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The impact of migration on tuberculosis in the United States

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SUMMARY

Due to greater exposure to *Mycobacterium tuberculosis* infection before migration, migrants moving to low-incidence settings can experience substantially higher tuberculosis (TB) rates than the native-born population. This review describes the impact of migration on TB epidemiology in the United States, and how the TB burden differs between US-born and non-US-born populations. The United States has a long history of receiving migrants from other parts of the world, and TB among non-US-born individuals now represents the majority of new TB cases. Based on an analysis of TB cases among individuals from the top 30 countries of origin in terms of non-US-born TB burden between 2003 and 2015, we describe how TB risks vary within the non-US-born population according to age, years since entry, entry year, and country of origin. Variation along each of these dimensions is associated with more than 10-fold differences in the risk of developing active TB, and this risk is also positively associated with TB incidence estimates for the country of origin and the composition of the migrant pool in the entry year. Approximately 87 000 lifetime TB cases are predicted for the non-US-born population resident in the United States in 2015, and 5800 lifetime cases for the population entering the United States in 2015.

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RÉSUMÉ

En raison de leur exposition plus importante à l'infection à *Mycobacterium tuberculosis* avant la migration, les migrants allant vers des pays à faible incidence peuvent avoir des taux de tuberculose (TB) considérablement plus élevés que la population née sur place. Cette revue décrit l'impact de la migration sur l'épidémiologie de la TB aux Etats-Unis et la manière dont le poids de la TB diffère entre les populations nées aux Etats-Unis et les autres. Les Etats-Unis ont une longue histoire d'accueil de migrants des autres régions du monde, et la TB parmi les individus nés hors des Etats-Unis représente maintenant la majorité des nouveaux cas de TB. En nous basant sur l'analyse des cas de TB parmi les individus venant des 30 principaux pays d'origine en termes de poids de la TB des patients nés hors des Etats-Unis entre 2003 et 2015, nous décrivons comment les risques de TB varient au sein des populations non nées aux Etats-Unis en fonction de leur âge, des années écoulées depuis leur arrivée, de l'année d'entrée et du pays d'origine. Les variations en fonction de chacun de ces facteurs sont associées avec des différences de plus de 10 fois le risque de développer une TB active, et ce risqué est également positivement associé aux estimations d'incidence de la TB dans le pays d'origine et à la composition du reservoir de migrants pendant l'année d'entrée. Environ 87 000 cas de TB au cours de la vie sont prédits pour la population née hors des Etats-Unis et résidant aux Etats-Unis en 2015, et 5800 cas au cours de la vie pour la population entrée aux Etats-Unis en 2015.

RESUMEN

Debido a una mayor exposición a *Mycobacterium tuberculosis* antes de la migración, los migrantes que se desplazan hacia entornos con baja incidencia de la enfermedad pueden presentar tasas de tuberculosis (TB) notablemente más altas que la población natural del pais de acogida. En el presente art´ıculo se describe la repercusión de la migración en las caracter´ısticas epidemiológicas de la TB en los Estados Unidos y la medida en que la carga de morbilidad por TB difiere entre las poblaciones naturales de los Estados Unidos y las poblaciones nacidas en el extranjero. Los Estados Unidos tienen una larga historia de acogida de migrantes de otras regiones del mundo y en la actualidad, la TB en las personas nacidas en el extranjero representa la mayor´ıa de los casos nuevos de la enfermedad. A partir de un estudio realizado del 2003 al 2015 sobre la carga de morbilidad por TB en la población nacida en el extranjero, proveniente de los 30 países de origen más frecuente, se describe la forma como var´ıan los riesgos de TB en estas poblaciones en función de la edad, los aos transcurridos desde su llegada al país, el año de entrada y el país de origen. La variación en cada una de estas dimensiones se asocia con má s de 10 veces más de diferencias en el riesgo de contraer la TB activa y este riesgo también se correlaciona de manera positiva con las estimaciones de incidencia de TB en el país de origen y la composición de la totalidad de los migrantes en el año de entrada. Se pronostican cerca de 87 000 casos de TB alguna vez durante toda la vida en la población nacida en el extranjero residente en los Estados Unidos en el 2015 y 5800 casos durante toda la vida en la población que entró a los Estados Unidos en el 2015.

Keywords

TB; migration; incidence trends

DESPITE INCREASING EFFORTS to strengthen tuberculosis (TB) services in high-burden countries,[1] progress has been variable. Panel A of Figure 1 shows time trends in World Health Organization (WHO) TB incidence estimates from 2000 to 2015 for the 30 most populous countries in 2015.[2] While some high-burden countries have experienced sustained declines in TB incidence, the gap between high- and low-burden countries is generally growing, and now spans several orders of magnitude. Among the 30 countries represented in Figure 1A, the 10 countries with the highest average incidence experienced an average annual decline of 0.9% between 2000 and 2015, while the 10 countries with the lowest average incidence experienced an average annual decline of 2.8%. For countries such as the United States, evidence suggests that current low incidence levels are the product of a long ongoing decline in incidence from historical values that were substantially higher than they are today.[3–5] For the countries shown in Panel A of Figure 1, 2015 incidence estimates differ by a multiple of 260 between highest and lowest. Other measures of TB burden (prevalence, mortality) show similar wide variation.

For several low-incidence settings, immigration is an important factor in TB epidemiology, where migrants may originate from countries with substantially higher TB burden.[6] In Panel B of Figure 1, recent incidence trends in the United States are contrasted with incidence trends for the 30 countries with the greatest number of non-US-born persons living in the United States. The WHO incidence estimates for most of these countries substantially exceed rates reported for the United States, with an average incidence in 2015 that is 22 times higher than in the United States. As TB disease can develop many years after infection, migrants exposed to high rates of tuberculous infection in their country of origin face elevated risks of future active disease after US arrival compared with US-born individuals, due to the possible reactivation of latent tuberculous infection (LTBI) acquired earlier in life.

Using the United States example, we review the epidemiological differences between native-born and non-native-born residents of low-incidence countries, and describe the implications for future TB trends in these settings. All new analyses were undertaken as secondary analyses of de-identified data, and no patient consent was required.

TUBERCULOSIS BURDEN AMONG US-BORN AND NON-US-BORN INDIVIDUALS LIVING IN THE UNITED STATES

In 2016, 6351 TB cases reported in the United States occurred among non-US-born individuals, representing 69% of the 9252 total cases with recorded nativity (nativity information was missing in 3% of the total 9547 cases),[7] although non-US-born individuals constitute only 14% of the population.[8] These differences imply an incidence rate ratio of 14 for non-US-born compared to US-born individuals (respectively 14.52 and 1.04 cases per 100 000 population). Figure 2 shows total TB cases and TB incidence rates among US and non-US-born individuals living in the United States by calendar year (A) and age group (B), based on data from the National TB Surveillance System[9] and the American Community Survey.[10] For both non-US-born and US-born groups, TB incidence rates have been decreasing over time and increase with age (except for the 0–4 years age group). Averaged

over 2000–2016, incidence rates in the non-US-born were nine times higher than in the US-born. This ratio varies with age: it is 17–23 times higher in those aged 15–24 years (when many non-US-born individuals enter the United States) and 4–8 times higher in 45–54 year olds. Over the 2000– 2016 period, incidence rates in the US-born dropped more rapidly than in the non-US-born, with this accelerated decline concentrated in older age groups (Figure 2).

All individuals applying to immigrate to the United States receive a comprehensive medical examination for TB, and individuals diagnosed with active TB are required to complete a course of directly observed treatment before entry to the United States.[11,12] This examination requires a culture-based diagnostic algorithm, which replaced an earlier smear-based algorithm in 2007.[13] A study conducted among prospective immigrants during the introduction of the new algorithm found that 54% of TB diagnoses were smear-negative, and potentially would have been missed under the older algorithm. Introduction of the new algorithm was also correlated with a 38% decline in annual TB cases among non-US-born persons within 1 year of arrival.[14] However, this algorithm will only identify TB among individuals applying for lawful permanent residence in the United States, who are required to undergo screening. In contrast, most individuals entering the United States are not required to undergo this screening, including individuals entering on student, work, or tourist visas, and undocumented migrants. Individuals in these groups may enter the country with prevalent disease, and rates of TB notifications are several times higher among individuals in their first year in the United States than in subsequent years. Over the period 2000–2010, the incidence rate for individuals in the country for <1 year was 4.5 times higher than in individuals in the country for 1–4 years. This ratio fell to 3.3 during the 2010–2016 period, possibly reflecting the higher sensitivity of culture-based diagnosis in the TB medical examination.

Active TB among individuals entering the country cannot explain differentials in TB case notifications more than a couple of years after entry.[15–17] Empirical evidence suggests that reactivation of LTBI is the primary cause of the difference in TB incidence between US-born and established non-US-born populations. The National Health And Nutrition Examination Survey (NHANES) provides population-based evidence on LTBI prevalence among US-born and non-US-born groups, with both tuberculin skin test (TST) and interferon-gamma release assay (IGRA) data collected during the 2011–2012 survey.[18] These data demonstrate TST positivity to be 13.7 times higher among non-US-born than in US-born individuals (20.5% vs. 1.5%) and IGRA positivity to be 5.7 times higher (15.9% vs. 2.8%).[19] These results are consistent with the 1999–2000 NHANES, which found TST positivity to be 9.5 times higher among non-US-born than in US-born individuals (18.1% vs. 1.9%). These results should be interpreted carefully given imperfect test sensitivity and specificity—in particular, TST specificity will be lower among non-US-born individuals vaccinated with bacille Calmette-Gue´rin in childhood.[20] However, taken together, these results suggest substantially higher LTBI prevalence for non-US-born individuals. Compared to US-born individuals, non-US-born individuals have different prevalences of diabetes, smoking, and human immunodeficiency virus (HIV) infection, which may contribute to minor differences in population-average LTBI progression rates.[21,22]

Molecular epidemiology studies provide another opportunity to decompose the causes of incident TB, with cases linked to a cluster of cases via a common genotype attributed to recent transmission, and unlinked cases assumed to arise from LTBI reactivation. Given the limitations of earlier genotype-based clustering approaches,[23–25] recent US studies have incorporated clinical and demographic data, as well as spatiotemporal proximity, to better identify TB clusters.[26] A study applying this 'plausible source case' approach to all genotyped TB cases in the United States during 2011–2014 revealed substantial differences between US-born and non-US-born cases, with 27.4% of all US-born genotyped TB cases estimated to be attributable to recent transmission within the United States, compared with 7.5% of non-US-born genotyped TB cases.27 If one assumes that 92.5% of all non-US-born cases are attributable to LTBI reactivation rather than recent transmission, and that the large majority of these latent tuberculous infections were acquired before entry into the United States, these results imply that approximately two thirds of all US TB cases arise from reactivation of LTBI acquired abroad. The plausible source case approach has been incorporated into routine TB surveillance, with national estimates for 2015–2016 associating 26.2% of US-born cases and 8.1% of non-US-born cases with recent transmission.[7] As TB incidence during 2016 was approximately 14 times higher among non-US-born than US-born populations, these results suggest that TB incidence due to recent infection could be 4–5 times higher among non-US-born than among US-born individuals, with incidence from recent infection of 0.27 (1.04 × 0.262) per 100 000 for the US-born, and 1.17 (14.5 × 0.081) for the non-US-born, although recent infection represents a smaller proportion of all non-US-born TB cases.

The plausible source case approach has known limitations for younger children and for infections acquired abroad, and cannot be applied to clinically diagnosed cases (27% of all cases in 2015–2016). These factors imply that the results should be interpreted cautiously. Applying similar calculations to those shown above to reactivation disease suggests that TB incidence due to LTBI reactivation could be 17–18 times higher among non-US-born than among US-born individuals (0.77 (1.04 × 0.738)/100 000 in the US-born, and 13.3 (14.5 × 0.919) in the non-US-born), driven by higher LTBI prevalence. With assortative mixing within population groups,[28] elevated TB incidence among non-US-born individuals means that members of non-US-born communities face greater exposure to infectious TB cases than US-born individuals. Consistent with this explanation, US-born children of non-US-born parents have been estimated to experience TB incidence rates six times higher than US-born children of US-born parents.[29] Non-US-born individuals may also face greater exposure to infection outside of the United States.[30]

TRENDS IN TUBERCULOSIS BURDEN WITHIN MIGRANT GROUPS

Migrants to the United States are a diverse population, including 'immigrants' (individuals granted lawful permanent residence, categorized as family reunification, employment sponsorship, refugees, and asylum seekers), non-immigrant visa holders and parolees, and undocumented migrants. These groups differ in terms of previous TB exposure, access to preventive and treatment services, and average duration of US residence. Understanding the relationship between immigration class and TB incidence could help explain observed patterns in TB epidemiology; however, this relationship is difficult to study directly, as

questions describing immigration class on the standardized TB case reporting form are often not completed, and do not reflect immigration status at time of diagnosis or exposure to screening at time of entry to the country.

Evidence to stratify the size of the non-US-born population by immigration class is also weak. While the US Department of Homeland Security reports data on individuals legally entering the country in different migrant categories, it is unclear what proportion of these individuals subsequently emigrate, and little information is available on entry or exit of undocumented migrants. Moreover, while the US Census Bureau conducts large surveys describing the composition of the US population, these surveys do not record immigration status. In European settings, higher TB incidence has been observed among undocumented migrants than legal immigrants.[31,32] In the United States, a multisite study of individuals newly diagnosed with TB found that 61% of non-US-born individuals were legal permanent residents, 3% had temporary visas, and 25% were undocumented.[33] A study estimating the distribution of TB cases among legal entrants <1 year since arrival based on TB incidence in the country of origin found that 42% of cases occurred among legal immigrants, and 58% among short-term non-immigrant visitors.[34] These studies use data collected during 2000–2008, before the revised TB medical screening instructions, and these proportions may have changed over recent years.

Country of origin will also influence TB outcomes in the United States, and is routinely reported for incident TB cases. Figure 3 shows trends in TB incidence and population volume for individuals living in the United States from the top 15 countries of origin in terms of total TB cases over the period from 2003 to 2015. TB case data were drawn from the National TB Surveillance System (NTSS),[7] and population estimates calculated from American Community Survey data.[10] Taken together, individuals from these countries represented 73% of all non-US-born TB cases over the period shown, and 43% of all TB cases, irrespective of nativity. Within each panel, a black line joins consecutive years from 2003 to 2015. Diagonal grey lines represent isoclines of absolute case numbers, with greater number of cases in the top right of the plot and lower numbers in the bottom left. While the pattern varies between countries and years, two trends are apparent for each country of origin: progressively increasing population volume, and decreasing incidence rates. These two trends have competing effects on the total number of TB cases, such that the trend in overall TB cases diagnosed in the United States is declining rapidly among persons from some countries (e.g., Mexico, South Korea, Ecuador, Peru), stagnant for others (e.g., the Philippines, India, Ethiopia, Honduras), and even increasing slightly among persons from China. This figure also demonstrates the unequal distribution of TB cases among countries of origin, with 53% of TB cases in non-US-born individuals coming from the top five countries (Mexico, the Philippines, India, Viet Nam and China), and 22% from Mexico alone. Averaged over the most recent 5 years of data (2011–2015), annual TB incidence rates for individuals from these five countries were respectively 11.0, 41.0, 24.8, 37.7, and 21.3/100 000 (Figure 3).

Variation in total TB cases by country of origin is largely explained by differences in population size. For example, the number of individuals from Mexico living in the United States is approximately equal to the combined total for all other countries in Figure 3.

However, there are also marked differences in TB incidence between individuals from different countries. The causes of these differences can be hard to disentangle, given that groups from different countries will also differ in terms of age distribution and years since entry into the United States, factors known to influence TB risk. To unpack these different effects, we fit regression models to a data set of all reported TB cases between 2003 and 2015 for individuals from the top 30 countries of origin in terms of TB cases, stratified by country of origin, age, years since entry, and entry year, controlling for population size. TB case counts were modelled with a Poisson Generalized Additive Regression Model with log link function, which assumes the different predictors interact multiplicatively. We parameterized the effects of age, years since entry, and entry year with penalized B-splines to allow flexibility in the estimated relationships. In addition, the validity of these results depends on the validity of demographic information reported by individuals for TB case reporting[35] and American Community Survey,[10] as well as the completeness of both of these data sources.

We used the fitted models to estimate incidence risk ratios (IRRs) comparing different groups. Figure 4 shows risk ratios for TB incidence by age, years since entry, and entry year, controlling for other effects. We used average incidence in the study population (non-US-born individuals from the top 30 countries of origin in terms of TB cases, 2003–2015) as the reference category, to quantify how each risk factor produced deviations from this general population risk. These panels also show unadjusted risk ratios estimated directly from the raw data, without controlling for other effects.

Panel A shows differences in TB incidence attributable to age. Non-US-born individuals aged 2–12 years experienced the lowest TB risk, with adjusted IRRs <0.2 compared to population-average incidence for non-US-born individuals. Older age groups experienced the highest risks, with adjusted IRRs increasing exponentially above 40 years of age, and with adjusted IRRs >3.0 for all ages >75 years. These patterns likely result from two effects: greater cumulative exposure to tuberculous infection among older individuals, and variation in susceptibility to LTBI reactivation as a function of age. Infants are known to experience elevated risks of developing active TB compared to healthy adults, and older children are thought to experience reduced risks of developing active TB,[36] consistent with these results. Older adults with LTBI may also experience increasing risks of developing active TB.[37]

Panel B of Figure 4 shows a rapid decline in the adjusted IRR after the year of arrival, with a 65% reduction in incidence risk by Year 2 after arrival, a 90% reduction by Year 10, and a 98% reduction by Year 30. As noted previously, prevalent TB among non-immigrant individuals entering the country may explain part of the sharp reduction in reported incidence after the arrival year,[15] but only over the initial 1–2 years. However, ongoing declines in incidence risk are apparent up to 60 years after entry. Non-US-born individuals typically migrate from a country with a higher TB burden than the United States, and will experience a sharp drop in exposure to *M. tuberculosis* infection upon entry into the United States. As a consequence, the longer an individual resides in the United States, the longer the average time since infection for individuals with LTBI. As the risk of developing active disease declines with increasing time since infection,[38,39] this may explain the prolonged decline in the adjusted IRR with increasing years since entry. These results suggest that

incidence risk continues to decline beyond the 10–15 year periods examined in observational trials (Figure 4).[38,39]

Panel C of Figure 4 shows the time trend in incidence risk attributable to entry year, revealing an ongoing, approximately log-linear decline. This decline represents a 4.9% average annual reduction in TB risk, for a 96% reduction over the period 1950– 2015. The rate of decline over the last 10 years has been more rapid, with a 6.8% average annual reduction in TB risk. A major part of this decline will likely represent reductions in TB burden between successive migration cohorts, and progressive improvements in measures to prevent transmission and treat exposed contacts. The recent acceleration in this rate of decline may reflect the more sensitive pre-arrival TB screening introduced in 2007.[11]

The Table reports adjusted IRRs by country of origin, controlling for age, years since entry, and entry year, with Mexico (the country of origin with most TB cases) as the reference category. There is wide variation in incidence risk between countries, with a 49-fold difference between the highest and lowest countries in the analysis (Somalia and Cuba). Moreover, this analysis will understate the total variation in incidence risk by country of origin. As the analysis focuses on the top 30 countries by TB cases, it excludes countries of origin with low-incidence rates (Table 1).

The TB burden among migrants entering the United States will reflect their previous exposure to TB, as well as TB prevention or treatment services received before entry. Panel A of Figure 5 shows 2015 WHO incidence estimates for the top 30 countries of origin graphed against incidence estimates for non-US-born US residents from that country in the same year.2 Panel B shows a similar comparison, with WHO estimates compared to incidence for non-US-born US residents with <5 years since entry. In both graphs, the diagonal lines represent isoclines with a fixed ratio of incidence in the country of origin relative to the United States (Figure 5).

These figures demonstrate the positive relationship between incidence among a migrant group in the United States and incidence in their country of origin, with incidence in the country of origin commonly far higher than for individuals residing in the United States. Across the 30 countries, TB incidence in the country of origin is 6.8 times higher than in migrants from that country living in the United States, and 3.1 times higher than in migrants entering the United States within the previous 5 years. This ratio varies widely between countries, from 1.3 to 17.5 for all migrants, and from 0.3 to 10.3 for migrants <5 years since entry. One explanation for this variation will be differences in the mix of migrants entering the United States, such as differences in immigration class. Migrants do not represent a random sample from their country of origin, and if these individuals are drawn from parts of the population with lower (or higher) TB exposure this will translate into lower (or higher) TB incidence in the United States.

To quantify these relationships, we revised the regression model used to create Figure 4 and the Table, replacing country identifiers with 1) logged WHO-estimated incidence in the country of origin in the year of entry to the United States, and 2) refugees as a proportion of legal migrants in that year. As both variables are only available from 1990, the regression

was restricted to individuals entering the United States from 1990 onwards. Both predictors exhibited a positive relationship with TB incidence in the United States. A 10% higher TB incidence in the country of origin was associated with a 4.8% (95% confidence interval [CI] 4.7–4.9) higher incidence for individuals from that country of origin in the United States, and a 10% increase in the proportion of refugees among legal migrants was associated with a 6.6% (95%CI 6.2–7.0) increase in incidence for individuals from that country of origin in the United States. A second regression model was fit to understand whether this relationship weakened for increasing years since entry, by including a separate term in the regression for each year up to 10 years since entry. Results are shown in Figure 6. For both incidence in the country of origin and the proportion of refugees, there is no clear downward trend over time to suggest that these factors are associated with a persistent increase in TB incidence (Figure 6).

While these analyses demonstrate a relationship between incidence in the country of origin and incidence after migration to the United States, they are not causal, and could be confounded by other factors affecting TB incidence rates. When we refit these regressions including country fixed effects (effectively predicting TB incidence in the United States as a function of changes in incidence (as compared to incidence level) in the country of origin), coefficient estimates were small and not statistically significant.

IMPLICATIONS FOR FUTURE TRENDS IN TUBERCULOSIS

Non-US-born individuals have represented an increasing share of total TB cases in the United States over recent years. Many factors may influence future trends in the number of TB cases among non-US-born individuals, including the future size, composition, and visa category of migrating cohorts, and TB prevention and care provided to migrating individuals. These factors will be subject to economic fluctuations and public policy decisions, and are therefore difficult to predict precisely. However, US Census forecasts assume rising migration volume in coming years, with an increasing share of migrants from higher TB burden settings such as sub-Saharan Africa and South Asia.[40] On their own, these factors might imply increasing TB incidence in the non-US-born population. However, declining TB burden in migrants' countries of origin represents a counter-vailing effect. While global TB incidence has declined at approximately 1.5% per year, country-level trajectories vary widely (Figure 1). If global goals for reinvigorated TB control in high-burden settings are achieved,1 this would produce accelerated declines in TB burden among migrants entering the United States. While current pre-arrival screening is effective for identifying and treating active disease among immigrants and refugees,41 it is unlikely that further gains can be made without considering predeparture TB screening among non-immigrant visa applicants, or screening and treatment of LTBI among individuals seeking to enter the country.

While TB trends among individuals entering the country are unpredictable, a large proportion of TB cases in the near term will occur in individuals already living in the country. For example, of all non-US-born TB cases arising during 2010–2015, 74% occurred among the 41 million non-US-born individuals resident in the country before the start of the period. TB incidence for this group can be predicted based on observed trends. Using the

adjusted risk ratios shown in Figure 4 to project future TB cases among the non-US-born individuals resident in the country in 2015 implies a total of 87 000 future TB cases, with 41 000 of these occurring in the following decade (Figure 7). For the cohort of individuals entering as new migrants in 2015, this implies a total of 5800 incident TB cases over their lifetime, 4.6 times more than the approximately 1300 TB cases arising in their entry year. While it is difficult to validate these long-term projections, refitting the model to pre-2006 data and using this model to project TB cases for the 2006– 2015 period reproduced total cases to within 2% (Figure 7).

DISCUSSION

Similar to other low-incidence settings,[42] TB incidence in the United States has become increasingly concentrated in the non-US-born population. This has come about through a long secular decline in TB incidence in the United States, concomitant with the development of effective strategies for TB detection and treatment. As a consequence, LTBI prevalence in the US-born population is low, and exposure to infectious sources is also low. In contrast, TB burden has not declined as rapidly in many of the settings from which individuals migrate to the United States, with slow or stagnant reductions in TB burden in higher-burden countries. The composition of the migrant pool has also shifted towards higher-burden settings, dominated by European migration up until the 1970s, and is now largely composed of individuals from Latin American and Asian countries. While improvements in pre-immigration screening and post-arrival surveillance can identify prevalent TB before or shortly after entry to the United States, the progressive divergence of US TB trends compared to those in the major countries of origin means that migrants enter the United States with a substantially higher burden of LTBI than the US-born population. Given the potential for late reactivation many years after initial infection, the consequences of this elevated LTBI burden will play out over the life course. For the five countries of origin that represent the majority of non-US-born TB cases (Mexico, the Philippines, India, Viet Nam and China), their contributions to US TB epidemiology reflect large resident populations as well as elevated TB exposure for these individuals before arrival.

Improvements in the detection and treatment of active TB in non-US-born residents would have important benefits for affected individuals and their contacts,[43] but would have little effect on overall population-level incidence trends, as most cases of active TB arise from reactivation of old infections. As it stands, incident TB among migrants is less likely to be associated with local disease outbreaks than TB arising among US-born individuals,[44,45] and the large majority of new non-US-born TB cases arise from LTBI reactivation rather than recent infection.[27] Several studies in different settings have demonstrated that migrants represent a negligible risk of onward transmission.[28,46,47] While migrants face elevated individual health risks due to TB, there is therefore minimal additional risk to the wider community. Due to the risks of reactivation TB, LTBI is a focus for intervention in low-incidence settings such as the United States,[48,49] and targeted testing and treatment of LTBI among migrants from high TB prevalence countries is recommended.[50]

Achieving TB elimination (less than 1 TB case per million annually) is a prominent goal of US TB policy.[51] The United States has a long history of receiving migrants from other parts

of the world; based on extrapolation of recent and current trends, it is expected that the large reservoir of LTBI in the United States plus migration of individuals with high LTBI burden will challenge the ability of the United States to reach TB elimination within this century.[52,53] This challenge provides motivation to identify more effective approaches to detect and treat LTBI among high-burden groups in the United States,[54] and to ensure that TB policy and programming is tailored to the ongoing need for TB prevention services. Potential actions to hasten TB elimination in the United States are not confined to national borders,[55] and the relationships described in this paper demonstrate the interlinkage of TB epidemiology in the United States with TB epidemiology in high-burden countries of origin. Given this connection, investments to strengthen TB prevention and care worldwide would also produce benefits in the United States.[56]

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References

1. World Health Assembly. Post-2015 global TB strategy and targets. A67/62 Geneva, Switzerland: World Health Organization, 2014 http://www.who.int/tb/strategy/End_TB_Strategy.pdf. Accessed September 2018.
2. World Health Organization. WHO TB database Geneva, Switzerland: WHO, 2015.
3. Grigg ER. The arcana of tuberculosis with a brief epidemiologic history of the disease in the USA. Am Rev Tuberc 1958; 78: 151–172. [PubMed: 13559649]
4. Grigg ER. The arcana of tuberculosis; with a brief epidemiologic history of the disease in the USA. III. Am Rev Tuberc 1958; 78: 426–453. [PubMed: 13571601]
5. Hermans S, Horsburgh CR, Wood R. A century of tuberculosis epidemiology in the Northern and Southern Hemisphere: the differential impact of control interventions. PLOS ONE 2015; 10: e0135179. [PubMed: 26288079]
6. United Nations Population Division. International migration report, 2013 Geneva, Switzerland: United Nations Department of Economic and Social Affairs, Population Division, 2013.
7. US Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2016 Atlanta, GA, USA: US Department of Health and Human Services, 2017.
8. US Census Bureau. Table S0501: Selected characteristics of the native and foreign-born populations. 2016 American Community Survey 1-year estimates Washington DC, USA: US Census Bureau, 2017.
9. US Centers for Disease Control and Prevention. Online Tuberculosis Information System (OTIS), National Tuberculosis Surveillance System, United States, 1993–2014. CDC WONDER On-line Database, January 2016 Atlanta, GA, USA: US CDC, 2016 https://wonder.cdc.gov/tb.html. Accessed September 2018.
10. Ruggles S, Genadek K, Goeken R, Grover J, Sobek M. Integrated Public Use Microdata Series: American Community Survey. Version 6.0 Minneapolis, MN, USA: University of Minnesota, 2015 10.18128/D010.V6.0. Accessed September 2018.
11. US Centers for Disease Control and Prevention. CDC immigration requirements: technical instructions for tuberculosis screening and treatment Atlanta, GA, USA: CDC, 2009.
12. Posey DL, Naughton MP, Willacy EA, et al. Implementation of new TB screening requirements for US-bound immigrants and refugees—2007–2014. MMWR 2014; 63: 234–236. [PubMed: 24647399]
13. US Centers for Disease Control and Prevention. Technical instructions for panel physicians Atlanta, GA, USA: CDC, 1991.

14. 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: 420–428. [PubMed: 25775314]
15. Walter ND, Painter J, Parker M, et al. Persistent latent tuberculosis reactivation risk in United States immigrants. Am J Resp Crit Care 2014; 189: 88–95.
16. Tsang CA, Langer AJ, Navin TR, Armstrong LR. Tuberculosis among foreign-born persons diagnosed ⩾10 years after arrival in the United States, 2010–2015. MMWR 2017; 66: 295–298. [PubMed: 28333913]
17. Cain KP, Benoit SR, Winston CA, MacKenzie WR. Tuberculosis among foreign-born persons in the United States. JAMA 2008; 300: 405–412. [PubMed: 18647983]
18. National Center for Health Statistics. National Health and Nutrition Examination Surveys (NHANES): Laboratory procedures manual Atlanta, GA, USA: National Center for Health Statistics, US Centers for Disease Contrrol and Prevention, 2011.
19. Miramontes R, Hill AN, Yelk Woodruff RS, et al. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011– 2012. PLOS ONE 2015; 10: e0140881. [PubMed: 26536035]
20. Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. Ann Intern Med 2008; 149: 177–184. [PubMed: 18593687]
21. Bosdriesz J, Lichthart N, Witvliet M, Busschers W, Stronks K, Kunst A. Smoking prevalence among migrants in the US compared to the US-Born and the population in countries of origin. PLOS ONE 2013; 8: e58654. [PubMed: 23520525]
22. Cunningham S, Ruben JD, Venkat Narayan K. Health of foreign-born people in the United States: a review. Health Place 2008; 14: 623–635. [PubMed: 18242116]
23. Glynn JR, Vynnycky E, Fine PE. Influence of sampling on estimates of clustering and recent transmission of *Mycobacterium tuberculosis* derived from DNA fingerprinting techniques. Am J Epidemiol 1999; 149: 366–371. [PubMed: 10025480]
24. Murray M Sampling bias in the molecular epidemiology of tuberculosis. Emerg Infect Dis 2002; 8: 363–369. [PubMed: 11971768]
25. Murray M, Alland D. Methodological problems in the molecular epidemiology of tuberculosis. Am J Epidemiol 2002; 155: 565–571. [PubMed: 11882530]
26. 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: 799–807. [PubMed: 26464470]
27. Yuen CM, Kammerer JS, Marks K, Navin TR, France AM. Recent transmission of tuberculosis—United States, 2011– 2014. PLOS ONE 2016; 11: e0153728. [PubMed: 27082644]
28. Sandgren A, Schepisi MS, Sotgiu G, et al. Tuberculosis transmission between foreign- and native-born populations in the EU/EEA: a systematic review. Eur Respir J 2014; 43: 1159–1171. [PubMed: 24114966]
29. Pang J, Teeter LD, Katz DJ, et al. Epidemiology of tuberculosis in young children in the United States. Pediatrics 2014; 133: e494–504. [PubMed: 24515517]
30. Cobelens FG, van Deutekom H, Draayer-Jansen IW, et al. Risk of infection with Mycobacterium tuberculosis in travellers to areas of high tuberculosis endemicity. Lancet 2000; 356: 461–465. [PubMed: 10981889]
31. Wolff H, Janssens JP, Bodenmann P, et al. Undocumented migrants in Switzerland: geographical origin versus legal status as risk factor for tuberculosis. J Immigr Minor Health 2010; 12: 18–23. [PubMed: 19582582]
32. Heldal E, Kuyvenhoven JV, Wares F, et al. Diagnosis and treatment of tuberculosis in undocumented migrants in low- or intermediate-incidence countries. Int J Tuberc Lung Dis 2008; 12: 878–888. [PubMed: 18647446]
33. Davidow AL, Katz D, Ghosh S, et al. Preventing infectious pulmonary tuberculosis among foreign-born residents of the United States. Am J Public Health 2015; 105: e81–e88.
34. Liu Y, Painter JA, Posey DL, et al. Estimating the impact of newly arrived foreign-born persons on tuberculosis in the United States. PLOS ONE 2012; 7: e32158-e.

35. Yelk Woodruff RS, Pratt RH, Armstrong LR. The US National Tuberculosis Surveillance System: a descriptive assessment of the completeness and consistency of data reported from 2008 to 2012. JMIR Public Health Surveill 2015; 1: e15. [PubMed: 27227133]
36. Marais BJ, Gie RP, Schaaf HS, et al. The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era. Int J Tuberc Lung Dis 2004; 8: 392–402. [PubMed: 15141729]
37. Vynnycky E, Borgdorff MW, Leung CC, Tam CM, Fine PE. Limited impact of tuberculosis control in Hong Kong: attributable to high risks of reactivation disease. Epidemiol Infect 2008; 136: 943–952. [PubMed: 17678555]
38. Sutherland I The ten-year incidence of clinical tuberculosis following 'conversion' in 2550 individuals aged 14 to 19 years. TSRU Progress Report The Hague, The Netherlands: International Union Against Tuberculosis, 1968.
39. Ferebee SH, Mount FW. Tuberculosis morbidity in a controlled trial of the prophylactic use of isoniazid among household contacts. Am Rev Respir Dis 1962; 85: 490–510. [PubMed: 13892318]
40. US Census Bureau. Methodology, assumptions, and inputs for the 2014 National Projections Washington DC, USA: US Census Bureau, 2014 https://www2.census.gov/programs-surveys/popproj/technical-documentation/methodology/methodstatement14.pdf. Accessed September 2018.
41. Aldridge RW, Yates TA, Zenner D, White PJ, Abubakar I, Hayward AC. Pre-entry screening programmes for tuberculosis in migrants to low-incidence countries: a systematic review and meta-analysis. Lancet Infect Dis 2014; 14: 1240–1249. [PubMed: 25455991]
42. Pareek M, Greenaway C, Noori T, Munoz J, Zenner D. The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. BMC Med 2016; 14: 48. [PubMed: 27004556]
43. Heuvelings CC, de Vries SG, Greve PF, et al. Effectiveness of interventions for diagnosis and treatment of tuberculosis in hard-to-reach populations in countries of low and medium tuberculosis incidence: a systematic review. Lancet Infect Dis 2017; 17: e144–e158. [PubMed: 28291722]
44. Haddad MB, Mitruka K, Oeltmann JE, Johns EB, Navin TR. Characteristics of tuberculosis cases that started outbreaks in the United States, 2002–2011. Emerg Infect Dis 2015; 21: 508–510. [PubMed: 25695665]
45. Mindra G, Wortham JM, Haddad MB, Powell KM. Tuberculosis outbreaks in the United States, 2009–2015. Public Health Rep 2017; 132: 157–163. [PubMed: 28147211]
46. Aldridge RW, Zenner D, White PJ, et al. Tuberculosis in migrants moving from high-incidence to low-incidence countries: a population-based cohort study of 519 955 migrants screened before entry to England, Wales, and Northern Ireland. Lancet 2016; 388: 2510–2518. [PubMed: 27742165]
47. Diel R, Ru¨ sch-Gerdes S, Niemann S. Molecular epidemiology of tuberculosis among immigrants in Hamburg, Germany. J Clin Microbiol 2004; 42: 2952–2960. [PubMed: 15243044]
48. LoBue P, Mermin J. Latent tuberculosis infection: the final frontier of tuberculosis elimination in the USA. Lancet Infect Dis 2017; 17: e327–e333. [PubMed: 28495525]
49. Lönnroth K, Migliori GB, Abubakar I, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. Eur Respir J 2015; 45: 928–952. [PubMed: 25792630]
50. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for latent tuberculosis infection in adults: US Preventive Services Task Force Recommendation Statement. JAMA 2016; 316: 962–969. [PubMed: 27599331]
51. Blomquist ET. Program aimed at eradication of tuberculosis. Public Health Rep 1963; 78: 897–905. [PubMed: 14062221]
52. Hill AN, Becerra JE, Castro KG. Modelling tuberculosis trends in the USA. Epidemiol Infect 2012; 140: 1862–1872. [PubMed: 22233605]
53. 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: 2011–2020. 10.1093/aje/kwy094. Accessed September 2018. [PubMed: 29762657]

54. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for latent tuberculosis infection in adults: US Preventive Services Task Force recommendation statement. JAMA 2016; 316: 962–969. [PubMed: 27599331]

55. Posey DL, Marano N, Cetron MS. Cross-border solutions needed to address tuberculosis in migrating populations. Int J Tuberc Lung Dis 2017; 21: 485–486. [PubMed: 28399961]

56. Schwartzman K, Oxlade O, Barr RG, et al. Domestic returns from investment in the control of tuberculosis in other countries. New Engl J Med 2005; 353: 1008–1020. [PubMed: 16148286]

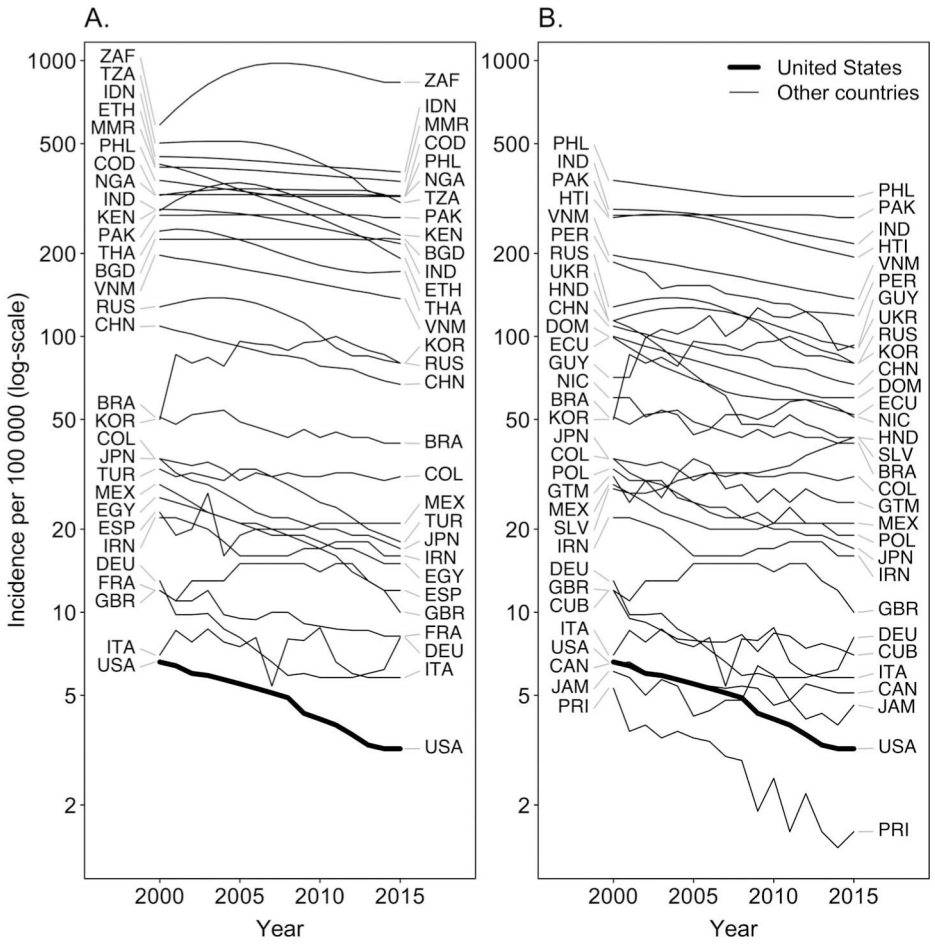

Figure 1.

Population-level TB incidence trends from 2000 to 2015 for selected countries. **A)** WHO TB incidence trends (log scale) from 2000 to 2015 for the top 30 most populous countries in 2015. **B)** WHO TB incidence trends (log scale) from 2000 to 2015 for the 30 countries with the greatest number of non-US-born persons currently living in the United States, in comparison to WHO TB incidence estimates for the United States. Three letter codes represent country ISO3 identifiers. ZAF = South Africa; TZA = Tanzania; IDN = Indonesia; ETH = Ethiopia; MMR = Myanmar; PHL = The Philippines; COD = Congo (Democratic Republic of the); NGA = Nigeria; IND = India; KEN = Kenya; PAK = Pakistan; THA = Thailand; BGD = Bangladesh; VNM = Viet Nam; RUS = Russia; CHN = China; BRA = Brazil; KOR = Korea; COL = Colombia; JPN = Japan; TUR = Turkey; MEX = Mexico; EGY = Egypt; ESP= Spain; IRN= Iran; DEU= Germany; FRA= France; GBR= Great Britain; ITA= Italy; USA= United States; HTI = Haiti; PER = Peru; GUY = Guyana; UKR = Ukraine; DOM = Dominican Republic; ECU = Ecuador; NIC = Nicaragua; HND = Honduras; SLV = El Salvador; GTM = Guatemala; POL = Poland; CUB = Cuba; CAN = Canada; JAM = Jamaica; PRI = Puerto Rica; WHO = World Health Organization; TB = tuberculosis; ISO = International Organization for Standardization.

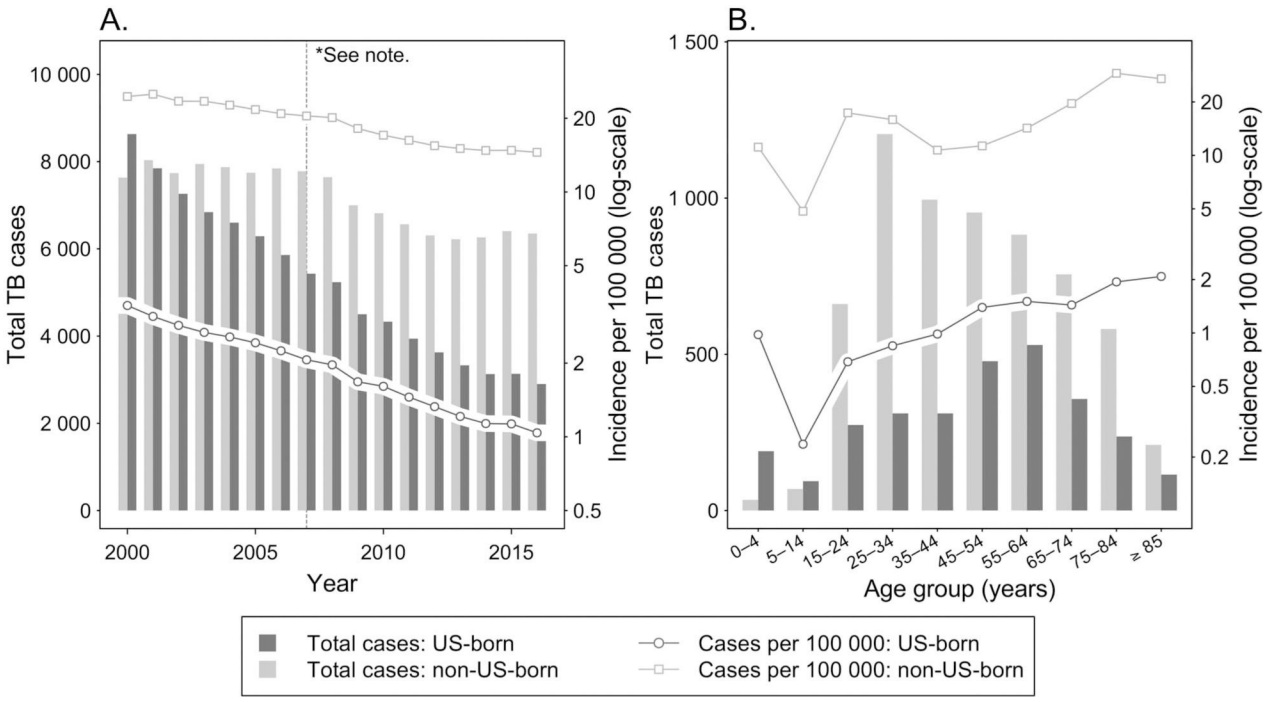

Figure 2.

Trends in TB cases and TB incidence rates for US-born and non-US-born individuals residing in the United States from 2000 to 2016. **A)** Total annual TB cases and TB incidence rate for US-born and non-US-born individuals living in the United States for each year from 2000 to 2016. *Note: vertical dashed line indicates date of introduction of revised medical screening instructions for prospective immigrants and refugees. **B)** Total annual TB cases and TB incidence rate for US-born and non-US-born in 10-yearly age groups for 2016. TB incidence rates calculated as reported TB cases divided by population size for a given year and population group. TB case numbers sourced from the National TB Surveillance System[9] and population estimates derived from the American Community Survey.[10] TB = tuberculosis.

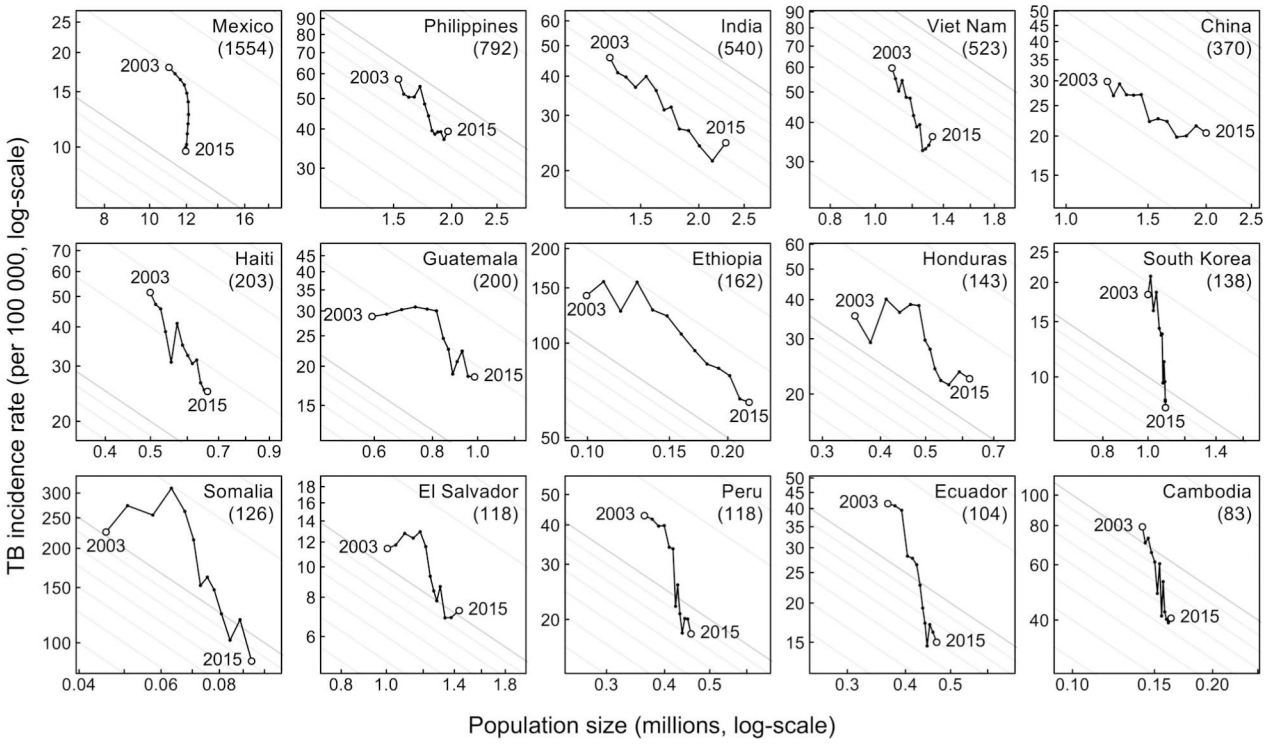

Figure 3.

Time series of TB incidence and population size for non-US-born individuals living in the United States for the top 15 countries of origin by TB cases, from 2003 to 2015.* *Grey diagonal lines represent lines of equal total TB cases (log scale). TB incidence calculated as total TB cases divided by resident population size, for each year and country of origin. Values in parentheses under each country name represent the average annual number of TB cases reported for individuals living in the United States from each country of origin over the period 2003–2015. TB case numbers sourced from the National TB Surveillance System[9] and population estimates derived from the American Community Survey.[10]

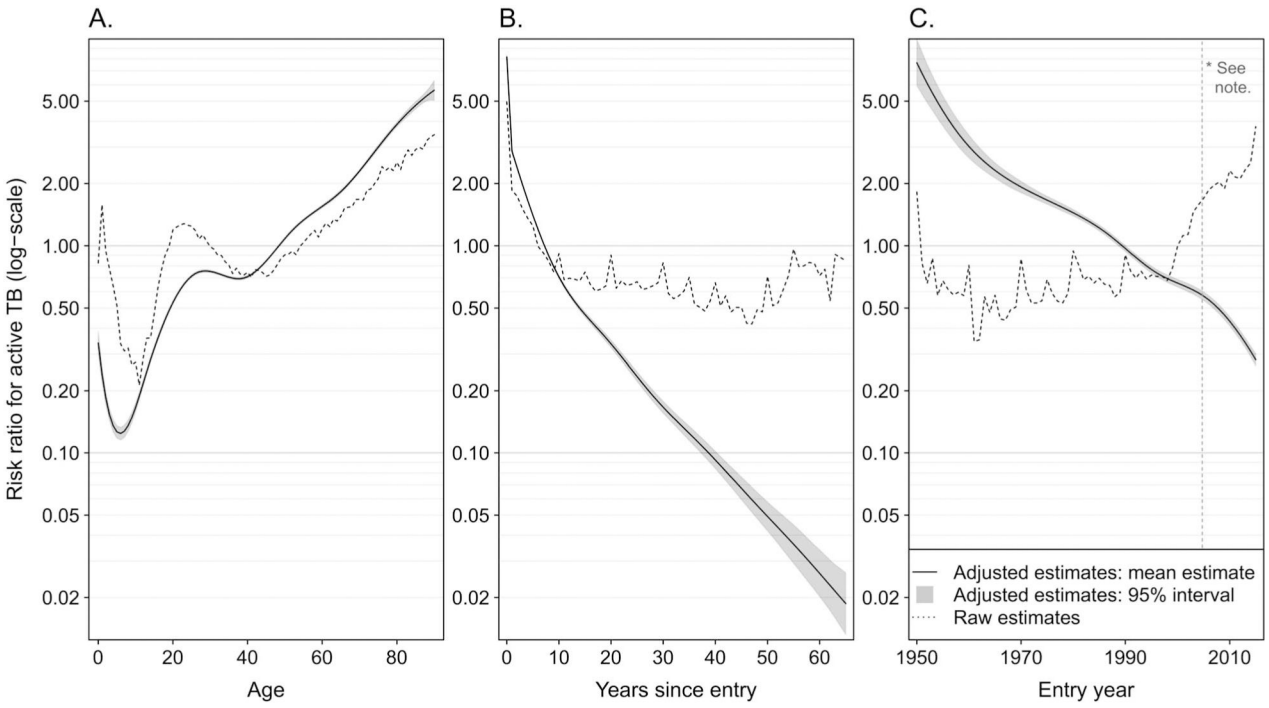

Figure 4.

RRs for TB incidence for the non-US-born population by age, years since entry and entry year, controlling for other effects.**RRs for TB incidence among non-US-born individuals from the top 30 countries of origin between 2003 and 2015, with overall average incidence in the study population as the reference category. Adjusted RRs estimated from a regression model estimating effects by country of origin, age, years since entry, and calendar year, assuming smooth effects for age and year since entry. Raw RRs estimated directly from the raw data, not controlling for other effects. **A)** Adjusted and raw IRRs as a function of individual age. **B)** Adjusted and raw IRRs as a function of years since entry into the United States. **C)** Adjusted and raw IRRs as a function of entry year into the United States. Note: vertical dashed line indicates date of introduction of revised medical screening instructions for prospective immigrants and refugees. RR = risk ratio; TB = tuberculosis; IRR = incidence RR.

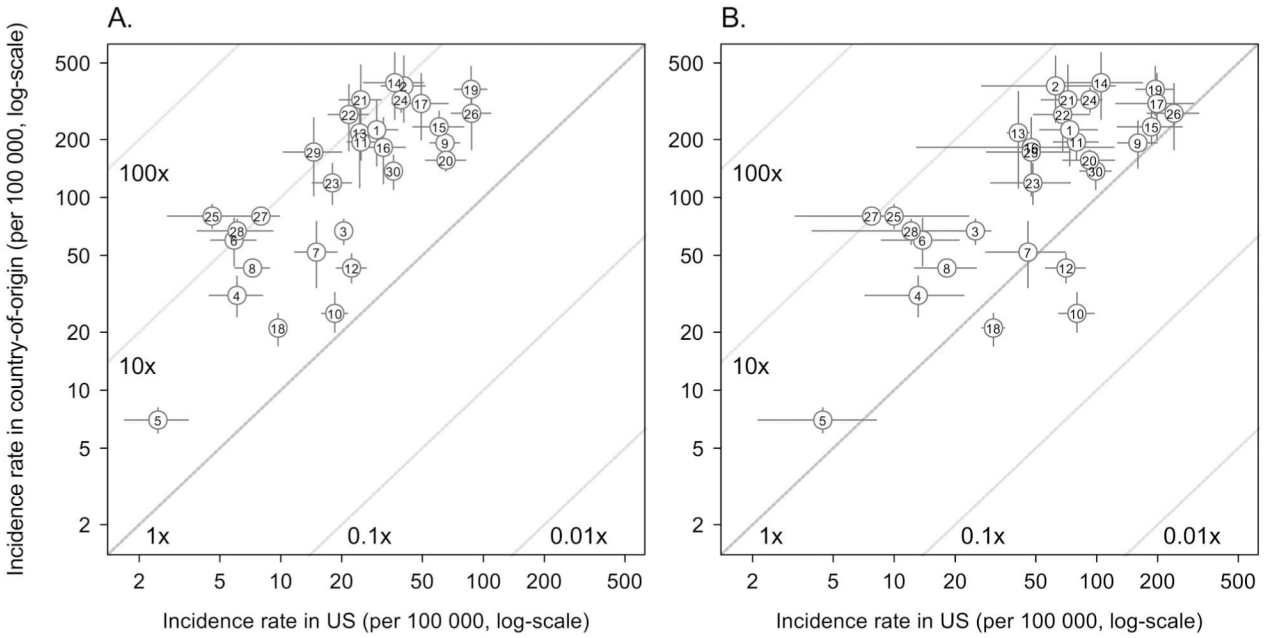

Figure 5.

Incidence for individuals living in the United States from each of the top 30 countries of origin graphed against WHO incidence estimates for each country, 2015. **A)** compares 2015 TB incidence estimates for non-US-born individuals living in the United States from each of the top 30 countries of origin (horizontal axis) to WHO incidence estimates for the same country in the same year (vertical axis). **B)** compares 2015 TB incidence estimates for recent migrants (<5 years since entry) from each of the top 30 countries of origin (horizontal axis) to WHO incidence estimates for the same country in the same year (vertical axis). Horizontal bars represent confidence intervals for TB incidence in individuals living in the United States, and vertical bars represent uncertainty intervals reported with WHO incidence estimates. Diagonal dotted lines represent isoclines with a fixed ratio of incidence in the country of origin relative to the United States (labels for each isocline represent ratio of incidence in the country of origin to incidence for individuals living in the United States). Numbers within plotting symbols represent country identifiers: 1 = Bangladesh; 2 = Cambodia; 3 = China; 4 = Colombia; 5 = Cuba; 6 = Dominican Republic; 7 = Ecuador; 8 = El Salvador; 9 = Ethiopia; 10 = Guatemala; 11 = Haiti; 12 = Honduras; 13 = India; 14 = Indonesia; 15 = Kenya; 16 = Laos; 17 = Liberia; 18 = Mexico; 19 = Myanmar; 20 = Nepal; 21 = Nigeria; 22 = Pakistan; 23 = Peru; 24 = Philippines; 25 = Russia; 26 = Somalia; 27 = South Korea; 28 = Taiwan; 29 = Thailand; 30 = Viet Nam; WHO = World Health Organization; TB = tuberculosis.

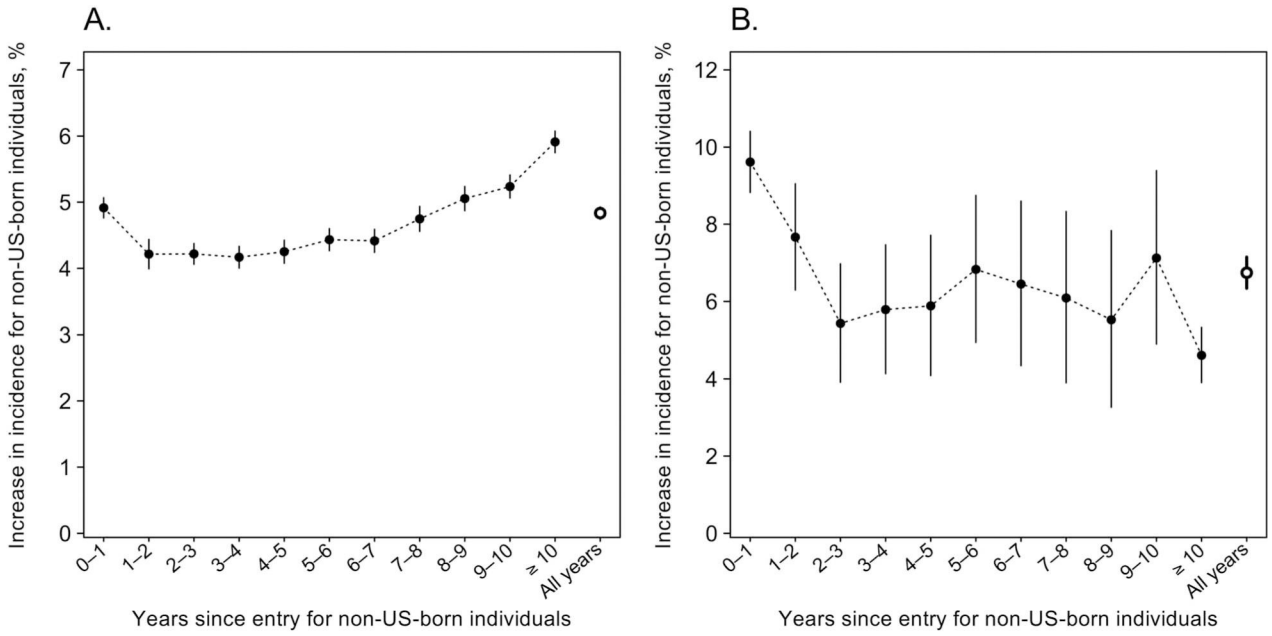

Figure 6.

Increase in TB incidence among non-US-born individuals associated with a 10% increase in TB incidence in the country of origin, and a 10 percentage point increase in refugees among the migrant pool at entry year. **A)** shows the percentage increase in TB incidence in non-US-born populations associated with a 10% increase in TB incidence in the country of origin at the entry year. **B)** shows the percentage increase in TB incidence in non-US-born populations associated with a 10% increase in refugees as a proportion of all legal migrants from a given country in the entry year. Results represent first differences estimated from a regression model controlling for TB incidence in the country of origin, percentage refugee, age, years since entry, and calendar year, assuming smooth effects for age and year since entry. TB = tuberculosis.

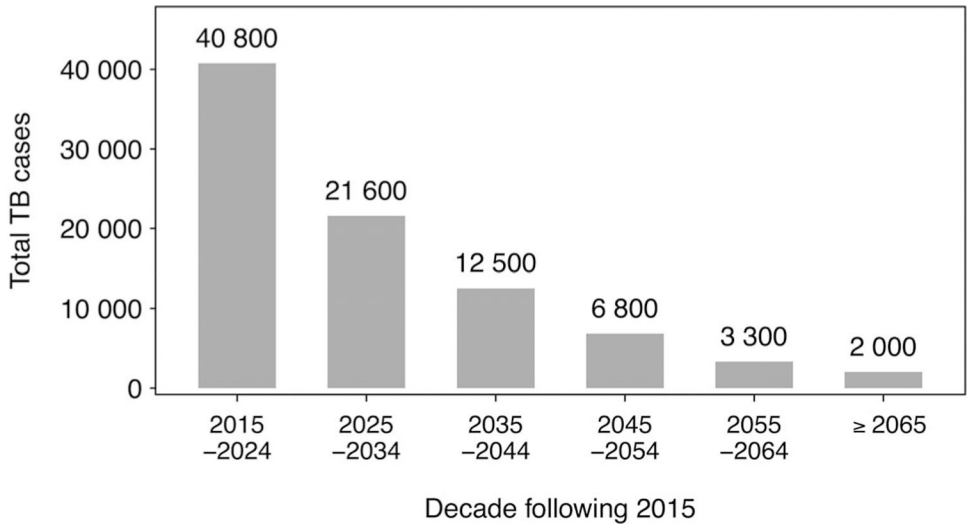

Figure 7.

Projected future number of incident TB cases among the cohort of non-US-born individuals resident in the United States in 2015 by decade.* *Projections based on current non-US-born population size and composition, assuming no emigration, that current all-cause mortality rates apply, and that changes in TB incidence rates associated with age and years since entry follow the risk ratios presented in Figure 4. TB = tuberculosis.

Table 1

RRs for TB incidence by country of origin, controlling for other effects [*]

Country	aRR (95%CI) [†]	RR (95%CI) [‡]	Country	aRR (95%CI) [†]	RR (95%CI) [‡]
Cuba	0.20 (0.18–0.22)	0.27	Pakistan	1.73 (1.62–1.84)	1.99
Russia	0.39 (0.35–0.43)	0.52	Bangladesh	1.77 (1.63–1.91)	2.29
Colombia	0.40 (0.37–0.44)	0.49	Honduras	1.92 (1.83–2.01)	2.20
Taiwan	0.53 (0.48–0.59)	0.61	Haiti	2.24 (2.16–2.34)	2.65
Dominican Republic	0.61 (0.58–0.65)	0.69	Indonesia	2.54 (2.33–2.77)	3.19
El Salvador	0.70 (0.66–0.74)	0.74	Philippines	2.69 (2.62–2.75)	3.42
South Korea	0.82 (0.78–0.86)	0.98	Laos	2.95 (2.75–3.16)	2.65
Mexico (reference)	1.00 (1.00–1.00)	1.00	Viet Nam	3.03 (2.95–3.12)	3.32
China	1.17 (1.13–1.21)	1.79	Liberia	3.24 (2.96–3.54)	4.02
Nigeria	1.29 (1.19–1.39)	1.71	Cambodia	4.12 (3.88–4.39)	4.18
Thailand	1.59 (1.46–1.72)	1.58	Myanmar	4.57 (4.30–4.86)	7.32
India	1.66 (1.61–1.70)	2.36	Nepal	4.85 (4.52–5.21)	7.23
Ecuador	1.66 (1.57–1.76)	1.87	Ethiopia	5.85 (5.59–6.12)	7.59
Guatemala	1.70 (1.63–1.77)	1.85	Kenya	6.48 (6.05–6.94)	7.83
Peru	1.72 (1.63–1.81)	2.17	Somalia	9.58 (9.11–10.08)	13.18

[*] RRs for TB incidence among non-US-born individuals from the top 30 countries of origin between 2003 and 2015, with Mexico (the country of origin with the highest number of TB cases) as the reference category.

[†] Estimated from a regression model estimating effects by country of origin, age, year since entry, and calendar year, assuming smooth effects for age and year since entry, with 95% confidence intervals shown in parentheses.

[‡] Estimated directly from the raw data, not controlling for other effects.

RR = risk ratio; TB = tuberculosis; CI = confidence interval; aRR = adjusted RR.