ORIGINAL ARTICLE

Impact of Effective Global Tuberculosis Control on Health and Economic Outcomes in the United States

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Abstract

Rationale: Most U.S. residents who develop tuberculosis (TB) were born abroad, and U.S. TB incidence is increasingly driven by infection risks in other countries.

Objectives: To estimate the potential impact of effective global TB control on health and economic outcomes in the United States.

Methods: We estimated outcomes using linked mathematical models of TB epidemiology in the United States and migrants' birth countries. A base-case scenario extrapolated country-specific TB incidence trends. We compared this with scenarios in which countries achieve 90% TB incidence reductions between 2015 and 2035, as targeted by the World Health Organization's End TB Strategy ("effective global TB control"). We also considered pessimistic scenarios of flat TB incidence trends in individual countries.

Measurements and Main Results: We estimated TB cases, deaths, and costs and the total economic burden of TB in the United States. Compared with the base-case scenario, effective global TB control would avert 40,000 (95% uncertainty interval, 29,000–55,000) TB cases in the United States in 2020–2035. TB incidence rates in 2035 would be 43% (95% uncertainty interval, 34–54%) lower than in the base-case scenario, and 49% (95% uncertainty interval, 44–55%) lower than in 2020. Summed over 2020–2035, this represents 0.8 billion dollars (95% uncertainty interval, 0.6–1.0 billion dollars) in averted healthcare costs and $2.5 billion dollars (95% uncertainty interval, 1.7–3.6 billion dollars) in productivity gains. The total U.S. economic burden of TB (including the value of averted TB deaths) would be 21% (95% uncertainty interval, 16–28%) lower (18 billion dollars [95% uncertainty level, 8–32 billion dollars]).

Conclusions: In addition to producing major health benefits for high-burden countries, strengthened efforts to achieve effective global TB control could produce substantial health and economic benefits for the United States.

Keywords: latent tuberculosis; immigration; economic burden of disease; mathematical model

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At a Glance Commentary

Scientific Knowledge on the Subject: Strengthening tuberculosis (TB) control in high-burden settings would provide major health benefits in affected countries. However, there is little evidence on the indirect benefits for low-burden countries that receive migrants from high-burden settings. A previous study of the benefits to the United States of improved TB control in Mexico, Haiti, and the Dominican Republic found that these benefits could be considerable.

What This Study Adds to the Field: This mathematical modeling study found that U.S. TB incidence rates in 2035 would be 43% lower compared with current trends if other countries achieve global TB control targets. The predicted reduction in TB rates represents 18 billion U.S. dollars in monetized health benefits and healthcare cost savings between 2020 and 2035.

Tuberculosis (TB) is the leading global cause of infectious disease deaths (1). For a small fraction of those infected with *Mycobacterium tuberculosis* (*Mtb*), active disease develops rapidly after exposure. For the rest, latent TB infection (LTBI) confers an ongoing risk of TB, such that exposures early in life can result in active disease many years later (2, 3). TB in the United States arises predominantly among non–U.S.-born individuals, and although annual TB cases among U.S.-born individuals have been declining steadily, annual TB cases among non–U.S.-born individuals have stabilized at 6,200–6,400 since 2012 (4–6). Future projections of U.S. TB incidence suggest stagnation of historical rates of decline and an increasing fraction of cases arising among the non–U.S.-born population (7–9). *Mtb* exposure within the United States is low, and most TB cases in non–U.S.-born residents are attributed to reactivation of long-standing LTBI (10, 11), which was likely acquired before entry to the United States. U.S. TB policy and services are centered on LTBI testing and treatment for non–U.S.-born residents and other high-risk populations (12, 13), with these epidemiological dynamics and accompanying control strategies mirroring those in other low-burden, high-income countries (14).

TB incidence trends in migrants' birth countries determine their cumulative *Mtb* exposure before entry, which in turn will determine the risks of TB from LTBI reactivation they face after entry. Mathematical modeling has demonstrated the sensitivity of U.S. TB epidemiology to TB trends among migrants (9, 15), and the potential benefits to the United States of better TB control in selected countries (16–18), raising the question of whether TB treatment and prevention in countries contributing most to the U.S. TB burden should be considered in parallel to massive efforts to test and treat migrants for LTBI after U.S. arrival.

This study describes how future TB outcomes in the United States—where one in seven residents is born abroad (19)—will be influenced by the success or failure of TB control in migrants' birth countries. In this study, we compare a base-case scenario—assuming current TB incidence trends continue—with an optimistic scenario in which birth countries (individually or collectively) achieve 90% TB incidence reductions between 2015 and 2035, as envisioned by the World Health Organization (WHO) End TB Strategy (20). We also examine a pessimistic scenario wherein TB incidence rates in birth countries remain at current levels.

Methods

Modeling Framework

We adapted an existing transmission dynamic model of TB in the U.S. resident population (9) (Figures E1 and E2 and Table E1 in the online supplement). The model simulates U.S. TB epidemiology and health services based on data reported to the U.S. Centers for Disease Control and Prevention on TB trends and mortality, LTBI prevalence, and TB services (6, 21). To estimate TB epidemiology among future migrants, we constructed models for the 30 countries from which the greatest number of non–U.S.-born TB cases were reported in 2000–2017, with one additional model representing the remaining countries. Models were parameterized to match country demography (22), TB incidence (23), and LTBI prevalence (24) (Figures E3 and E4). Using these models, we generated TB burden time trends for migrants entering the United States. Migration volumes and age distributions were calculated from American Community Survey data (25) (Figure E5). We calibrated the simulated TB epidemiology of migrating cohorts to reproduce trends in U.S. TB cases from each country during 2000–2017 (Figures E6–E8). Future migration volume was assumed to increase slowly (average 0.8% annually) following U.S. Census projections (26).

Scenarios

We assumed current epidemiological trends in each country would continue until 2020 and created scenarios for the subsequent trajectory of TB epidemiology, operationalized as changes in TB incidence trends (annual number of true incident TB disease cases per 100,000) between 2020 and 2035.

Base-case scenario. This scenario assumed that future TB incidence in each country would follow recent trends, estimated from the average annual percentage change in WHO-estimated incidence rates over 2007–2017 (23). For countries with increasing incidence, we assumed that mean incidence rates would not increase by more than 2% annually and allowed for uncertainty in these trends (Figure E9).

Optimistic scenario (achievement of WHO End TB Strategy goal). This scenario assumed each country would strengthen TB control to achieve a major target of the WHO's End TB Strategy (a 90% decline in TB incidence rates from 2015 levels by 2035) (20).

Pessimistic scenario (stagnation at current incidence levels). This scenario assumed countries with declining TB incidence trends would experience setbacks in TB control such that TB incidence rates in 2035 would be unchanged from those in 2020. Countries with increasing historical incidence trends were assumed to follow the same trend as the base-case scenario.

Optimistic and pessimistic scenarios were implemented by *1*) modifying the average duration of TB disease (representing improved/worsened TB case detection) and *2*) allowing for resolution of LTBI (representing expanded LTBI treatment). For the optimistic scenario, we adjusted the magnitude of changes so that each mechanism contributed 50% of the required reduction in incidence rates,

representing a TB control strategy targeting multiple epidemic mechanisms. For the pessimistic scenario, we assumed there would be no expansion of LTBI treatment and that TB treatment access would deteriorate to produce the required stagnation in incidence rates. Figure E10 compares LTBI prevalence estimates in 2015 and 2035. Optimistic and pessimistic scenarios were implemented for each country individually, for the set of five countries representing the greatest number of non–U.S.-born TB cases in the United States (Mexico, the Philippines, India, Vietnam, and China) (6), and for all countries collectively.

Outcomes

We estimated future outcomes for individuals entering and/or residing in the United States and calculated differences between optimistic and pessimistic scenarios and the base-case scenario. We did not assess costs or health outcomes realized outside of the United States. Health outcomes included incident TB cases, prevalent *Mtb* infection or disease among migrants, incident *Mtb* infections from transmission in the United States, TB deaths, life-years lost from TB mortality, and quality-adjusted life-years lost from TB. Economic outcomes included TB- and LTBI-related direct medical costs and productivity losses, including those from premature mortality (27). Total costs for each of these categories were calculated by multiplying the number of modeled events (TB and LTBI treatments and TB deaths) by estimates of unit costs and productivity losses adjusted for age and calendar year. Total economic burden (28) was calculated as the sum of direct medical costs, nonmortality productivity losses, and the economic value of TB deaths (total TB deaths multiplied by the Value of a Statistical Life [VSL] [29], estimated as 5.7 million U.S. dollars after adjusting for the age distribution of TB deaths), discounted annually at 3% (28). Costs were updated to 2018 U.S. dollars using personal consumption expenditure for health (for medical costs) and changes in average weekly earnings (productivity and VSL). *See* online supplement for additional details.

To capture consequences realized beyond the end of our 15-year time horizon, we conducted sensitivity analyses that included lifetime outcomes, in addition to the outcomes calculated for 2020–2035. These were estimated by simulating future outcomes for all individuals residing in the United States (U.S.-born and non–U.S.-born) after 2035 for the rest of their lifetime, assuming no further immigration or TB transmission.

Statistical Analysis

The analytic model was coded in R (version 3.5.2) and C++ via the Rcpp package (version 1.0.0) (30, 31). Bayesian evidence synthesis was used to calibrate models to data on population demography, TB epidemiology, and TB services (32) (Figures E11A and E11B). Using this approach, uncertainty in study outcomes is represented by a large number of simulated epidemic trajectories (33), which were estimated using incremental mixture importance sampling via the IMIS package (version 0.1) (34). Uncertainty in parameters not included in model calibration (e.g., unit costs and VSL estimates) was introduced by second-order Monte Carlo simulation. For each outcome of interest, point estimates were calculated as the mean value obtained from the distribution of simulated epidemic trajectories. Ninety-five percent uncertainty intervals were calculated as the 2.5th and 97.5th percentiles of the outcome distribution.

Results

Figure 1A shows reported U.S. TB cases and modeled TB estimates from 2000 to 2035 with the base-case scenario. Over 2020–2035, modeled U.S.-born TB cases declined at an average of 3.2% (95% uncertainty interval, 2.5 to 3.8) per year, whereas non–U.S.-born and total TB cases were relatively flat (averaging a 0.6% [95% uncertainty interval, −0.6% to 1.9%] increase and a 0.3% [95% uncertainty interval, −0.9% to 1.3%] decline per year, respectively). During this period, the fraction of TB cases among non–U.S.-born individuals increased to 83% (95% uncertainty interval, 80–85%), with 25% (95% uncertainty interval, 20–31%) among non–U.S.-born individuals within 2 years of U.S. arrival (Figure 1B) (compared with 70% and 17%, respectively, in 2017) (6).

Future TB Incidence

Figure 2A shows future U.S. TB incidence estimates when the three scenarios are applied to all countries collectively. In the base-case scenario, the overall incidence was projected to be 2.9 (95% uncertainty interval, 2.5 to 3.2) per 100,000 in 2020 and to decline to 2.5 (95% uncertainty interval, 2.1 to 3.1) per 100,000 by 2035, a 12% (95% uncertainty interval, −5% to 24%) reduction. In the optimistic scenario (assuming all countries achieve WHO End TB Strategy incidence targets for 2035), this reduction was projected to be 49% (95% uncertainty interval, 44 –55%) for an incidence rate of 1.4 (95% uncertainty interval, 1.2–1.7) per 100,000 in 2035, which is 43% (95% uncertainty interval, 34–54%) lower than the base-case scenario in the same year. In the pessimistic scenario (with incidence in all countries stagnating at current levels), the U.S. incidence rate was projected to be approximately level, dropping by just 1% (95% uncertainty interval, −13% to 12%) over 2020–2035 for an incidence rate of 2.9 (95% uncertainty interval, 2.5 to 3.2) per 100,000 in 2035, which is 12% (95% uncertainty interval, 4% to 23%) higher than the base-case scenario.

Figures 2B and 2C show TB incidence projections by scenario for U.S.-born and non–U.S.-born populations. U.S.-born incidence rates were projected to be 0.91 (95% uncertainty interval, 0.79–1.03) per 100,000 in 2020 and to decline by 43% (95% uncertainty interval, 36–48%) in the base-case scenario, reaching 0.51 (95% uncertainty interval, 0.43–0.61) per 100,000 in 2035. U.S.-born trends showed minor differences between optimistic and pessimistic scenarios, producing a 55% (95% uncertainty interval, 53–58%) reduction and a 40% (95% uncertainty interval, 33–44) reduction in incidence rates over 2020–2035, respectively. These modest differences are not surprising because the U.S.-born population is only indirectly impacted through changes in secondary transmission from non–U.S.-born individuals. Incidence rates for the non–U.S.-born population were projected to be 15 (95% uncertainty interval, 13 to 17) per 100,000 in 2020 and to remain stagnant, with an estimated decline of 7% (95% uncertainty interval, −10% to 22%) to reach 14 (95% uncertainty interval, 11 to 17) per 100,000 in 2035. The two alternative scenarios were projected to diverge rapidly, with a 51% (95% uncertainty interval, 46% to 58%) reduction 2020–2035 with the optimistic scenario and a potential 5% (95% uncertainty interval, −5% to 19%) increase with the pessimistic scenario.

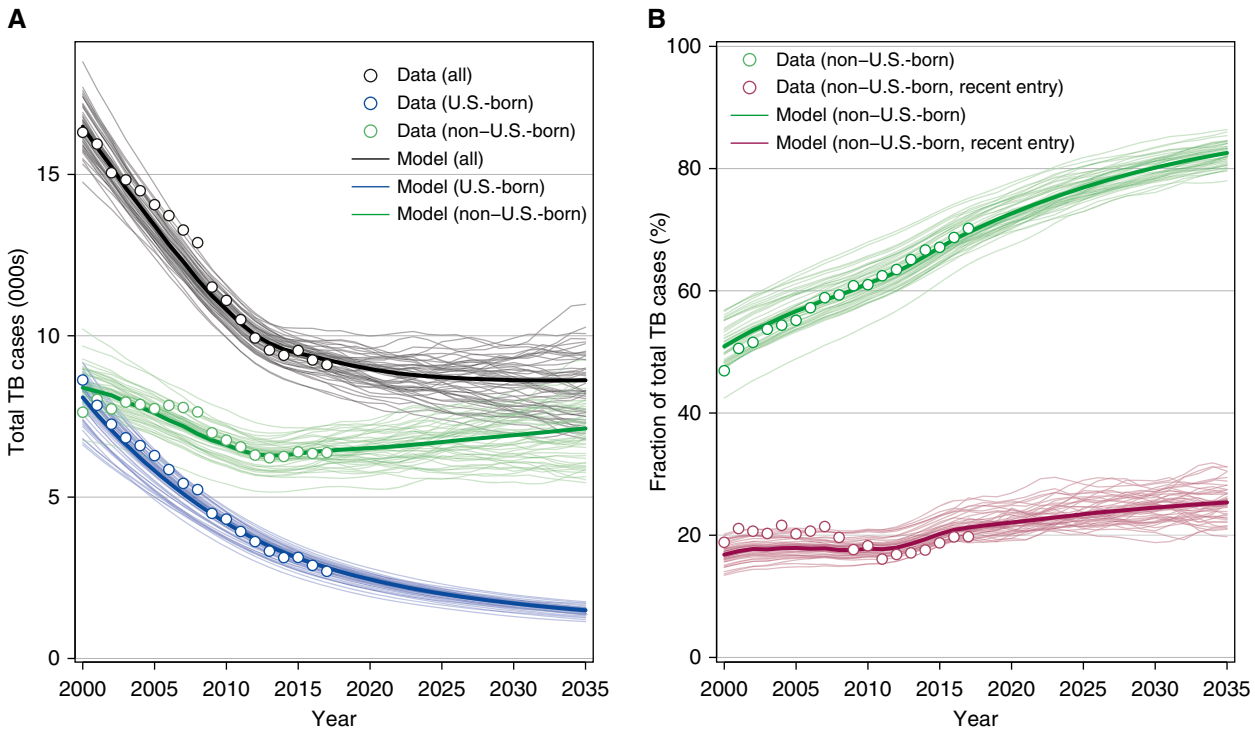

Figure 1. Estimated tuberculosis (TB) cases in the United States compared with reported data and projected cases to 2035 in the base-case scenario. (*A*) Total annual TB cases for U.S.-born, non–U.S.-born, and total populations (2000–2035). (*B*) Contribution of non–U.S.-born individuals and recent migrants to total annual U.S. TB cases (2000–2035). Lines represent multiple simulated epidemic trajectories. Recent entry indicates TB diagnosis with 2 years of U.S. entry.

Figure E12 shows U.S. TB incidence rate projections for optimistic and pessimistic scenarios applied to Mexico, the Philippines, India, Vietnam, and China collectively while all other countries follow their base-case trends. These results largely mirror Figure 2, with smaller but still substantial changes in incidence for total and non–U.S.-born populations. In the total population, the optimistic scenario produced U.S. TB incidence declines of 33% (95% uncertainty interval, 25% to 41%) over 2020–2035 (compared with 12% [95% uncertainty interval, −5% to 24%] under the base-case scenario), whereas the pessimistic scenario produced an estimated 7% (95% uncertainty interval, −9% to 18%) decline.

TB Cases Averted

In the base-case scenario, 148,352 (95% uncertainty interval, 127,065–173,106) U.S. TB cases are projected for the 2020–2035 period (32,810 [95% uncertainty interval, 28,396–37,286] U.S.-born and 115,541 [95% uncertainty interval, 96,385–136,823] non–U.S.-born). Table 1 shows total U.S. TB cases averted over the period of 2020–2035 for optimistic and pessimistic scenarios compared with the base-case scenario, for countries individually, for the top five countries, and for all countries collectively (Table E2 shows results for the top 30 countries). The countries with the highest number of TB cases averted under the optimistic scenario—Mexico and the Philippines—were those projected to contribute a large number of future migrants to the United States that currently have flat or rising TB incidence trends. The countries with the highest number of additional TB cases in the pessimistic scenario—Vietnam, China, and India—were those with rapidly declining current TB incidence trends. The 39,795 (95% uncertainty interval, 28,603–55,142) TB cases averted if all countries achieve the WHO End TB Strategy targets represent 27% (95% uncertainty interval, 21–34%) of all TB cases projected for the base-case scenario over 2020–2035. Of these averted cases, 7.1% (95% uncertainty interval, 5.9–8.6%) were projected to result from secondary infections averted among U.S.-born individuals, and 59% (95% uncertainty interval, 53–65%) of this reduction could be achieved if the top five countries achieved the WHO End TB Strategy targets.

Table E3 extends these results to include reductions in lifetime TB cases occurring after the end of 2035. In general, these values are 30–35% higher than those in Table 1, with 52,770 (95% uncertainty interval, 38,044–71,693) cases averted by the optimistic scenario over this extended time horizon.

Other Outcomes

Compared with the base-case scenario over 2020–2035, the optimistic scenario is projected to reduce total numbers of those entering the United States with prevalent *Mtb* by 27% (95% uncertainty interval, 21–34%), incident *Mtb* infections within the United States by 12% (95% uncertainty interval, 11–14%), TB deaths by 21% (95% uncertainty interval, 16–29%), life-years and quality-adjusted life-years lost to TB by 24% (95% uncertainty interval, 18–31%), TB healthcare costs by 16% (95% uncertainty interval, 13–21%), TB-related productivity losses by 23% (95% uncertainty interval, 18–29%), and the overall economic burden of TB by 21%

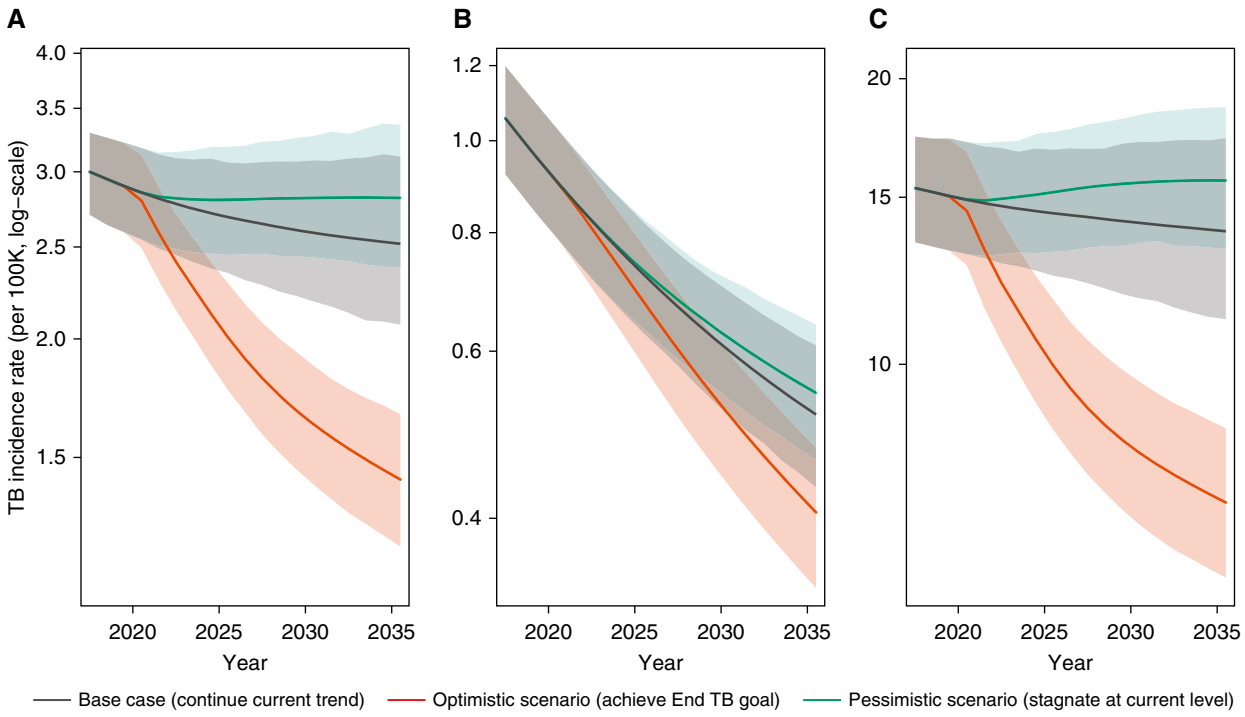

Figure 2. Projections of future tuberculosis (TB) incidence for the total population, U.S.-born population, and non–U.S.-born population in different scenarios for TB trends applied to all birth countries. (*A*) Total population. (*B*) U.S.-born population. (*C*) Non-U.S.-born population. Vertical axes are scaled to represent percentage changes equally in each panel. Solid lines represent best estimates for each scenario. Shaded regions represent 95% uncertainty intervals.

(95% uncertainty interval, 16–28%). Table 2 presents cumulative estimates for each outcome over the period 2020–2035, describing the incremental impact of the optimistic and pessimistic scenarios for all countries and the top five countries collectively. Table E4 shows results for the extended time horizon.

Discussion

TB is concentrated in low- and middle-income countries, and disparities between rich and poor countries have grown in recent years (23). These disparities, combined with migration from low- to high-income countries, mean that large numbers of individuals migrate to countries where *Mtb* exposure is orders of magnitude lower than in their birth countries. These individuals face lower TB risks than in their birth countries but higher risks than native-born individuals. The net effect for high-income countries is that TB is increasingly concentrated among migrant populations, with population TB trends sensitive to changes in migrant population size and *Mtb* exposure (35, 36).

Our study describes what could happen in the United States if TB control efforts are substantially improved—or stagnate—in the countries from which individuals migrate to the United States. In our optimistic scenario, in which all countries reduce TB incidence rates by 90% between 2015 and 2035 (20), we predict 40,000 (95% uncertainty interval, 29,000–55,000) fewer U.S. TB cases between 2020 and 2035 or 53,000 (95% uncertainty interval, 38,000–72,000) fewer TB cases including lifetime outcomes. Extrapolating incidence trends achieved in the optimistic scenario produces a high probability that the United States would reach the preelimination target of less than 1.0 TB case per 100,000 by 2050. In the base-case scenario, this threshold is unlikely to be reached before 2100. These impacts can be benchmarked against prior analyses examining radically strengthened TB services within the United States (9) in which large improvements in TB and LTBI detection and treatment were projected to have an impact on TB incidence approximately equal to that projected for the optimistic scenario. Even if the optimistic scenario is restricted to the top five countries (Mexico, the Philippines, India, Vietnam, and China), the reduction in TB incidence by 2035 is substantial, with 24,000 (95% uncertainty interval, 16,000–34,000) TB cases averted during 2020–2035.

Economic impacts estimated for these scenarios are similarly large, with 0.8 billion dollars (95% uncertainty interval, 0.6–1.0 billion dollars) in healthcare costs averted and 2.5 billion dollars (95% uncertainty interval, 1.7–3.6 billion dollars) in productivity gains accruing by 2035 in the optimistic scenario applied to all countries. Healthcare averted costs and productivity gains rise to 1.2 billion dollars (95% uncertainty interval, 0.9–1.5 billion dollars) and 3.7 billion dollars (95% uncertainty interval, 2.6–5.3 billion dollars), respectively, if lifetime outcomes are included. Over the 2020–2035 period, the optimistic scenario is estimated to reduce the total economic burden of TB in the United States by 18 billion dollars [(95% uncertainty interval, 8–32 billion dollars]), reflecting the large number of TB deaths averted in this scenario (3,600 [95% uncertainty interval, 2,300–5,500]) and the high value placed on mortality reductions.

In the pessimistic scenario applied to all countries, U.S. TB incidence trends are

Table 1. Cumulative TB Cases Averted during 2020–2035 for Optimistic and Pessimistic Scenarios Compared with the Base-Case Scenario

Country	Optimistic Scenario (Meet WHO End TB Strategy Goal) [*n (95% Uncertainty Interval)*]			Pessimistic Scenario (Stagnate at Current Incidence Level) [*n (95% Uncertainty Interval)*]		
	U.S.-Born	Non–U.S.-Born	Total Population	U.S.-Born	Non–U.S.-Born	Total Population
Mexico	413 (247 to 672)	5,563 (3,477 to 8,514)	5,976 (3,750 to 9,068)	−18 (−74 to 0)	−261 (−1,086 to 0)	−278 (−1,156 to 0)
Philippines	684 (379 to 1,193)	8,769 (4,985 to 15,072)	9,453 (5,383 to 16,196)	−27 (−112 to 0)	−365 (−1,507 to 0)	−393 (−1,635 to 0)
Vietnam	195 (104 to 333)	2,522 (1,371 to 4,194)	2,717 (1,496 to 4,529)	−76 (−164 to −13)	−1,064 (−2,146 to −192)	−1,140 (−2,294 to −204)
India	239 (138 to 402)	2,999 (1,799 to 4,823)	3,237 (1,949 to 5,239)	−99 (−195 to −20)	−1,340 (−2,518 to −283)	−1,439 (−2,725 to −305)
China	165 (96 to 282)	2,074 (1,228 to 3,367)	2,239 (1,328 to 3,644)	−77 (−148 to −23)	−1,055 (−1,957 to −326)	−1,132 (−2,094 to −349)
Haiti	48 (27 to 83)	605 (355 to 1,037)	653 (382 to 1,118)	−28 (−53 to −10)	−376 (−675 to −150)	−404 (−719 to −160)
Guatemala	75 (44 to 123)	1,016 (612 to 1,633)	1,091 (662 to 1,762)	−16 (−39 to 0)	−234 (−536 to 0)	−250 (−574 to 0)
Ethiopia	27 (13 to 50)	341 (164 to 617)	368 (177 to 665)	−46 (−77 to −26)	−622 (−992 to −369)	−668 (−1,059 to −395)
Honduras	45 (27 to 74)	603 (373 to 940)	648 (400 to 1,007)	−10 (−24 to 0)	−145 (−336 to 0)	−154 (−356 to 0)
South Korea	14 (8 to 22)	193 (115 to 293)	207 (124 to 314)	−4 (−9 to −1)	−69 (−136 to −13)	−74 (−144 to −14)
All countries	2,834 (1,946 to 4,281)	36,961 (26,535 to 50,979)	39,795 (28,603 to 55,142)	−589 (−1,069 to −210)	−8,150 (−14,298 to −2,899)	−8,739 (−15,326 to −3,114)
Top five countries	1,696 (1,111 to 2,644)	21,930 (14,824 to 31,487)	23,626 (15,966 to 34,109)	−297 (−580 to −82)	−4,084 (−7,660 to −1,137)	−4,381 (−8,242 to −1,214)

Definition of abbreviations: TB = tuberculosis; WHO = World Health Organization.

Table lists results for the top 10 countries for non–U.S.-born persons with TB in the United States individually as well as all countries and the top five countries collectively. Table E2 lists results for the top 30 countries for non–U.S.-born persons with TB in the United States.

Table 2. Cumulative Health and Economic Outcomes for Optimistic and Pessimistic Scenarios for 2020–2035 Compared with the Base-Case Scenario

Outcome	Base-Case Scenario [*n (95% Uncertainty Interval)*]	Optimistic Scenario (Meet WHO End TB Strategy Goal) [*n (95% Uncertainty Interval)*]		Pessimistic Scenario (Stagnate at Current Incidence Level) [*n (95% Uncertainty Interval)*]	
		All Countries	Top Five Countries	All Countries	Top Five Countries
Prevalent *Mtb* among migrants*, thousands	8,045 (6,799 to 9,490)	7,072 (5,992 to 8,340)	7,600 (6,420 to 8,963)	8,187 (6,936 to 9,652)	8,108 (6,860 to 9,566)
Incremental difference vs. base-case	—	−973 (−1,200 to −772)	−445 (−563 to −344)	141 (41 to 250)	63 (19 to 115)
New *Mtb* infections in the United States, thousands	338 (282 to 398)	245 (206 to 289)	283 (239 to 327)	358 (305 to 422)	348 (292 to 410)
Incremental difference vs. base-case scenario	—	−93 (−129 to −66)	−55 (−80 to −38)	20 (7 to 36)	10 (3 to 19)
TB deaths	16,811 (12,722 to 20,461)	13,196 (9,707 to 15,991)	14,282 (10,644 to 17,244)	17,522 (13,305 to 21,188)	17,214 (13,067 to 20,831)
Incremental difference vs. base-case scenario	—	−3,615 (−5,501 to −2,348)	−2,529 (−3,977 to −1,584)	712 (249 to 1,296)	403 (108 to 794)
Life-years lost to TB, thousands	297 (224 to 363)	226 (171 to 275)	252 (190 to 307)	311 (235 to 378)	305 (229 to 371)
Incremental difference vs. base-case scenario	—	−70 (−103 to −47)	−45 (−68 to −29)	15 (5 to 26)	8 (2 to 15)
QALYs lost to TB, thousands	332 (259 to 403)	253 (197 to 304)	282 (220 to 339)	349 (274 to 420)	341 (267 to 412)
Incremental difference vs. base-case scenario	—	−80 (−115 to −54)	−50 (−76 to −33)	17 (6 to 30)	9 (2 to 17)
Healthcare costs, 2018 USD, millions	4,629 (4,017 to 5,317)	3,866 (3,376 to 4,483)	4,188 (3,651 to 4,822)	4,793 (4,170 to 5,449)	4,710 (4,101 to 5,380)
Incremental difference vs. base-case scenario	—	−763 (−1,040 to −552)	−442 (−630 to −301)	163 (57 to 287)	81 (23 to 152)
Productivity losses, 2018 USD, millions	10,869 (8,496 to 13,215)	8,373 (6,607 to 9,974)	9,363 (7,361 to 11,209)	11,410 (8,882 to 13,720)	11,148 (8,740 to 13,444)
Incremental difference vs. base-case scenario	—	−2,496 (−3,638 to −1,662)	−1,506 (−2,256 to −974)	540 (189 to 967)	279 (75 to 521)
Total economic burden, 2018 USD, millions	83,954 (39,967 to 136,235)	65,996 (32,417 to 104,072)	72,112 (35,270 to 114,628)	87,582 (42,263 to 140,883)	85,942 (41,159 to 138,288)
Incremental difference vs. base-case scenario	—	−17,957 (−31,540 to −7,886)	−11,842 (−21,567 to −5,069)	3,628 (1,061 to 7,652)	1,988 (453 to 4,437)

Definition of abbreviations: LTBI = latent TB infection; *Mtb* = *Mycobacterium tuberculosis*; QALY = quality-adjusted life year; TB = tuberculosis; USD = U.S. dollars; WHO = World Health Organization.

Incremental differences calculated by subtracting the value estimated for the base-case scenario from the value estimated for optimistic and pessimistic scenarios. Negative values represent improvement in a given metric, and positive values represent deterioration (e.g., negative incremental deaths averted implies fewer deaths under the optimistic scenarios).

*Includes individuals with LTBI as well as active TB.

predicted to flatten, threatening TB prevention and control goals and resulting in extra TB cases (9,000 [95% uncertainty interval, 3,000–15,000]), TB deaths (700 [95% uncertainty interval, 200–1,300]), healthcare costs (0.16 billion dollars [95% uncertainty interval, 0.06–0.29 billion dollars]), productivity losses (0.55 billion dollars [95% uncertainty interval, 0.19–0.97 billion dollars]), and total economic burden (3.6 billion dollars [95% uncertainty interval, 1.1–7.7 billion dollars]) by 2035 compared with the base-case scenario. For both optimistic and pessimistic scenarios, the economic consequences should be compared with the costs of efforts to strengthen global TB control (37, 38).

This study presents stylized scenarios for the success or failure of global TB control, based on major policy statements and targets (20, 39). These scenarios do not consider country-specific factors that shape TB control strategy or how implementation challenges will be confronted. Evidence suggests that these challenges will be substantial, requiring technical and programmatic innovation as well as major new investment (38, 40). Moreover, we did not investigate the relative capabilities of different countries to achieve TB control goals. These capabilities will differ, such that even if global-level goals are met, progress will vary across countries. Country-specific analyses are required to assess realistic goals for TB control and optimal policy portfolios for pursuing them (41). Although we did not model the impact of U.S. policy changes (9, 42), our results are broadly supportive of existing policies that target screening and treatment for non–U.S.-born individuals migrating to or residing in the United States (43, 44) and the potential expansion of these policies (45). Finally, although analyses allowed for uncertainty in many inputs, several key factors are difficult to predict, including domestic TB policy, long-term immigration trends, and changes in the composition of migrant inflows (such as increasing refugee numbers) that affect TB risk.

Although this study focused on outcomes in the United States, strengthening TB control in high-burden countries will principally reduce the human suffering and early deaths from TB experienced by communities in these countries. There is a strong ethical rationale for efforts to support global TB control (46), and this compelling motivation has driven both financial investments and political engagement, exemplified by the Post-2015 Global TB Strategy adopted by the World Health Assembly in 2014. Our study highlights additional justifications for the United States and other high-income, low-transmission countries to support TB control in high-burden settings—based on the potential for substantial domestic health and economic benefits—and confirms the common stake that all countries have in accelerating global TB elimination. ■

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