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Epidemiology of Tuberculosis in the United States

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INTRODUCTION

What is now recognized as tuberculosis (TB) has been part of the human experience for all of recorded history, although it was not until the early 19th century that the various clinical presentations of the disease were first postulated to be one condition, and not until later in that century that TB was recognized as an infectious disease caused by *Mycobacterium tuberculosis* complex.[1,2] In addition to the understanding of TB as an infectious disease that was transmissible person to person, researchers applied age-period-cohort methods in the 1930s to demonstrate that the burden of TB in a given cohort at a young age could help to predict the TB burden in that cohort later in life.[3,4] This observation was some of the earliest evidence that TB could remain "latent" in the body for many years after initial infection before progressing to clinically evident TB disease; this is now commonly known as latent TB infection (LTBI).

However, research in the last 10–20 years has drawn into question the classical model of TB as having two clinical states: LTBI and "active" TB disease. Rather, evidence now supports a model where infection with *M. tuberculosis* complex (i.e., "TB infection") is recognized to exist on a clinical spectrum.[5–7] Patients who reside on a part of the spectrum where the cell-mediated immune response to TB infection can be detected through in-vivo (i.e., tuberculin skin testing; TST) or in-vitro (i.e., interferon-gamma release assay; IGRA) testing, but whose degree of tuberculous lesions remain below the limit of detection of available methods (e.g., radiography or microbiologic testing) are diagnosed as having LTBI.[5–8] Correspondingly, those persons whose tuberculous disease is severe enough to be detectable are classified as having TB disease.[5–7] However flawed a dichotomization might be in terms of the true pathophysiology of TB, it can nonetheless be useful when studying TB

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epidemiology because it is helpful to think of LTBI as potentially preventable TB disease, even if infected individuals are not now showing any signs of illness or able to transmit the infection to others.

In the United States, TB prevention activities have first focused on early detection and treatment of TB cases, in order to cure the patient and prevent further TB transmission.[9] The second priority is contact investigation around infectious TB cases, to identify other TB disease or LTBI cases and offer treatment to reduce the risk of those individuals progressing to TB disease.[9] Finally, as program resources allow, the third priority is to conduct targeted TB infection testing among high-risk populations to identify persons with remotely acquired LTBI and offer treatment.[9]

U.S. TB MORBIDITY, MORTALITY, AND DISABILITY-ADJUSTED LIFE YEARS

MORBIDITY

TB DISEASE

DIAGNOSIS AND VERIFICATION OF TB CASES FOR INCLUSION IN OFFICIAL COUNTS: The U.S. government began systematically tracking TB morbidity nationwide in 1953, shortly after the widespread introduction of anti-TB chemotherapy drugs.[10] Definitive diagnosis of TB requires compatible clinical signs and symptoms (e.g., persistent cough, unexplained weight loss, night sweats) in combination with laboratory and diagnostic imaging results consistent with TB.[11] TB disease requires a minimum of 6 months of treatment following diagnosis, and cases are often not detected immediately because of the slow progression of the disease and TB's mimicry of more common illnesses such as community-acquired pneumonia.[11] This long treatment period makes it is especially important in describing the morbidity of TB to distinguish between incidence (new disease cases observed during a period of interest) and prevalence (all disease cases observed during the period). For TB, the more useful concept is incidence, and TB incidence is commonly described in terms of case counts and incidence rates. CDC uses U.S. Census Bureau official census and midyear postcensal estimates for population denominator data in the calculation of incidence rates, and rates are typically expressed in CDC TB surveillance data in terms of cases per 100,000 persons in the population of interest during the period of interest.[12] While both measures are useful, this review will focus on annual incidence rates in order to account for the effect of changes in the size of the underlying population.

In order for U.S. TB surveillance reporting areas to verify a TB case for surveillance purposes, the case must meet the criteria for one of the three diagnostic classifications of TB: laboratory confirmation via positive culture or direct testing of a clinical specimen (81%), meeting clinical case criteria in the absence of laboratory confirmation (14%), or expert opinion of a healthcare provider for cases that do not meet either the laboratory or clinical criteria (5%).[12]

MORBIDITY TRENDS: U.S. TB incidence rates (Figure 1) consistently decreased at annual percent declines from 2.1% to 11.1% from the introduction of systematic national surveillance in 1953 (52.6 cases per 100,000 persons) to 1985 (9.3). In 1986, the incidence

rate increased (9.5) for the first time over the preceding year (previous recorded increases in 1963 and 1975 were artifacts caused by changes in TB surveillance practices or one-time immigration events).[10,12] This 1.6% increase in incidence rate could not be explained by either an administrative change in reporting criteria or a one-time immigration event.[12] Although declines resumed during 1987–1988, they were much slower (0.4–1.1% annual decline in case count and 1.3–2.0% annual decline in incidence rate).[12] In 1989, a marked increase occurred in incidence rate (3.7%), followed by less dramatic increases during 1990–1992 (1.5–2.3% annual increase in case count and 0.1–0.9% annual increase in incidence rate).[12] This increase prompted considerable concern, including a Congressional investigation.[10] In 1987, the U.S. Department of Health and Human Services established the Advisory Committee (later Council) for the Elimination of TB (ACET) to "provide recommendations for the development of new technology, application of prevention and control methods, and management of state and local tuberculosis programs targeted toward the elimination of tuberculosis as a public health problem."[13] In response, CDC and ACET created a strategic plan for the elimination of TB in the United States, establishing for the first time a national goal of TB elimination (defined as <1 TB case per 1,000,000 population).[13] Major factors that fueled the U.S. TB resurgence were the emergence of human immunodeficiency virus (HIV), the spread of multidrug-resistant (MDR) TB (a problem first noted in 1978), and reductions in resources for U.S. TB control programs.[14–31] A federal task force created the first National Action Plan to combat MDR TB in 1993.[32] This initial plan has subsequently been updated and built upon with other strategic planning documents, most recently in 2015.[33] As a result of these efforts, primary MDR TB (i.e., MDR TB in a patient with no prior history of TB disease) has constituted <2% of U.S. TB cases since 1995.[12]

Beginning in 1993, the annual incidence rate began to decline again each year until 2015, when it increased slightly from 2.9 to 3.0 before beginning to decrease again in 2016 (2.9) and 2017 (2.8).[12] An analysis of incidence rate trends during this period found that there are three distinct periods based on average annual percent change (APC) during 1993–2012: 1993–2000 (APC = −7.3%), 2000–2007 (APC = −3.7%), and 2007–2012 (APC = −6.7%).[34] The relatively steep 2007–2012 decline included an abrupt drop in 2009 from 4.2 to 3.8 (−10%) that raised concerns about potential underascertainment of TB cases; however, extensive investigations did not find evidence to support underdetection of TB cases.[35–37] One hypothesis for the abrupt decline was that the contemporaneous U.S. economic recession resulted in changes in migration patterns that influenced the TB incidence rate.[35] Another potential explanation was the introduction of new technical instructions for overseas panel physicians screening for TB among non-U.S.–born persons who were seeking legal permanent residency in the United States.[38] Since 2012, though, the APC has been only −2.2%.[34] This slowing trend has been observed across geographic and national origin strata, although it is notable that during the entire 1993–2017 period, incidence rates among U.S.-born persons declined at a substantially faster pace than rates among non-U.S.–born persons; in fact, incidence rates for non-U.S.–born persons during 2013–2017 were essentially flat.[34] These data indicate that the percentage of U.S. TB cases occurring among non-U.S.–born persons has been steadily increasing.

LTBI ESTIMATES—While LTBI has been viewed as an important aspect (and a particular challenge) of TB epidemiology, measuring and reducing LTBI has historically been considered a tertiary priority in the U.S. TB control program.[9] The highest program priority is prompt detection and treatment of TB disease cases in order to prevent further transmission, followed by contact investigation to identify and treat persons recently infected with TB to prevent progression to TB disease.[9] However, more recent experience including the results of multiple statistical models have reinforced the outsized effect of LTBI on the long-term epidemiology of TB disease, particularly in low-incidence countries.[39–41] Unlike TB disease, LTBI is a condition that exists without clinical signs or symptoms. Accordingly, rather than incidence, prevalence is the preferred approach to describing LTBI morbidity. Also unlike TB disease, because LTBI cases will not come to the attention of the public health system without some form of active case-finding, traditional case-based public health surveillance is ill-suited to generating LTBI prevalence estimates.

Beginning in 1971, CDC has conducted periodic TB infection prevalence surveys as part of the National Health and Nutrition Examination Survey (NHANES), which is an annual survey that assesses the health and nutritional status of U.S. residents as part of a continuous program to meet emerging public health needs.[42–44] The 2011–2012 NHANES estimated that 4.7% of the civilian, noninstitutionalized U.S. population aged ≥6 years were infected with TB, which corresponds to approximately 13.3 million persons.[44] An estimated 5.0% of males and 4.4% of females were infected based on TST results, with the highest prevalence of infection among persons 45–64 years of age.[44] Based on TST results, groups with higher LTBI prevalence included non-U.S.–born persons (20.5%), Hispanics (12.3%) and non-Hispanic Asians (22.2%).[44] LTBI prevalence estimates using IGRA resulted in similar patterns as for TST.[44] In all populations, LTBI prevalence estimates did not significantly differ from the NHANES 1999–2000 estimates.[43,44]

In addition to supporting periodic NHANES estimates, CDC continues to explore other innovative approaches to estimating LTBI prevalence. One of these approaches takes advantage of an established, field-validated method using routinely collected U.S. TB surveillance data, linked to molecular genotyping information, to classify TB cases as being attributed to recent transmission (occurring in the preceding 2 years) by using this recent transmission estimate as the basis for “back-calculation” of the underlying LTBI prevalence.[45–47] Other approaches using mathematical modeling have also been published.[48]

MODELING THE FUTURE—Given the numerous key determinants of U.S. TB incidence rates, CDC and its partners have developed several advanced statistical models to explain and predict incidence rate trends.[39–41] These models include many of the known predictors for TB incidence, and they indicate that without any changes in current U.S. TB control practices, incidence rate declines will continue to slow, with the main contributor to this trend being the prevalence of LTBI in the United States, particularly among non-U.S.–born persons.[39–41]

MORTALITY AND DISABILITY

The United States has made considerable progress in reducing deaths attributed in TB (Figure 2). In 1953, the TB mortality rate was 12.4 deaths per 100,000 persons; however, within 10 years the rate had declined over 60% to 4.9 in 1963.[12] After another decade, the rate had dropped by a similar degree to 1.8 in 1973, and this trend continued similarly into the early 1980s before slowing during the TB resurgence of the late 1980s.[12] After the end of the resurgence, the mortality rate rapidly declined again until reaching 0.2 in 2003, where it has remained since then.[12] A similar, although slower, trend has occurred with case fatality ratios, declining from 23.4% in 1953 to approximately 5.0–6.0% in the last several years.[12] Statistical modeling of TB mortality rates predicts that the mortality rate will remain close to 0.2 until at least 2025 before the pace of decline in mortality begins to accelerate again.[41]

Reliance on vital statistics (death certificate) data for TB mortality estimates has prompted concerns that these estimates might represent persons who died *with* TB (i.e., TB was not the actual cause of death) rather than persons who died *from* TB; however, recently published research has found that most (72%) persons who die with TB did in fact have a TB-related death.[49] Delayed diagnosis is the major risk factor for TB mortality; almost three fourths of persons who died from TB did so before diagnosis or within a month of treatment initiation.[49] Other risk factors include HIV infection (or not knowing the patient's HIV status), particularly severe forms of TB disease, preexisting comorbidities, use of immunosuppressive medications, multidrug resistance, and exclusion of pyrazinamide from the initial treatment regimen (possibly because of concern about hepatotoxicity).[49,50]

In the last two decades, public health programs have increasingly understood the importance of long-term effects of disease in patients who survive. The disability-adjusted life year (DALY) is a summary measure combining years of life lost to premature death with time lived in less than perfect health, which the DALY calculation refers to as "disability."[51] Figure 3 shows the TB DALY and DALY rate (per 100,000 population) estimates for the United States, the Group of Seven (G7) industrialized countries, and for all WHO-member states.[51] The U.S. DALY rate is on average >200 times lower than the global rate and nearly four times lower than the G7 rate; the U.S. rate also declined by nearly half between 2000 and 2015.[51] This suggests that the United States has been more effective at preventing TB death and disability than the world in general or even the comparably developed economies of the G7 countries; however, it is not clear what factors have led to the U.S. success in this regard.

U.S. TB RISK FACTORS

RISK FACTORS FOR ACQUISITION OF TB INFECTION

The beginning and end of the TB epidemiologic cycle is transmission of the infection to a new host, and one of the most important goals of public health programs is to prevent uninfected persons from becoming infected. This primary prevention goal is the top priority of the U.S. TB program. Only persons with respiratory forms of TB are considered infectious; however, nearly 80% of all U.S. TB cases reported in 2017 had a respiratory site

of disease.[12] Over 70% of 2017 pulmonary TB cases were sputum-culture positive, which is an indication of infectiousness.[12] The risk at a population level of becoming infected with TB is directly related to the concentration (case or incidence rate) of infectious TB cases to which that person is exposed.

The strongest risk factor for becoming infected with TB is the country in which a person is born or spends most of his or her life. For example, a person born in sub-Saharan Africa, where most countries report TB incidence rates ≥300 cases per 100,000 population, has about 100 times the risk on average of being exposed to someone with TB than a person who was born in the United States, where the incidence rate in 2017 was 2.8 cases per 100,000.[12,52] As a nation of immigrants, this difference is particularly striking in the United States when comparing U.S.-born and non-U.S.–born persons. During 2011–2012, NHANES estimated the overall prevalence of TB infection (based on a conservative TB infection definition requiring that both TST and IGRA results be positive) in the United States at approximately 2%; however, when stratified by origin of birth, the TB infection prevalence among non-U.S.–born persons using the double-positive definition was about 9%, which is considerably higher than the estimate among U.S.-born persons (0.6%).[44] As a result, non-U.S. birth is the major defining risk factor for >70% of U.S. TB cases, while the approximately 30% of cases occurring among U.S.-born persons typically involve one or more clinical or social risk factors such as immunocompromise, homelessness, or substance misuse.[12]

This difference in risk of infection is further demonstrated through the birth cohort effect.[3,4,12] However, even when stratifying by origin of birth among U.S. TB disease cases reported during 1996–2016 and controlling for age and period effects, all successive birth cohorts had lower age-specific incidence rates than all previous cohorts.[53] This strong birth-cohort effect is the consequence of steady reductions over time in the risk of TB exposure for each successive cohort.[53]

The next most important risk factor for acquiring TB infection is documented close contact with a TB patient; the risk of infection increases proportionately to the amount of time spent in close contact with persons who have infectious TB disease.[54] Accordingly, any circumstances that can lead to crowding can increase the risk of TB infection and disease, e.g., estimated TB rates among persons experiencing homelessness (36–47 cases per 100,000) and incarceration (8–29 cases per 100,000).[55–57] Two analyses of data from the 1999–2000 NHANES cycle identified associations between tobacco smoking or exposure to secondhand tobacco smoke and acquiring TB infection; however, this association has not been identified in subsequent NHANES cycles.[58,59]

Occupation can also increase risk of exposure to TB. Healthcare workers are at least theoretically at particular risk for TB exposure, although only a small proportion of U.S. TB cases are reported among healthcare workers, and these individuals often have other risk factors for acquiring TB infection, such as birth outside of the United States.[60] A recent analysis in Canada, which has similar TB epidemiology to the United States, found that occupational exposure to TB (based on workers' compensation claims) was relatively uncommon.[61]

PROGRESSION OF TB INFECTION TO TB DISEASE

HIV coinfection played a major role in the resurgence of TB in the late 1980s and early 1990s.[17,19,21] Systematically assessing the degree of coinfection has been challenging because of low rates of HIV testing of TB patients and incomplete reporting of these data to CDC; however, efforts to promote testing and treatment for HIV infection have been largely successful.[62] In 1993, only 30% of TB patients were tested for HIV, but nearly half of those tested were HIV-positive.[12] In contrast, by 2017 nearly 90% of TB patients had been tested for HIV, and only 5.5% were positive.[12] Even among this small proportion of coinfected patients, it is unclear how many are substantially immunocompromised given the widespread availability of highly effective antiretroviral therapy.

Individuals who misuse alcohol or drugs or who smoke tobacco are also at higher risk of progressing to TB disease, which could be because of a combination of factors including impaired overall health status.[63–67] Use of TNF-α inhibitors for conditions such as rheumatoid arthritis is also associated with progression to TB disease.[68] Additional risk factors for progression to TB disease include diabetes mellitus (19.1% of reported TB cases) and other non-HIV immunocompromising conditions, including end-stage renal disease and history of solid organ transplantation (7.5%).[12,69–80]

DISCUSSION

As the U.S. TB control program enters a new decade, a combination of old and new approaches are needed to maintain and accelerate progress toward eliminating TB in the United States. Traditional programmatic priorities focused on early detection of TB cases, prompt treatment of TB cases to prevent further transmission, and early identification and treatment of recently infected persons to reduce the risk of progression to TB disease have been highly successful in reducing TB incidence among U.S.-born persons; however, the decline in TB incidence among the non-U.S.–born has been much slower, largely because U.S.-based efforts to reduce recent transmission are substantially less effective in reducing TB incidence among non-U.S.–born populations that were most likely infected many years before arriving in the United States. Accordingly, more emphasis is needed on testing for and treating LTBI in high-risk populations such as the non-U.S.–born. However, while epidemiologic models have demonstrated that stopping recent transmission in the United States alone will not be sufficient to achieve TB elimination, it is equally clear from the TB resurgence in the late 1980s and early 1990s that control measures aimed at reducing recent transmission must be maintained to prevent a reversal of the substantial gains in TB control achieved during the last 70 years.

While it cannot be at the expense of transmission control activities, wherever possible TB control programs should increase their investments in testing for and treating LTBI among high-risk populations in order to accelerate progress toward TB elimination in the United States.[81] More sensitive and specific tests are needed for TB infection to ensure that LTBI cases are not missed and persons without LTBI are not treated unnecessarily.[81] Continued progress is also needed on developing LTBI treatment regimens that are less expensive, shorter, and less toxic than current treatments.[81] In addition, development of diagnostic tests that can distinguish which LTBI cases are more likely to progress to TB disease would help

to prioritize LTBI cases for treatment.[82] Finally, improvement of overseas TB screening of persons seeking entry into the United States to include more visa types and broaden testing for TB infection beyond children could substantially reduce the burden of TB among non-U.S.–born persons living in the United States.[83]

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REFERENCES

1. Dubos RJ, Dubos J. The white plague; tuberculosis, man and society Boston: Little, Brown; 1952.
2. Koch R Die Atiologic der Tuberkulose. Berliner KlinischeWochenschrift 1882;15:221–230.
3. Frost WH. The age selection of mortality from tuberculosis in successive decades. 1939. Am J Epidemiol 1995;141(1):4–9; discussion 3. [PubMed: 7801964]
4. Andvord KF, Wijsmuller G, Blomberg B. What can we learn by following the development of tuberculosis from one generation to another? 1930. Int J Tuberc Lung Dis 2002;6(7):562–568. [PubMed: 12102293]
5. Dutta NK, Karakousis PC. Latent tuberculosis infection: myths, models, and molecular mechanisms. Microbiol Mol Biol Rev 2014;78(3):343–371. [PubMed: 25184558]
6. Drain PK, Bajema KL, Dowdy D, et al. Incipient and Subclinical Tuberculosis: a Clinical Review of Early Stages and Progression of Infection. Clin Microbiol Rev 2018;31(4).
7. Sousa J, Saraiva M. Paradigm changing evidence that alter tuberculosis perception and detection: Focus on latency. Infect Genet Evol 2018.
8. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis 2017;64(2):111–115. [PubMed: 28052967]
9. CDC. Essential components of a tuberculosis prevention and control program. Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR Recomm Rep 1995;44(RR-11): 1–16.
10. U.S. Congress Office of Technology Assessment. The Continuing Challenge of Tuberculosis, OTA-H-574 In. Washington, DC: U.S. Government Printing Office; 1993.
11. Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis 2016;63(7):e147–e195. [PubMed: 27516382]
12. CDC. Reported Tuberculosis in the United States, 2017 Atlanta, GA: CDC;2018.
13. CDC. A strategic plan for the elimination of tuberculosis in the United States. MMWR Morb Mortal Wkly Rep 1989;38(16):269–272. [PubMed: 2495428]
14. Villarino ME, Geiter LJ, Simone PM. The multidrug-resistant tuberculosis challenge to public health efforts to control tuberculosis. Public Health Rep 1992;107(6):616–625. [PubMed: 1454973]
15. Kent JH. The epidemiology of multidrug-resistant tuberculosis in the United States. Med Clin North Am 1993;77(6):1391–1409. [PubMed: 8231419]
16. Brudney K, Dobkin J. Resurgent tuberculosis in New York City. Human immunodeficiency virus, homelessness, and the decline of tuberculosis control programs. Am Rev Respir Dis 1991;144(4): 745–749. [PubMed: 1928942]
17. CDC. Nosocomial transmission of multidrug-resistant tuberculosis among HIV-infected persons--Florida and New York, 1988–1991. MMWR Morb Mortal Wkly Rep 1991;40(34):585–591. [PubMed: 1870559]

18. Reichman LB. The U-shaped curve of concern. Am Rev Respir Dis 1991;144(4):741–742. [PubMed: 1928940]
19. Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant Mycobacterium tuberculosis infections. Factors in transmission to staff and HIV-infected patients. JAMA 1992;268(10):1280–1286. [PubMed: 1507374]
20. Daley CL, Small PM, Schecter GF, et al. An outbreak of tuberculosis with accelerated progression among persons infected with the human immunodeficiency virus. An analysis using restriction-fragment-length polymorphisms. N Engl J Med 1992;326(4):231–235. [PubMed: 1345800]
21. Dooley SW, Villarino ME, Lawrence M, et al. Nosocomial transmission of tuberculosis in a hospital unit for HIV-infected patients. JAMA 1992;267(19):2632–2634. [PubMed: 1573751]
22. Edlin BR, Tokars JI, Grieco MH, et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. N Engl J Med 1992;326(23): 1514–1521. [PubMed: 1304721]
23. Pearson ML, Jereb JA, Frieden TR, et al. Nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis. A risk to patients and health care workers. Ann Intern Med 1992;117(3):191–196. [PubMed: 1352093]
24. Snider DE Jr., Roper WL. The new tuberculosis. N Engl J Med 1992;326(10):703–705. [PubMed: 1736110]
25. Frieden TR, Sterling T, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. N Engl J Med 1993;328(8):521–526. [PubMed: 8381207]
26. Landesman SH. Commentary: tuberculosis in New York City--the consequences and lessons of failure. Am J Public Health 1993;83(5):766–768. [PubMed: 8484468]
27. Buskin SE, Gale JL, Weiss NS, Nolan CM. Tuberculosis risk factors in adults in King County, Washington, 1988 through 1990. Am J Public Health 1994;84(11):1750–1756. [PubMed: 7977912]
28. Cantwell MF, Snider DE Jr., Cauthen GM, Onorato IM. Epidemiology of tuberculosis in the United States, 1985 through 1992. JAMA 1994;272(7):535–539. [PubMed: 8046808]
29. Brown RE, Miller B, Taylor WR, et al. Health-care expenditures for tuberculosis in the United States. Arch Intern Med 1995;155(15):1595–1600. [PubMed: 7618981]
30. Jereb JA, Klevens RM, Privett TD, et al. Tuberculosis in health care workers at a hospital with an outbreak of multidrug-resistant Mycobacterium tuberculosis. Arch Intern Med 1995;155(8):854–859. [PubMed: 7717794]
31. CDC. CDC Timeline 1940s−-1970s https://www.cdc.gov/museum/timeline/1940-1970.html. Accessed September 28, 2018.
32. CDC. National action plan to combat multidrug-resistant tuberculosis. MMWR Recomm Rep 1992;41(RR-11):5–48.
33. U.S. Government. National Action Plan for Combating Multidrug-Resistance Tuberculosis In: 2015.
34. Armstrong LR, Winston CA, Stewart B, Tsang CA, Langer AJ, Navin TR. Changes in tuberculosis epidemiology, United States, 1993–2017. Int J Tuberc Lung Dis 2019;In Press.
35. Winston CA, Navin TR, Becerra JE, et al. Unexpected decline in tuberculosis cases coincident with economic recession - United States, 2009. BMC Public Health 2011;11.
36. Winston CA, Navin TR, Becerra JE, LoBue PA. No rebound in tuberculosis in the United States in 2010. Int J Tuberc Lung Dis 2011;15(9):1272.
37. Chen MP, Shang N, Winston CA, Becerra JE. A Bayesian analysis of the 2009 decline in tuberculosis morbidity in the UnitedStates. STAT MED 2012;31(27):3278–3284. [PubMed: 22415632]
38. Liu Y, Posey DL, Cetron MS, Painter JA. Effect of a culture-based screening algorithm on tuberculosis incidence in immigrants and refugees bound for the United States: a population-based cross-sectional study. Ann Intern Med 2015;162(6):420–428. [PubMed: 25775314]
39. Hill AN, Becerra JE, Castro KG. Modelling tuberculosis trends in the USA. Epidemiol Infect 2012;140(10):1862–1872. [PubMed: 22233605]

40. Shrestha S, Hill AN, Marks SM, Dowdy DW. Comparing drivers and dynamics of tuberculosis in California, Florida, New York, and Texas. Am J Respir Crit Care Med 2017;196(8):1050–1059. [PubMed: 28475845]
41. Menzies NA, Cohen T, Hill AN, et al. Prospects for Tuberculosis Elimination in the United States: Results of a Transmission Dynamic Model. Am J Epidemiol 2018;187(9):2011–2020. [PubMed: 29762657]
42. CDC. About the National Health and Nutrition Examination Survey https://www.cdc.gov/nchs/nhanes/about_nhanes.htm. Accessed November 3, 2018.
43. Bennett DE, Courval JM, Onorato I, et al. Prevalence of tuberculosis infection in the United States population: The national health and nutrition examination survey, 1999–2000. Am J Respir Crit Care Med 2008;177(3):348–355. [PubMed: 17989346]
44. Miramontes R, Hill AN, Woodruff RSY, et al. Tuberculosis infection in the United States: Prevalence estimates from the national health and nutrition examination survey, 2011–2012. PLoS ONE 2015;10(11).
45. France AM, Grant J, Kammerer JS, Navin TR. A Field-Validated Approach Using Surveillance and Genotyping Data to Estimate Tuberculosis Attributable to Recent Transmission in the United States. AM J EPIDEMIOL 2015;182(9):799–807. [PubMed: 26464470]
46. Yuen CM, Kammerer JS, Marks K, Navin TR, France AM. Recent transmission of tuberculosis - United States, 2011–2014. PLoS ONE 2016;11(4).
47. Haddad MBRK, Lash TL, Hill AN, Kammerer JS, Winston CA, Castro KG, Gandhi NR, Navin TR. Simple Estimates for Local Prevalence of Latent Tuberculosis Infection, United States, 2011–2015 Emerg Infect Dis 2018;24(10).
48. Houben RMGJ, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. PLoS Med 2016;13(10):e1002152. [PubMed: 27780211]
49. Beavers SF, Pascopella L, Davidow AL, et al. Tuberculosis mortality in the United States: Epidemiology and prevention opportunities. Ann Am Thorac Soc 2018;15(6):683–692.
50. Hannah HA, Miramontes R, Gandhi NR. Sociodemographic and clinical risk factors associated with tuberculosis mortality in the United States, 2009–2013. PUBLIC HEALTH REP 2017;132(3):366–375. [PubMed: 28394707]
51. WHO. Global Health Estimates 2016: Disease burden by Cause, Age, Sex, by Country and by Region, 2000–2016 2018; http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html, 2018.
52. WHO. Global Tuberculosis Report 2018 Geneva: World Health Organization;2018.
53. Iqbal SA, Winston CA, Bardenheier BH, Armstrong LR, Navin TR. Age-Period-Cohort Analyses of Tuberculosis Incidence Rates by Nativity, United States, 1996–2016. Am J Public Health 2018;108(S4):S315–S320. [PubMed: 30383432]
54. Wanyeki I, Olson S, Brassard P, et al. Dwellings, crowding, and tuberculosis in Montreal. Social science & medicine (1982) 2006;63(2):501–511. [PubMed: 16480805]
55. Bamrah S, Yelk Woodruff RS, Powell K, Ghosh S, Kammerer JS, Haddad MB. Tuberculosis among the homeless, United States, 1994–2010. Int J Tuberc Lung Dis 2013;17(11):1414–1419. [PubMed: 24125444]
56. Lambert LA, Armstrong LR, Lobato MN, Ho C, France AM, Haddad MB. Tuberculosis in jails and prisons: United States, 2002–2013. Am J Public Health 2016;106(12):2231–2237. [PubMed: 27631758]
57. Mindra G, Wortham JM, Haddad MB, Salinas JL, Powell KM, Armstrong LR. Tuberculosis Among Incarcerated Hispanic Persons in the United States, 1993–2014. J Immigr Minor Health 2017;19(4):982–986. [PubMed: 27900592]
58. Horne DJ, Campo M, Ortiz JR, et al. Association between smoking and latent tuberculosis in the U.S. population: an analysis of the National Health and Nutrition Examination Survey. PLoS ONE 2012;7(11):e49050. [PubMed: 23145066]
59. Lindsay RP, Shin SS, Garfein RS, Rusch ML, Novotny TE. The Association between active and passive smoking and latent tuberculosis infection in adults and children in the united states: results from NHANES. PLoS ONE 2014;9(3):e93137. [PubMed: 24664240]

60. Lambert LA, Pratt RH, Armstrong LR, Haddad MB. Tuberculosis among healthcare workers, United States, 1995–2007. Infect Control Hosp Epidemiol 2012;33(11):1126–1132. [PubMed: 23041811]
61. Youakim S The occupational risk of tuberculosis in a low-prevalence population. Occupational medicine (Oxford, England) 2016;66(6):466–470.
62. Albalak R, O'Brien RJ, Kammerer JS, et al. Trends in tuberculosis/human immunodeficiency virus comorbidity, United States, 1993–2004. Arch Intern Med 2007;167(22):2443–2452. [PubMed: 18071166]
63. Oeltmann JE, Oren E, Haddad MB, et al. Tuberculosis outbreak in marijuana users, Seattle, Washington, 2004. Emerg Infect Dis 2006;12(7):1156–1159. [PubMed: 16836841]
64. Oeltmann JE, Kammerer JS, Pevzner ES, Moonan PK. Tuberculosis and substance abuse in the United States, 1997–2006. Arch Intern Med 2009;169(2):189–197. [PubMed: 19171816]
65. Volkmann T, Moonan PK, Miramontes R, Oeltmann JE. Tuberculosis and excess alcohol use in the United States, 1997–2012. Int J Tuberc Lung Dis 2015;19(1):111–119. [PubMed: 25519800]
66. Smith GS, Van Den Eeden SK, Baxter R, et al. Cigarette smoking and pulmonary tuberculosis in northern California. J Epidemiol Community Health 2015;69(6):568–573. [PubMed: 25605864]
67. Davies PDO, Yew WW, Ganguly D, et al. Smoking and tuberculosis: The epidemiological association and immunopathogenesis. Trans R Soc Trop Med Hyg 2006;100(4):291–298. [PubMed: 16325875]
68. Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. N Engl J Med 2001;345(15):1098–1104. [PubMed: 11596589]
69. Epstein DJ, Subramanian AK. Prevention and Management of Tuberculosis in Solid Organ Transplant Recipients. Infect Dis Clin North Am 2018;32(3):703–718. [PubMed: 30146031]
70. Gras J, De Castro N, Montlahuc C, et al. Clinical characteristics, risk factors, and outcome of tuberculosis in kidney transplant recipients: A multicentric case-control study in a low-endemic area. Transplant Infect Dis 2018;20(5).
71. Santoro-Lopes G, Subramanian AK, Molina I, Aguado JM, Rabagliatti R, Len O. Tuberculosis Recommendations for Solid Organ Transplant Recipients and Donors. Transplantation 2018;102(2S Suppl 2):S60–S65. [PubMed: 29381579]
72. Natori Y, Ferreira VH, Nellimarla S, et al. Incidence, Outcomes, and Long-term Immune Response to Tuberculosis in Organ Transplant Recipients. Transplantation 2019;103(1):210–215. [PubMed: 29944616]
73. Gavelli F, Patrucco F. Diabetes and tuberculosis: A closer and closer relationship. Clin Respir J 2018;12(11):2622–2623. [PubMed: 30246931]
74. Hayashi S, Chandramohan D. Risk of active tuberculosis among people with diabetes mellitus: systematic review and meta-analysis. Trop Med Int Health 2018;23(10):1058–1070. [PubMed: 30062731]
75. Lin SY, Tu HP, Lu PL, et al. Metformin is associated with a lower risk of active tuberculosis in patients with type 2 diabetes. Respirology 2018;23(11):1063–1073. [PubMed: 29943489]
76. Nguyen CH, Pascopella L, Barry PM. Association between diabetes mellitus and mortality among patients with tuberculosis in California, 2010–2014. Int J Tuberc Lung Dis 2018;22(11):1269–1276. [PubMed: 30355405]
77. Siddiqui AN, Hussain S, Siddiqui N, Khayyam KU, Tabrez S, Sharma M. Detrimental association between diabetes and tuberculosis: An unresolved double trouble. Diabetes Metab Syndr Clin Res Rev 2018;12(6):1101–1107.
78. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: Evidence from a systematic review and meta-analysis 11 Medical and Health Sciences 1117 Public Health and Health Services. Syst Rev 2018;7(1).
79. Moran E, Baharani J, Dedicoat M, et al. Risk factors associated with the development of active tuberculosis among patients with advanced chronic kidney disease. J Infect 2018;77(4):291–295. [PubMed: 29928915]

80. Okada RC, Barry PM, Skarbinski J, Chitnis AS. Epidemiology, detection, and management of tuberculosis among end-stage renal disease patients. Infect Control Hosp Epidemiol 2018;39(11): 1367–1374. [PubMed: 30231948]

81. LoBue PA, Mermin JH. Latent tuberculosis infection: the final frontier of tuberculosis elimination in the USA. Lancet Infect Dis 2017;17(10):e327–e333. [PubMed: 28495525]

82. Zak DE, Penn-Nicholson A, Scriba TJ, et al. A blood RNA signature for tuberculosis disease risk: a prospective cohort study. LANCET 2016;387(10035):2312–2322. [PubMed: 27017310]

83. Maloney SA, Fielding KL, Laserson KF, et al. Assessing the performance of overseas tuberculosis screening programs: a study among US-bound immigrants in Vietnam. Arch Intern Med 2006;166(2):234–240. [PubMed: 16432095]

KEY POINTS

- Public health efforts have been successful in reducing TB morbidity and mortality through an approach largely focused on preventing TB transmission within the United States.
- Future U.S. TB prevention efforts should include a focus on testing for and treating latent tuberculosis infection in order to prevent progression to tuberculosis disease.
- Measures to prevent TB transmission in the United States must be maintained to avoid potential increases in recent transmission that could lead to large outbreaks.

SYNOPSIS

Although considerable progress has been made in reducing U.S. tuberculosis incidence, the goal of eliminating the disease from the United States remains elusive. An enhanced focus on preventing new tuberculosis infections while also identifying and treating persons with existing tuberculosis infection is needed. Continued vigilance to ensure ongoing control of tuberculosis transmission remains key.

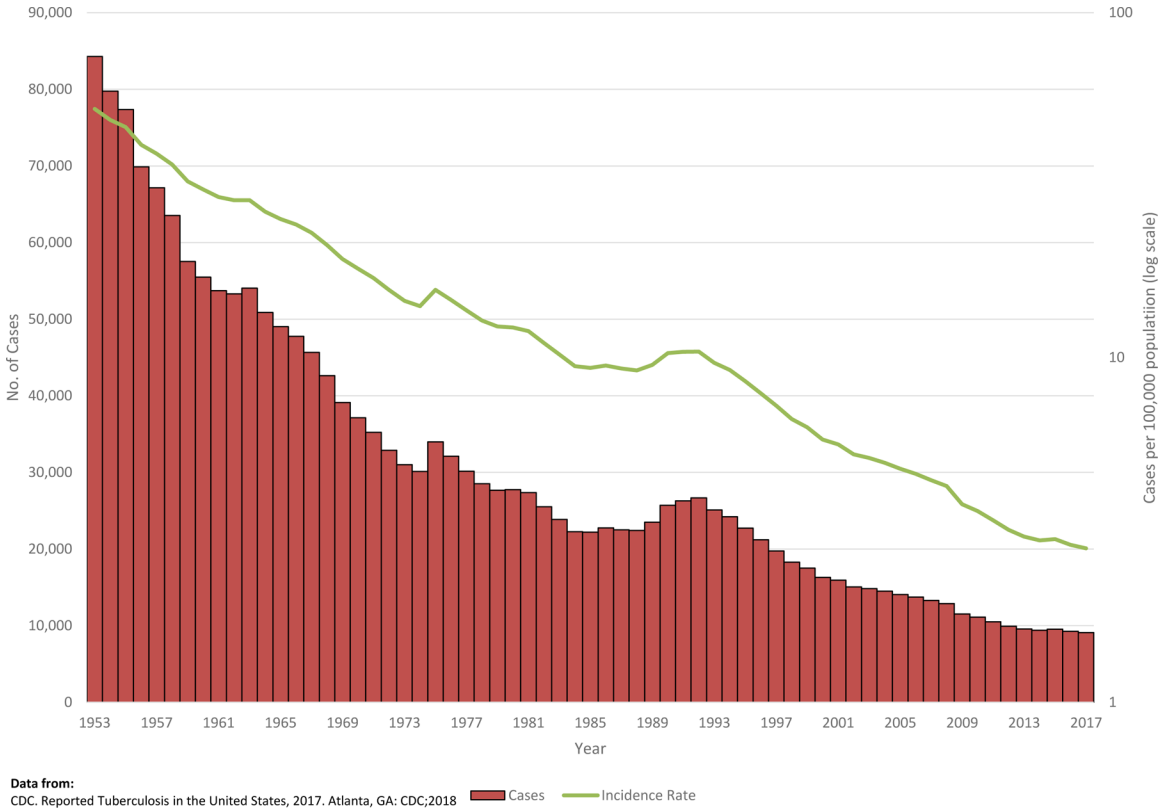

Figure 1:
Tuberculosis Cases and Incidence Rates --- United States, 1953–2017

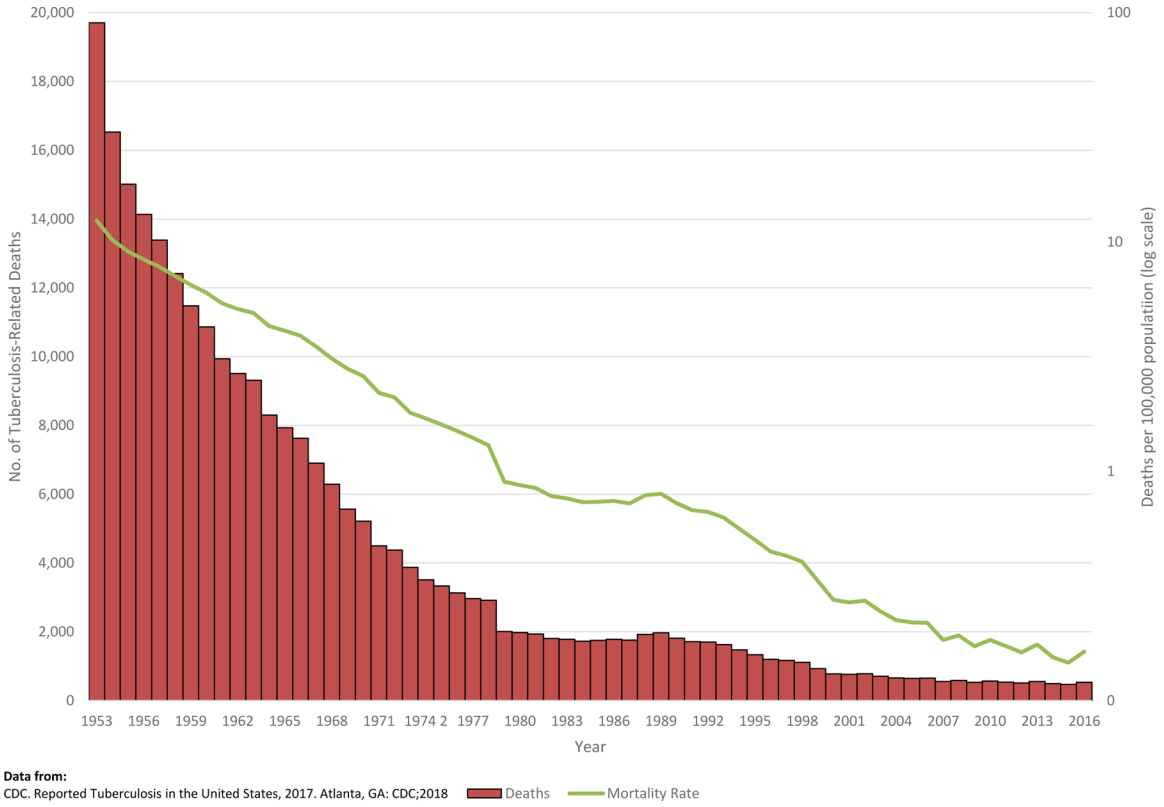

Figure 2:
Tuberculosis Deaths and Mortality Rates --- United States, 1953–2016

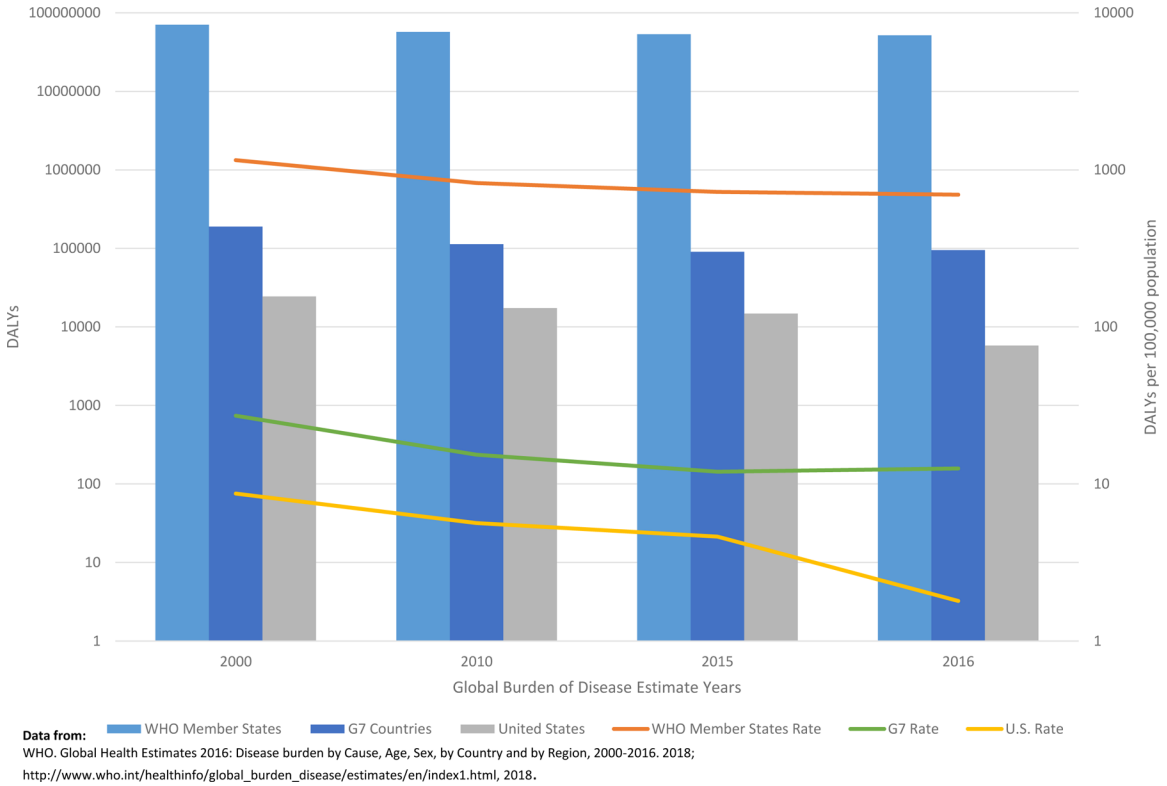

Figure 3:

Disability-Adjusted Life Years (DALYs) Lost to Tuberculosis and DALYs per 100,000 Population --- All WHO Member States, All G7 Countries, and United States, 2000–2016