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Estimating tuberculosis cases and their economic costs averted in the United States over the past two decades

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SUMMARY

BACKGROUND—Following a concerted public health response to the resurgence of tuberculosis (TB) in the United States in the late 1980s, annual TB incidence decreased substantially. However, no estimates exist of the number and cost savings of TB cases averted.

METHODS—TB cases averted in the United States during 1995–2014 were estimated: Scenario 1 used a static 1992 case rate; Scenario 2 applied the 1992 rate to foreign-born cases, and a pre-resurgence 5.1% annual decline to US-born cases; and a statistical model assessed human immunodeficiency virus and TB program indices. We applied the cost of illness to estimate the societal benefits (costs averted) in 2014 dollars.

RESULTS—During 1992–2014, 368 184 incident TB cases were reported, and cases decreased by two thirds during that period. In the scenarios and statistical model, TB cases averted during 1995–2014 ranged from approximately 145 000 to 319 000. The societal benefits of averted TB cases ranged from US$3.1 to US$6.7 billion, excluding deaths, and from US$6.7 to US$14.5 billion, including deaths.

CONCLUSIONS—Coordinated efforts in TB control and prevention in the United States yielded a remarkable number of TB cases averted and societal economic benefits. We illustrate the value of concerted action and targeted public health funding.

Abstract

A la suite d'une réponse concertée de santé publique à la résurgence de la tuberculose (TB) aux Etats-Unis à la fin des années 1980, l'incidence annuelle de la TB a considérablement décru. Il n'y a cependant pas d'estimations du nombre de cas de TB évités et des coûts épargnés.

Les cas de TB évités aux Etats-Unis entre 1995 et 2014 ont été estimés : le premier scénario a utilisé un taux statique de cas de 1992 ; le deuxième scénario a appliqué le taux de 1992 aux cas nés à l'étranger et un déclin annuel de 5,1% avant la résurgence, aux cas nés aux Etats-Unis ; un

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modèle statistique a évalué les indices des programmes pour le virus de l'immunodéficience humaine et TB. Nous avons appliqué le coût de la maladie afin d'estimer les bénéfices pour la société (coûts évités) en dollars 2014.

Entre 1992 et 2014, 368 184 cas de TB ont été déclarés et le nombre de cas a diminué de deux tiers pendant cette période. Dans les scénarios et le modèle statistique, le nombre de cas de TB évités entre 1995 et 2014 allait d'environ 145 000 à 319 000. Les bénéfices sociaux des cas de TB évités allaient de US$3,1à US$6,7 milliards, en excluant les décès, et de US$6,7 à US$14,5 milliards, en incluant les décès.

Les efforts coordonnés de prévention et de lutte contre la TB aux Etats-Unis ont abouti à un nombre remarquable de cas évités et de bénéfices sociaux. Nous illustrons la valeur d'une action concertée et d'un financement de santé publique ciblé.

Abstract

A raíz de la respuesta concertada de salud pública a la reaparición de la tuberculosis (TB) en los Estados Unidos al final de los años 1980, la incidencia anual de TB disminuyó de manera considerable. Sin embargo, no existen estimaciones sobre el número de casos evitados y el ahorro de costes.

Se llevó a cabo una estimación de los casos de TB evitados entre 1995 y el 2014 en los Estados Unidos; en la primera hipótesis se utilizó una tasa de incidencia estática a partir de 1992; en la segunda hipótesis se aplicó la tasa de 1992 a los casos nacidos en el extranjero y el 5,1% de la disminución anual en el país antes de la reaparición de la enfermedad a los casos nacidos en los Estados Unidos; y en un modelo estadístico se evaluaron los índices de los programas contra la TB y la infección por el virus de la inmunodeficiencia humana. Se aplicó el costo de la enfermedad con el fin de estimar la ganancia para la sociedad (costos evitados) en dólares del 2014.

De 1992 al 2014 se notificaron 368 184 casos nuevos de TB y se observó una disminución de dos tercios de los casos durante este período. Según las diferentes hipótesis y el modelo estadístico, el número de casos evitados de 1995 al 2014 osciló entre 145 000 y 319 000. Los casos evitados significaron una ganancia para la sociedad que osciló entre 3,1 y 6,7 mil millones de dólares al excluir las defunciones y entre 6,7 y 14,5 mil millones de dólares cuando se incluyeron.

En los Estados Unidos, los esfuerzos coordinados de control y prevención de la TB tuvieron como resultado un número notable de casos de TB evitados y considerables ganancias económicas para la sociedad. El estudio destaca el valor de la acción concertada y de la financiación orientada de la salud pública.

Keywords

TB; public health benefits and costs; low-incidence country; United States

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REPORTED TUBERCULOSIS (TB) CASES in the United States declined substantially from 1953 to 1985 (Figure 1). However, between 1985 and 1992, the country experienced an unprecedented reversal in that long-standing trend.[1] During this 8-year period, several outbreaks of multidrug-resistant TB (MDR-TB) occurred, predominantly affecting people with human immunodeficiency virus (HIV) infection in congregate settings (e.g., health care facilities and prisons).[2] TB incidence increased by 20%, with an estimated excess of 52 100 TB cases.[1] This situation required an urgent and comprehensive national reaction,[3,4] supported by new federal and state funding.[5] The Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) coordinated the national and multi-agency response, which included:

1. Training of health care providers to improve the ability to diagnose and treat persons with TB disease
2. Improving laboratory diagnostic methods with universal drug susceptibility testing (DST) of initial clinical specimens that were culture-positive for *Mycobacterium tuberculosis* complex[6,7]
3. Implementing infection control precautions in health care facilities and other congregate settings[8]
4. Strengthening state and local health department TB programs to undertake monitoring of treatment until cure and to conduct contact investigations,[4,9] and
5. Conducting programmatically relevant research.[10,11]

Following the implementation of these various measures, TB incidence decreased steadily between 1993 and 2014.[12]

The purpose of the present report is to quantify the public health benefits of the decline in TB incidence over the past two decades following the resurgence. We estimated the number and value of TB cases averted using two plausible scenarios. We also developed a statistical model using selected TB program indices.

MATERIALS AND METHODS

Data sources

We obtained the annual number of TB cases between 1953 and 2014 from data reported to the National Tuberculosis Surveillance System (NTSS) maintained by the CDC. NTSS includes diagnostic, clinical, and treatment data on TB cases from all 50 states, the District of Columbia, several large cities, and US territories.[13] CDC began collecting data on *M. tuberculosis* culture conversion, DST, and HIV status in 1993. Yearly TB cases were stratified by patient birthplace (i.e., US-born and foreign-born) and by drug resistance status (e.g., MDR-TB or extensively drug-resistant TB [XDR-TB], and non-MDR/XDR-TB).

We also used data reported by state TB programs to the CDC with the average number of persons having contact with infectious (pulmonary, sputum smear-positive) TB patients. From 1993 until 1999, these numbers are from an unpublished database of CDC TB Program Reports, and for 2000 until 2012 from Aggregate Reports for TB Program Evaluation (ARPE).[14]

Statistical analyses

We examined the total and annual percentage change (APC) in TB cases during 1992–2014, and constructed two scenarios to estimate the number of TB cases that might have occurred without the above-mentioned interventions. We developed a statistical model using selected TB program indices to further evaluate associations with TB cases averted. For each of the two scenarios and the statistical model, the estimated number of TB cases averted was calculated by subtracting the observed number of TB cases from the estimate.

Scenario 1: static 1992 TB case rate

We assumed that 1) the annual US TB incidence rate would remain static at the 1992 peak level of the resurgence (10.4 per 100 000 population); 2) the annual incidence rate of foreign-born TB cases would remain static at the 1992 rate (34.5/100 000); 3) US-born incident TB cases would be the difference of foreign-born estimated TB cases from total estimated TB cases; and 4) the number of averted MDR/XDR-TB US-born and foreign-born TB cases was calculable from actual annual proportions of TB cases who are MDR/XDR-TB among US-born and foreign-born TB cases, respectively.

Scenario 2: static 1992 TB case rate for foreign-born, 5.1% APC decline for US-born

We assumed that 1) annual US-born TB incident cases would decline by 5.1% annually (the historic trend before the TB resurgence, APC for 1953–1985, computed from NTSS data, Figure 1); 2) the annual incidence rate of foreign-born TB cases would remain static at the 1992 rate (34.5/100 000); 3) total TB cases were the sum of US-born and foreign-born estimated TB cases; and 4) the number of averted MDR/XDR-TB US-born and foreign-born TB cases was calculable from actual annual proportions of TB cases who are MDR/XDR-TB among US-born and foreign-born TB cases, respectively.

Statistical model of TB program indices

We developed a statistical model with five TB indices identified by previous analyses as being most associated with the decline in TB incidence[15,16] and HIV status. Indices included the percentage of TB cases alive at diagnosis and who:

1. had any use of directly observed therapy (DOT)
2. completed treatment and were alive within 1 year of treatment initiation, excluding TB that was meningeal, of the bone or joint, or the central nervous system, initially resistant to rifampin, or TB in children aged ≤14 years that was miliary or diagnosed by a blood specimen that was positive for *M. tuberculosis* on culture or nucleic acid amplification test
3. were initially *M. tuberculosis* culture-positive, for which DST was conducted on the *M. tuberculosis* isolate
4. were initially *M. tuberculosis* culture-positive and ever had documented *M. tuberculosis* sputum culture conversion
5. had HIV co-infection (alive or dead at diagnosis) (except in California, which did not report HIV-TB to CDC from 2005 to 2010), and

6. the average number of contacts elicited per *M. tuberculosis* sputum acid-fast bacilli smear-positive TB case.

Based on publications by McKenna et al.[15] and Lobato et al.,[16] we assumed that improvements in indices of effective TB control and prevention in year t_0 would affect the number of TB cases 2 years later (t_{0+2}). Using NTSS data beginning in 1993 and ARPE data through 2012, we developed a linear regression model to estimate the number of TB cases in year t_{0+2} from associations with the above TB program indices in time t_0. We found that two variables, sputum culture conversion and the percentage of TB patients who also had HIV, were statistically associated with the number of TB cases and had the greatest association with the decline in TB cases from 1995 to 2014.

This statistical model is represented as follows:

TB cases in year t_{0+2} = 32 207 − (314.3 * per cent sputum culture conversion in t_0) + (669.1 * per cent of patients with HIV in t_0). $R^2 = 0.99$

Using coefficients estimated in the model, and substituting in values for sputum culture conversion (65%) and the percentage of TB cases with HIV (16%) that represented values at the beginning of the time period, we estimated that there would be 22 485 (95% confidence interval [CI] 21 609–23 360) TB cases in each year if the sputum culture conversion rate remained static at 65% and if 16% of TB cases had HIV. The number of observed cases in each year was subtracted from the estimate of 22 485 and then summed to calculate the total number of averted TB cases.

Societal benefits of TB cases averted

We applied a cost of illness per estimated TB case averted to calculate the societal benefits (costs averted) in 2014 dollars of cases prevented for each scenario and the statistical model. In-patient and out-patient direct costs in 2010 dollars of non-MDR-TB reported and methods described in Shepardson et al.,[17] were updated to 2014 dollars by using the Consumer Price Index for Medical Care.[18] Direct costs in 2010 dollars of MDR- and XDR-TB were similarly updated to 2014 dollars.[19] The value of premature deaths due to MDR-TB was published previously;[19] however, there were no reported deaths among XDR-TB patients in that study, and we had to estimate non-MDR- and XDR-TB premature deaths as follows. For non-MDR-TB, we estimated, from an analysis of a cohort of >17 000 TB cases from 15 US study sites, that 72% of deaths with TB are because of TB;[20] and, from the NTSS, that 9% of TB patients die during treatment or are diagnosed with TB at death.[12] Thus, 72% × 9% = 6.48% of the value of premature life lost was attributed to TB. Productivity losses due to premature deaths,[21]* updated to 2014 US dollars using the change in average hourly earnings, were estimated at US$24 214 for non-MDR-TB patients (US$373 671 with death at age 65 × 6.48% of patients having deaths caused by TB) and at US$64 153 for XDR-TB patients (US$926 653 with death at age of 55, the average age at death for MDR-TB patients[19] multiplied by 6.92% of patients having deaths caused by TB—the actual

*The present value of future earnings, based on data from the Bureau of Labor Statistics Current Population Survey, and household production were discounted at 3% annually. These are estimates from persons surveyed and might not be representative of populations not surveyed, including institutionalized persons.

percentage in the published MDR-TB patient sample).[19] These costs were added to the societal costs for non-MDR-TB[17] and for XDR-TB.[19] Societal costs, including premature deaths for MDR-TB, were calculated at the individual age at death of patients.[19]

The costs used to estimate the value of cases averted are summarized in the Table. Direct medical costs in 2014 dollars are estimated at US$17 000 per non-MDR/XDR-TB case, US $150 000 per MDR-TB case, and US$482 000 per XDR-TB case. Societal cost estimates, excluding productivity losses due to premature deaths and rounded to the nearest thousand, are: US$20 000 per non-MDR/XDR-TB case, US$225 000 per MDR-TB case, and US$621 000 per XDR-TB case. Including lost productivity because of premature death, the societal costs are estimated at US$44 000 per non-MDR/XDR-TB case, US$282 000 per MDR-TB case, and US$664 000 per XDR-TB case.

To allow comparison of equal time periods for the two scenarios and the model, the number and societal benefits of TB cases averted for each year and for the total period of 1995 to 2014 were estimated.

RESULTS

Between 1992, when 26 673 cases were reported, and 2014, when 9421 cases were reported, a total of 368 184 incident TB cases occurred in the United States. The number of incident TB cases was reduced by nearly two thirds over the period, at an average APC decline of 4.6%. Actual annual TB incidence from 1953 to 2014 is depicted in Figure 1, with projections for scenarios 1 and 2.

The estimated annual number of averted TB cases for the two scenarios and the model are shown in Figure 2. Figure 3 shows the overall averted TB cases stratified by US-born and foreign-born persons for both scenarios (the number of averted foreign-born TB cases was the same for Scenarios 1 and 2). The total numbers of averted TB cases during 1995–2014 were respectively 318 948, 144 852, and 157 497 for scenarios 1 and 2 and the statistical model (Figure 2). Figure 4A shows increases in the annual percentage for four program indices, and a reduction in the annual percentage of HIV-infected TB cases during 1993–2012. Figure 4B shows the average number of contacts elicited per *M. tuberculosis* sputum acid-fast bacilli smear-positive TB case during 1993–2012.

The number and value of TB cases averted is greatest using Scenario 1, and much lower for both Scenario 2 and the statistical model. Excluding lost productivity because of premature death, the societal benefits of averted TB cases were estimated at respectively US$6.7, US $3.1 and US$3.4 billion for Scenario 1, Scenario 2, and the statistical model. Including lost productivity due to premature death, the societal benefits were respectively US$14.5, US $6.7 and US$7.3 billion (Figure 5).

DISCUSSION

Our analysis estimates that 144 852–318 948 TB cases were averted between 1995 and 2014, following the implementation of various TB control and prevention measures. In addition, we calculated the economic societal benefit accrued from the estimated averted cases over an extended period in TB incidence, including specific estimates for cases averted and the benefits of preventing difficult-to-treat forms of MDR-TB. In addition to preventing TB suffering and morbidity, the societal economic benefit, excluding the value of premature deaths, of averting TB cases ranged from US$3.1 to US$6.7 billion in 2014 US dollars. When we included the value of premature deaths lost to TB, the societal benefit of these public health program interventions ranged between US$6.7 and US$14.5 billion over the period 1995–2014.

Our scenarios and model were selected to be cautious and avoid exaggerating the long-term benefits of these public health interventions. While the upward trend in TB cases due to the resurgence in the late 1980s could have continued into the 1990s, we relied on two conservative scenarios in estimating the upper and lower bounds of the averted TB cases (Figure 1). The regression model provided additional information about the association between TB case trends and the proportion of sputum culture-positive patients who converted to culture-negative during treatment, and the percentage of TB cases with HIV. Coincidentally, the estimates of the number of TB cases averted using the regression model and Scenario 2 are similar, possibly providing additional validation to estimates from Scenario 2. Sputum culture conversion reflects good management of TB disease, suggesting that an effective treatment regimen is taken for a sufficient period. This index also signals the practice of universal DST to guide the selection of the most effective TB treatment regimen, instituted in 1993.[22] Recent evidence from a study in South Africa showed that prompt placement of TB patients on effective treatment rapidly reduces TB transmission.[23] McKenna et al. previously hypothesized that TB outbreaks affecting persons with HIV in the early 1990s were quelled by various measures that reduced TB transmission, including large investments in laboratory capacity and hospital infection control.[15] While transmission among persons with HIV likely declined as a result of infection control measures, we found that the percentage of TB cases with HIV has remained a significant predictor of TB cases throughout the past two decades.

Hill et al. estimated future TB trends in association with different interventions, and divided the population into US-born and foreign-born.[24] This stratification was maintained in two of our modeling scenarios, as the largest proportion of TB cases in the United States occurs in foreign-born persons (66% of reported TB cases in 2014). During the first decade following the peak annual TB incidence in 1992, when the larger proportion of cases occurred in US-born persons, the larger number of averted TB cases was also in the US-born population. However, by 2003, averted TB cases in the foreign-born population exceeded the US-born in our most conservative scenario. Despite the remarkable progress in averting TB cases, accelerated declines remain necessary in both populations.

There are limitations to the two scenarios and statistical model. First, they might mask state, local, and country of origin level effects on TB cases and trends within those smaller units. Future analyses will examine these in depth. Second, the number of TB cases among foreign-born persons varies by country of origin, and US population estimates and trends of foreign-born persons might lack accuracy. Third, the statistical model is unable to predict with precision the impact of individual interventions. Last, cost estimates exclude out-of-pocket costs to patients and the cost of investigating patients who present for medical attention with signs and symptoms of TB disease but are subsequently determined not to have TB disease, and the value of preventing secondary transmission from the averted TB cases.

As a country, the United States provided global public health leadership by developing and publishing in 1989 the national strategic plan for the elimination of TB in the United States.[25] Progress towards TB elimination, defined as annual TB incidence of fewer than one TB case per million population, was both reversed and threatened by the unprecedented resurgence of TB between 1985 and 1992. In response, various federal government agencies partnered with state and local public health departments, professional organizations, and academic institutions to design and implement research into new rapid laboratory diagnostic tools and treatment regimens, and used the data to develop, update, and implement evidence-based guidelines. Through CDC TB cooperative agreements with health departments in all 50 states, selected large cities, and US territories, the federal government has also provided technical and financial support to ensure prompt identification, treatment, and cure of persons with TB disease.[9,26] In addition, these various health jurisdictions have implemented updated policies to mitigate economic obstacles to the diagnosis and treatment of TB, and legal statutes aimed at reducing the risk of airborne *M. tuberculosis* transmission.[27] Furthermore, these various entities have provided assistance in responding to community and institutional TB outbreaks, implementing infection control and preventing TB transmission in health care and congregate settings such as correctional facilities and homeless shelters, as well as preventing TB disease progression in latently infected populations at high risk.[28] Successes have been described previously for New York City,[29] and for the rest of the country.[15,16] These combined efforts undertaken in partnerships among non-governmental organizations, federal, state, and local health departments have produced longstanding success since 1993 in reducing the incidence of TB. Widespread introduction of antiviral treatment for persons with HIV has also resulted in remarkable reductions in TB incidence in the United States and Europe.[30,31]

We document remarkable progress achieved in the United States over the past two decades to prevent suffering, morbidity, costs of direct medical care, and deaths due to TB disease. Sustaining these gains, while crucial, is insufficient for accelerated progress towards TB elimination. As previously reported,[24,25] an emphasis on targeted testing and treatment of persons with latent tuberculous infection is also required for TB elimination.

TB incidence in the United States is at its nadir, precariously accompanied by a renewed risk of complacency and the conditions that contributed to the 1985–1992 resurgence of TB.[1,32] The call to action by the US Institute of Medicine remains poignantly relevant 15 years later: ‘The question yet to be answered is whether the renewed opportunity that now presents itself to move toward elimination of tuberculosis will be seized or whether tuberculosis will be subject to another period of neglect until the next resurgence.’[32] This precise challenge is also being confronted globally by the World Health Organization's new End TB Strategy, which aims to ultimately eliminate TB.[33] The last two decades of progress against TB in the United States has demonstrated that achieving these ambitious targets demands both a comprehensive approach and unrelenting effort.

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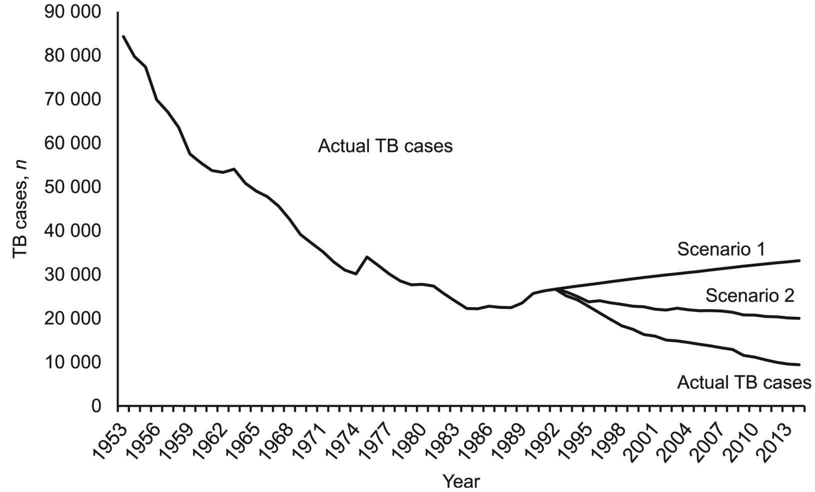

Figure 1.

US TB incidence (1953–2014) and TB cases averted (1992–2014) for Scenarios 1 (static 1992 TB case rate) and 2 (static 1992 TB case rate in foreign-born, 5.1% APC decline in US-born). TB = tuberculosis; APC = annual percentage change.

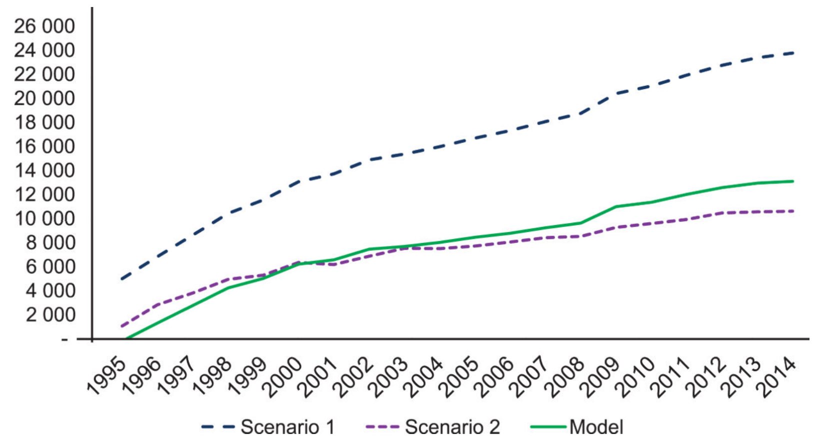

Figure 2.

The annual number of tuberculosis cases averted in the United States, 1995–2014. This image can be viewed online in color at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000007/art00016.

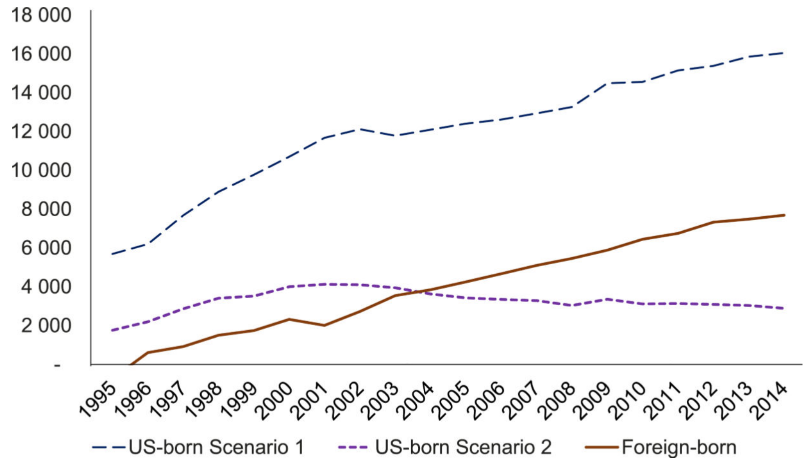

Figure 3.

The annual number of TB cases averted, US-born for Scenarios 1 and 2, and foreign-born for either scenario, 1995–2014. This image can be viewed online in color at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000007/art00016.

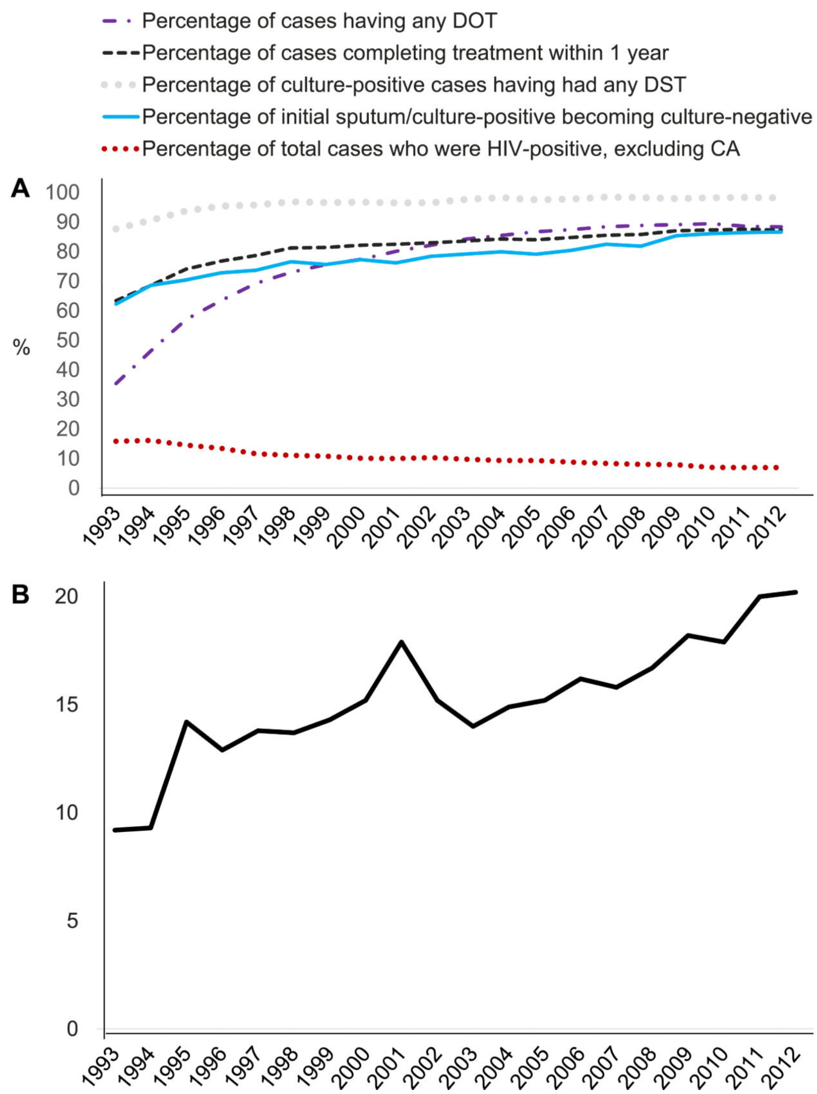

Figure 4.

Trends in TB program indices, 1993–2012; **A)** trends in TB indicators, 1993–2012; **B)** average number of contacts per TB case, 1993–2012. DOT=directly observed therapy; DST=drug susceptibility testing; HIV = human immunodeficiency virus; CA = California; TB = tuberculosis. This image can be viewed online in color at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000007/art00016.

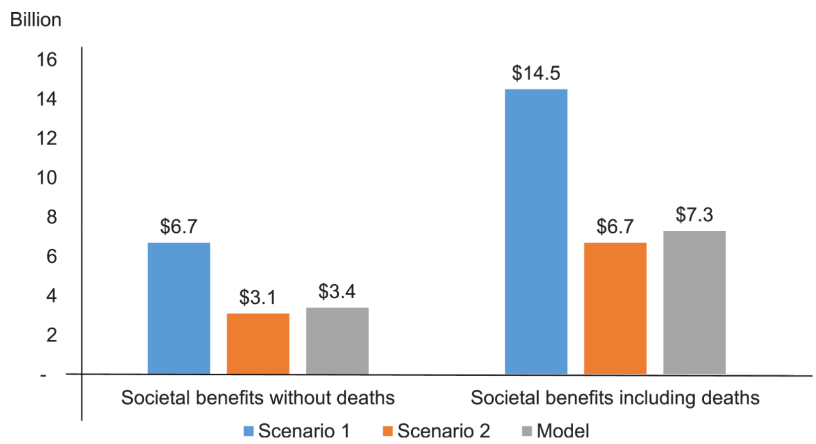

Figure 5.

Societal benefits in 2014 billion dollars of tuberculosis cases averted, excluding and including lost productivity due to premature deaths, 1995–2014. This image can be viewed online in color at http://www.ingentaconnect.com/content/iuatld/ijtld/2016/00000020/00000007/art00016.

Table

The cost of TB illness per case, 2014 US dollars

	Non-MDR-TB $US	MDR-TB $US	XDR-TB $US
Direct cost	17 000	150 000	482 000
Societal cost, excluding productivity lost due to premature deaths	20 000	225 000	621 000
Societal cost, including productivity lost due to premature deaths	44 000	282 000	664 000

TB = tuberculosis; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB.