resistant TB; PI, posterior interval.

^aNew infections represent incident *Mycobacterium tuberculosis* infections acquired through transmission, excluding prevalent cases of LTBI among arriving migrants.

^bPoint estimate represents posterior mean from Bayesian evidence synthesis.