The demography of tuberculosis in California in a time of transition:

In search of empirical evidence to guide public health agencies' efforts to target tuberculosis screening in immigrant communities

By

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Abstract

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This dissertation examines the relationships between immigration and the incidence of tuberculosis (TB) disease and prevalence of TB infection in California and in the United States (U.S.). The majority of TB cases in California occur among foreign-born persons from countries with high TB burdens. Although the incidence of TB is declining, the decline among immigrants has stalled, and relationships of this trend with changes in immigration patterns are not well characterized. Census data suggest that immigration to California has undergone notable transitions since the 1990s that have shaped the volume, demographic and socioeconomic composition of immigration streams to the state. The first two papers of this dissertation explore the relationships between changes in immigration and the incidence of TB using the decomposition method, and an innovative application of cohort analysis. The third paper examines the only nationally representative survey of new immigrants in the U.S. to determine gaps in TB screening and to assess the prevalence and risk of latent TB infection (LTBI) in immigrant subgroups by country of origin. This unique data source allowed for the assessment of important immigration, health, and socioeconomic variables.

The decomposition of the recent decline in the incidence of TB among the foreign-born in California shows that changes in the population composition associated with immigration shifts made a modest contribution to the decline, with the majority of the decline due to group-specific declines in rates. There was a notable difference between Hispanics/Latinos and Asians/Pacific Islanders, whereby the impact of immigration shifts was much greater in the former group. The cohort analysis shows that waves of immigration have had varying impacts on the incidence of TB in California, some cohorts contributing to increasing incidence, and others to decreasing incidence. This suggests that the slowing in the decline of the incidence of TB may be due, in part, to immigration cohort entry effects. Identifying cohorts with elevated risk of TB can help develop and test hypotheses on the epidemiologic reasons for the observed effects, and can provide an evidence base for selecting demographic subgroups in which to prioritize TB screening. The TB screening uptake and TB prevalence analysis confirmed gaps in testing for TB that varied significantly by country of origin. Substantial variation in the prevalence and risk of LTBI was also found, which may inform public health efforts to prioritize the targeted testing and treatment to specific subgroups of highest risk.

Dedication

This dissertation is dedicated to my parents, Sung-Hong and Sung-Aie Oh; my brother Jimin Oh; my wife Claudia Pereira-Oh; and our sons, Gabriel and Michael Pereira-Oh.

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List of abbreviations

ACS	American Community Survey
AIDS	Acquired immunodeficiency syndrome
aOR	Adjusted odds ratio
BCG	Bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention
CDPH	California Department of Public Health
CI	Confidence interval
DOT	Directly observed therapy
HIV	Human immunodeficiency virus
IGRA	Interferon gamma release assay
IPUMS	Integrated public use microdata sample
LTBI	Latent tuberculosis infection
MDR TB	Multidrug resistant tuberculosis
NHANES	National Health and Nutrition Examination Survey
NIS	New Immigrant Survey
OR	Odds ratio
RVCT	Report of Verified Case of Tuberculosis
TB	Tuberculosis
TST	Tuberculin skin test
WHO	World Health Organization
XDR TB	Extensively drug resistant tuberculosis

Introduction

This dissertation examines the relationships between contemporary changes in immigration to the United States (U.S.) and the incidence of tuberculosis (TB) in the foreign-born population of the state of California. It also investigates previously unexamined TB data from a unique and nationally representative survey of new immigrants in the U.S., to determine gaps in TB screening uptake and generate country of origin-specific TB infection prevalence estimates to help inform efforts to prioritize targeted testing and treatment interventions.

The global context of tuberculosis

Although largely absent from the public conscience in developed countries, this infectious disease remains a major global public health scourge. In the 21st century, the former "captain of these men of death" continues to reap its consumptive harvest, with an estimated 12 million prevalent cases of disease- including 8.6 million new cases- and 1.3 million deaths worldwide in 2012 (WHO, 2013). According to Global Disease Burden estimates, TB is the second-highest cause of death due to infectious disease, the seventh-highest cause of death overall, and eleventh-highest cause of disability adjusted life years, with the burden disproportionately affecting low-income countries (WHO, 2008). Despite the epidemiologic transition from the predominance of infectious diseases to chronic diseases (Omran, 1971), tuberculosis and other infectious diseases remain massive obstacles to human health and economic growth (Grimard & Harling, 2004).

An estimated one-third of the world's population is infected with *Mycobacterium tuberculosis* (WHO, 2013), an enormous reservoir for potential morbidity and mortality. Once infected, the risk of progression from latent TB infection (LTBI) to active disease remains present throughout the life course. This potentially lengthy latency period imbues TB epidemiology with temporal characteristics akin to chronic disease epidemiology (Wu et al., 2008). The annual probability of a person with LTBI developing active disease is estimated at 0.1%, and approximately 10% of persons with LTBI may develop TB disease in their lifetime (Schwartzman, 2002). The discovery in the 1940s and subsequent advancement of antibiotic therapies helped speed the decline of TB through the 1960s and 70s. However, several factors emerged in the 1980s that led to a reversal of the decline in TB. The HIV/AIDS epidemic, particularly in Sub-Saharan Africa, and health systems deterioration in the wake of sociopolitical upheavals (e.g., the breakup of the Soviet Union) led to resurgences of TB in many regions of the world. Resistance to anti-TB drugs led to multi- and extensively- drug resistant TB (MDR and XDR TB) strains that have posed grave new challenges to TB control efforts. In the context of increasing poverty, economic inequality, and other sociopolitical factors, the reverses suffered during the 1980s and 1990s heralded what some called a "new tuberculosis"- a social disease that medical interventions alone cannot eliminate (Farmer, 1998; Gandy & Zumla, 2002). Today, the reverse has slowed, but a mere twenty-one years since the World Health Organization (WHO) declared TB a "global emergency", the disease continues to pose major public health dilemmas, especially in the countries deemed "high burden" countries. The TB cases identified in these 22 countries together account for 80 percent of the world's incidence of this disease.[1] (WHO, 2009).

The burden of TB and approaches to its control in the U.S. and California

In the United States, TB was the leading cause of death in the 19th and into the early part of the 20th century (Binkin et al., 1999). While its morbid preeminence has since receded, nearly 10,000 new cases of TB were reported in the U.S. in 2012, an incidence of 3.2 cases per 100,000 population (CDC, 2013). Since 2002, the majority of TB case patients in the U.S. has been among foreign-born persons, and the proportion has steadily grown to 63 percent in 2012 (CDC, 2013). California has the largest number of TB cases in the nation, with 2,191 cases identified in 2012. Nearly four out of five TB cases in California occur among persons born outside the U.S. (Tuberculosis Control Branch, 2013).

The top two prioritized strategies of TB prevention and control in the U.S. are case finding and contact investigation (CDC, 2005a). Case finding refers to the prompt detection and chemotherapeutic treatment of cases of active TB disease. Contact investigation is the process of identifying persons who may have been recently exposed to patients with contagious TB, screening them, and treating those with evidence of latent TB infection (LTBI). A third strategy is targeted testing (i.e., screening) of groups at particularly high risk of TB (e.g., immigrants from high TB burden countries; health care workers; persons living with HIV infection; homeless persons). The planning, prioritization, implementation of the targeted testing strategy is left largely to the discretion of local health departments, given each county or metropolitan region's demographic composition, epidemiologic features, and resource availability. This multi-strategy system of TB control is organized in a hierarchy of federal, state and local entities. The Centers for Disease Control and Prevention (CDC) leads the formulation of TB policies and guidelines, but state TB control programs such the one housed in the California Department of Public Health (CDPH) as an important interface between federal and local levels of the TB control structure in the U.S. (Binkin et al., 1999).

Case finding efforts are not limited to interventions carried out on U.S. soil. To detect and treat TB disease in a group yet to arrive in the U.S., federal regulations require TB screening of adult immigrants and refugees bound for the U.S., as part of a comprehensive medical examination process (CDC, 2009). Persons with active, infectious disease must either complete a regimen of TB chemotherapy, or take sufficient treatment to render their disease non-infectious, before being cleared to travel to the U.S. Those with non-infectious or inactive disease can proceed with travel to the U.S., with a recommendation to present to the local public health agency for follow-up evaluation. In 2008, over 450,000 immigrants and 60,000 refugees arrived in the U.S. (DHS, 2009). Over the past two decades, studies in California and other states to assess the yield of case finding through this system of overseas screening and follow-up evaluation in the U.S. have shown that approximately 7 percent of immigrant arrivers with non-infectious TB identified in the medical examination are subsequently diagnosed with active disease in the U.S. within a few years of arrival (DeRiemer et al., 1998; LoBue & Moser, 2004;

[1] Afghanistan, Bangladesh, Brazil, Cambodia, China, Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, Philippines, Russian Federation, South Africa, Thailand, Uganda, Tanzania, Vietnam, and Zimbabwe.

Liu et al., 2009). While it is encouraging that this intervention does successfully identifies active TB, many more immigrants are either not screened because of their undocumented status, or they did not show signs of active disease at the time of the overseas screening process.

Local (i.e. county- or metropolitan area-level) public health agencies are a key organizational component of TB control in the U.S., as they have the legal responsibility to report diseases of public health significance, and provide the infrastructure (e.g., chest clinics, community health workers) to conduct case finding, clinical case management, contact investigation, directly observed therapy (DOT), and other TB-related services in the public sector. This interface between public health agency and patient is crucial, since it is at the local health department where TB expertise is concentrated, and many TB patients receive care. There are 61 health jurisdictions in California (58 counties and the three cities of Berkeley, Long Beach and Pasadena), most of which have their own TB control programs. At the state level, the CDPH TB Control Branch is tasked with a wide range of responsibilities including funding local TB programs, conducting surveillance and epidemiologic research, providing training and consultation for TB care providers, and facilitating communications among local health jurisdictions. My role as an epidemiologist in the Surveillance and Epidemiology Section of the TB Control Branch and my experience in investigating the epidemiologic features of TB in California left me well-placed to examine some gaps in the current understanding of TB among the foreign-born.

Immigration to California in a time of transition

With a population of over 36 million, California is a bellwether of U.S. demography and TB epidemiology. It is the top immigration destination in the country (Bohn, 2009), leads the nation in proportion of foreign-born persons at 27 percent (U.S. Census Bureau) and the number of TB cases, and its TB incidence rate is second only to Hawaii (CDC, 2009). High levels of immigration as well as internal migration (e.g., agricultural workers following work along the Central Valley; border zones near Mexico, relocations of refugees to burgeoning ethnic enclaves) contribute to a dynamic convergence of “imported” TB (i.e., the activation of infection acquired in the sending country) as well as potential foci of transmission. Foreign birth in a country with a high incidence of TB is an indicator to public health agencies of the likelihood that TB infection was acquired overseas, prior to arrival in the U.S. Among foreign-born TB cases in California, the most common countries of patient origin are Mexico (29%), the Philippines (22%), Vietnam (12%), China (8%) and India (6%) (Tuberculosis Control Branch, 2013). Previous analyses of temporal trends suggest that TB cases in the U.S. are declining among both the U.S.-born and the foreign born, but the decline among the foreign-born is slowing (Cain et al., 2008). In California, the incidence of TB among foreign born persons is nearly ten times higher than the incidence among native-born persons (16.8 vs. 1.7 cases per 100,000 population in 2012; Tuberculosis Control Branch, 2013). A number of previous studies of California data have suggested that these two groups represent parallel epidemiologic strands, with U.S.-born cases more likely to arise from recent transmission (in the U.S.), foreign-born cases more likely to be attributable to reactivation of infection, and little evidence for transmission between the strands (Chin et al, 1998; Borgdorff et al., 2000). Clearly, the prevention and control of TB in the California and in the U.S. requires continued efforts to identify and treat LTBI in order to reduce the future burden of cases of active TB disease.

The importance of targeted testing for latent TB infection

Crude extrapolation from estimates LTBI prevalence in the U.S. population based on the year 2000 National Health and Nutrition Examination Survey (NHANES) (Bennett et al, 2008), suggests that as many as 7 million people in the U.S. -about 2 million in California- are latently infected. In 2000, Institute of Medicine's exhortative report *Ending Neglect* (Geiter et al., 2000) and the CDC/American Thoracic Society's revised guidelines for target testing (CDC, 2000) underlined the increasing importance of screening immigrants who are already in the U.S. The guidelines specify the following at-risk populations as targets for screening efforts: *recent (i.e., within the prior 5 years) immigrants from high TB prevalence countries*, injection drug users, residents and employees of congregate settings (e.g., health care workers with exposure to TB in hospitals), mycobacteriology laboratory personnel, persons with certain clinical conditions or histories (e.g., silicosis, diabetes mellitus, chronic renal failure, cancer, extreme weight loss, gastric surgery; and young children under 4 yrs of age (CDC, 2000; Jasmer et al, 2002). Priority for recent immigrants was based on the observation that over half of TB cases in the U.S. among the foreign born were identified within five years of arrival (McKenna et al., 1995). However, subsequent findings in metropolitan ports of entry for immigrants such as San Francisco that two-thirds of TB cases among immigrants occurred in persons who been in the country for longer than five years at the time of TB diagnosis implies that long term immigrants may increasingly need to be screened in order to more successfully prevent TB among immigrants (Walter et al., 2008).

Declining TB disease rates and increasing epidemiological predominance of immigrants in the United States and other low-incidence countries have led to a shift in emphasis from the detection of active disease to the detection of latent infection (Nolan, 1999; Dasgupta & Menzies, 2005). Public health efforts to prevent the transition from LTBI to active disease are needed to complement the core activities of case finding (to interrupt transmission) and contact investigation (to promptly identify and treat recently infected persons) (Talbot et al., 2000). While early detection and treatment of active disease remains the primary means of controlling TB, it in insufficient as a strategy of TB elimination and must be complemented by a simultaneous and vigorous attack on LTBI (Dye & Williams, 2008). The consensus at the national TB control level is that the high rates of TB and elevated prevalence of LTBI in the foreign born warrant new approaches and interventions to reduce TB morbidity specifically in this group (Cain et al., 2007; Cain et al., 2008). Current TB control efforts in the U.S. tend to emphasize a foreign-born versus U.S.-born dichotomy, which, while useful in a crudely measure disparities in TB incidence, can hide important variations in health risks and demographic characteristics by country or region of origin. For example, South Asians as a group have an age profile skewed toward young adults and fewer sociobehavioral risk factors (e.g., homelessness, substance abuse) compared to other foreign-born persons with TB in the U.S. (Ashgar et al., 2008). Given its dynamic demographic changes and high immigration (Bohn, 2009), public health agencies in California could benefit from new analyses that will help refine in which immigrant subgroups the targeted testing and treatment of LTBI has been lagging, and which subgroups with high prevalence of LTBI to prioritize in future testing efforts. Local health departments may lack resources to undertake community-wide targeted testing programs in high-risk populations (Nolan, 1999) and therefore need guidance in focusing and implementing recommendations.

Opportunities to address social determinants of TB in California

The social determinants of TB have long been recognized. Friedrich Engels, Rudolf Virchow, and Salvador Allende are just a few of the observers from diverse disciplines who have pointed to the social origins of TB for the past century and a half (Waitzkin, 2005). Even after the advent of antibiotics and the rise in prominence of epidemiology, numerous voices from social science disciplines have cautioned public health scientists to include social processes and theories in conceptual frameworks of efforts to combat TB (Cassel, 1964; Farmer, 1997; Krieger, 1994; Krieger, 2000; Krieger, 2001). The evidence suggests that the current array of public health interventions in place to control and eliminate TB in California may not be sufficient to prevent new cases of TB among the foreign-born (Walter et al., 2008). In 2003, the CDC convened a national forum of TB researchers in public health, behavioral and social sciences in an attempt to synthesize what is known about social determinants of TB and to prioritize research directions (CDC, 2005b). At the forum, the director of the TB program of a major metropolitan area in California emphasized the importance of framing TB data in its full demographic context, including social determinants of TB. It is in this spirit that I chose to examine data of the New Immigrant Survey (NIS) as an integral part of this dissertation. The NIS is the first and only survey in the U.S. of a nationally representative sample of new immigrants. The NIS queried respondents on a range of social, economic and health topics, including educational attainment and childhood health status. The association of these social factors with TB outcomes was explored, with the objective to contribute to the relatively sparse literature on the social determinants of TB in the U.S. The influence of social factors on TB in immigrant populations in California has not been systematically analyzed.

Organization of this dissertation

This dissertation, based on TB surveillance data, Census population data, and NIS data, addresses the dearth of knowledge about the impact of population change on the stalling decline of TB among the foreign-born in California, and provides estimates of sending country-specific gaps in TB screening and prevalence of LTBI. In Paper One, the objective is to deconstruct the declining incidence of TB among immigrants in California between 2000 and 2010 into components of change using a methodology that has its origins in the social sciences and has been relatively underutilized in public health. Using this decomposition method, Paper One assesses the contributions to the decline in incidence of two epidemiologically important demographic characteristics: age, and duration of residence in the U.S. The results of this analysis highlight an important difference by race/ethnicity that characterizes the declining incidence of TB in California, and provide new insights into the impact of recent migration trends on the epidemiologic features of TB in this state.

Paper Two is an adaptation of cohort analysis – usually conceptualized as birth cohort – to assess the impact of immigration entry cohorts on declining trend in TB incidence in California between 2000 and 2011. The objective of this Paper Two was to identify such immigration entry cohort effects using a statistical technique that has shown promise in cohort analysis, and determine the magnitude of these effects. Paper Two presents evidence that some cohorts have contributed to increases in the incidence of TB in the first decade of the 21st century, while others did not have a significant impact or contributed to decreasing incidence. These findings highlight the direct influence of immigration selectivity and policy on the epidemiologic pattern on TB in California.

Paper Three addresses a major gap in the current knowledge of the variation of TB screening update, prevalence of LTBI and risks of LTBI among immigrants. It is the first to provide estimates specific to immigrants' countries of origin, and has the additional benefit of adjustment of the statistical relationships for important immigration-, health-, and socioeconomic- related factors. This paper highlights substantial variation by country of origin and provides public health agencies with important new information to help target and prioritize TB testing strategies. These three papers as a whole represent a novel and methodologically rigorous approach to a better clearer understanding of the epidemiologic features of TB and LTBI among immigrants in California and the U.S. It brings together epidemiology, demography, and social determinants of health to produce new insights on the decline of TB and practical information on how to speed the decline toward elimination.

Paper One

Contributions of changes in age and length of residence factors in the foreign-born population to decreasing tuberculosis incidence in California, 2000 to 2010

An application of the decomposition method

Abstract

Background Since the early 1990's, tuberculosis (TB) morbidity has steadily declined in California and in the United States (U.S.). The rate of decline in the foreign-born population is slower than the rate of decline in the native-born, suggesting disparities in the effectiveness of public health measures. The slowing decline is occurring in the context of slowing growth in international immigration to California in the first decade of the 21st century. No previous epidemiological analysis of TB has reported the influences of population structure changes (e.g., shifts in immigration) on the declining incidence of TB. This analysis aims to quantify the contributions of changes in two demographic characteristics that directly influence TB control measures, age and duration of residence in the U.S, to the recent decline in TB among immigrants in California.

Methods California TB case registry data and U.S. Census Bureau American Community Survey data from 2000 and 2010 were used to investigate TB incidence rates in specific demographic strata by age group, duration of residence category, and age and duration of residence simultaneously. Relative contributions of group-specific rate changes and group-specific population composition changes were quantified using the decomposition method. The analysis assessed the entire foreign-born population, as well as the Hispanic/Latino and Asian/Pacific Islander populations separately, to identify differences that could inform revisions of targeted TB testing and treatment guidelines.

Results The analysis included 8.9 million foreign-born persons in 2000 and 10.4 million in 2010. The 2,268 cases of TB in foreign-born persons in 2000 and 1,744 in 2010 yielded incidence rates of 25.3 and 16.8 per 100,000, respectively, an absolute decrease of 8.5. Decomposition on age and duration of residence factors simultaneously revealed that 92.2% of the rate decline was attributable to changes in the TB rate distribution and 7.8% to changes in the population composition. Stratified analyses by race/ethnicity showed that the population change contribution remained substantial in the Hispanic/Latino group (8.0%) but was minimal in the Asian/Pacific Islander group (0.8%). In both groups, the impact on incidence declines was concentrated in the recent immigrant arrivers, but among Hispanics/Latinos, population factors were predominant whereas among Asians/Pacific Islanders, precipitous rate declines were the dominant factor. Among immigrants with longer duration of residence in the U.S., evidence for upward pressures on TB incidence trends was found.

Conclusions Compositional changes in the immigrant population in the California made a modest contribution to the decline in the incidence of TB among immigrants in the first decade of the 21st century. Stark differences between Hispanic/Latino and Asian/Pacific Islander groups may have practical implications for the evidence-based prioritization of targeted TB testing and treatment interventions. The reductions in recent immigrants of prime working age may reverse with improving economic conditions. Expanding targeted TB testing and treatment of immigrants of longer duration of residence is probably warranted.

Background

After peaking during the height of the HIV epidemic in 1992, annual reports of TB cases in California and the rest of the United States (U.S.) have decreased in a nearly monotonic trend. TB disproportionally affects the immigrant population in California: 77% of the 2,325 case patients reported in 2011 were immigrants- yielding an incidence rate more than nine times higher than in the native-born population, at a time when 27% of the population was foreign-born (Westenhouse et al., 2012; American Community Survey, 2011). A disparity in incidence by nativity has been observed over the course of the first decade of the 21st century, whereby the pace of decline of TB in immigrants is declining more slowly or stagnating compared to that in the native-born. (Cain et al., 2007; Westenhouse el al., 2012). The overall decline in TB in California has been attributed, in part, to successful TB control measures. The reasons for the lagging decline in the immigrant population are not well understood. Important to the understanding of this dynamic, but not well characterized, process is the impact of demographic shifts in the immigrant population. Changes in the demographic structure of the immigrant population brought on by variations in immigration patterns including volume, age structure, and origin may have important impacts on the magnitude and trends of TB in the foreign-born, but these influences are not well described.

Recent observations of immigration streams into the U.S. and California suggest that the opening decade of the 21st century offers a timely opportunity to study the impact of demographic trends on the epidemiologic features of TB. This decade has seen an unprecedented surge in immigration to the U.S.: of the 40 million immigrants living in the country in 2010, nearly 14 million arrived in or after 2000, making it “the highest decade of immigration in American history” (Camarota, 2011). However, a subtle yet important subtext of this enormous volume of immigration to the U.S. is a recent trend, beginning in the late 1990s, characterized by increasing proportions of new immigrants choosing to settle in parts of the U.S. other than the traditional immigrant magnets of California, New York, Illinois, Texas, Florida and New Jersey. Thus, the first decade of the 21st century has seen slowing growth rates of the immigrant population in California, contrasted with rapid growth in new immigration destination states in regions such as the South and the Midwest (Bohn, 2009). North Carolina and Georgia, for example, experienced increases of 67 and 63 percent, in contrast to less than 15 percent growth in California (Camarota, 2011). The age composition of new immigrants in California has also changed in recent years. Whereas in the 1980s, California’s working-age (age 23 – 64) immigrant population grew 9.5 percent per year, this growth slowed to 4.4 percent per year in the 1990’s and further decelerated to 2 percent per year in the 2000’s (Bohn, 2009). Furthermore, the composition has changed along important socioeconomic dimensions such as educational level. In 1990, 19 percent of new arrivers were university graduates and 41 percent had less than a high school diploma. A trend toward more highly educated new immigrants meant that by 2007, those new arrivers with a university diploma (35 percent) outnumbered those with less than a high school degree (30 percent) (Bohn, 2009). Demographic shifts in the immigrant population in California are also occurring along lines of regions of origin and race and ethnicity. Compared to the 1990s, proportionally fewer newly arriving Latino immigrants in the U.S. chose to settle in California in the first half of the opening decade of the 2000s (Bohn, 2009). An analysis of Mexican immigration to the U.S. based on data sources on both sides of the border identified a decrease in the flow of immigrants from Mexico to the U.S. that began mid-decade and steeply declined by its end (Passel & Cohn, 2009).

The slowing decline of TB in the immigrant population of California has not been investigated from the perspective of these recent and dramatic demographic changes. The relationships between population structures of age at TB diagnosis, length of residence in the U.S. between arrival and TB diagnosis, and TB incidence are important to understand. It is reasonable to focus on these two demographic variables because they are among the primary characteristics by which risks for TB (both for infection and for progression from infection to disease) are assessed, and targeted testing and treatment of latent TB infection (LTBI) is recommended (CDC, 2000; CDC, 2005a). If age- and length of residence-specific TB incidence rates are constant over time, changes may simply reflect changes in the age and duration of residence profile of the immigrant population. In this scenario, the primary contributor to the changing incidence rate would be "rate schedule differences" (Preston et al., 2001). On the other hand, if age- and duration of residence-specific incidence rates are found to change over time, the difference may be influenced by shifts in the composition of the immigrant population by age and duration of residence due, in part, to new immigration. Very few published studies have examined the impact of changes in recent immigration patterns on the epidemiologic features of TB. Age and duration of residence have been assessed separately in previous studies, but in this analysis I investigate these two factors simultaneously, using a decades-old methodology developed in the social sciences that remains underutilized in epidemiology.

Methods

Individual-level demographic characteristics of reported cases of active TB in the years 2000 and 2010 were queried from a de-identified electronic database of Reports of Verified Case of Tuberculosis (RVCT) in the TB case registry of the California Department of Public Health. The RVCT has been the standard tool for the surveillance of confirmed active TB cases in the U.S. since 1985. The RVCT includes individual-level data on patient demographic characteristics, clinical characteristics, laboratory results, risks associated with acquiring TB infection and/or risk of progressing from infection to active disease (e.g., living in congregate settings, behavioral factors such as substance use), TB treatment, and treatment outcomes. In 1993, the RVCT was revised to include data on anti-TB drug resistance. In 2010, a further revision added variables capturing TB diagnostic results (i.e., nucleic acid amplification tests and interferon gamma release assays), the presence of medical conditions increasingly recognized as being associated with increased risk of progression to TB disease (e.g., diabetes), and immigration status at the time of TB diagnosis. Population estimates were derived from the U.S. Census Bureau American Community Survey (ACS) 1-year estimates for the years 2000 and 2010. I accessed these data on the Integrated Public Use Microdata Series (IPUMS) online database of the Minnesota Population Center, University of Minnesota (Ruggles et al., 2010).

The age and recentness of arrival of immigrants are important demographic characteristics in TB control interventions because TB incidence rates vary substantially by both factors and targeted testing and treatment of latent TB infection ("TB screening") recommendations in California and in the U.S. cite specific thresholds of these factors for prioritizing groups for TB screening. For example, California guidelines prioritize TB screening for, among other groups, foreign-born children under 18 years of age and persons who have immigrated within the last five years from high TB burden regions of the world (CDHS/CTCA, 2006); national guidelines also specify immigration within the last five years from a high TB-incidence country as warranting prioritization for TB screening (CDC, 2005). Age-specific TB incidence rates in the immigrant population vary by duration of residence in the country. Duration of residence can be conceptualized as an effect modifier of the relationship between age and TB incidence. Therefore, I investigated changes in both factors simultaneously.

Following the convention of most surveillance reports and epidemiological studies of TB in the U.S., the age categories used in this analysis were 0 to 4, 5 to 14, 15 to 24, 25 to 44, 45 to 64, and 65 years or older. The ages of TB case patients were determined by subtracting the month and year of birth from the month and year of the report date of the TB case. The analysis was limited to foreign-born persons. For TB case patients, the length of residence in the U.S. at the time of the TB case report was calculated by subtracting the month and year of self-reported arrival in the U.S. from the month and year of the TB case report. For the California population, the duration of residence was calculated using the IPUMS variable "yrsusa1", which ascertained "when did this person come to live in the United States?" These values were used in reference to each year of analysis (2000 and 2010) and were categorized into the following groups: in the U.S. for 0 to 2, 3 to 5, 6 to 10, 11 to 15, 16 to 20, 21 to 25, 26 to 30, 31 to 35, 36 to 40 and over 40 years.

To investigate the relative contributions of changes in age and duration of residence factors to change in the crude TB incidence between 2000 and 2010 I used the decomposition method, which was developed in the social sciences in the middle of the 20^{th} century. The decomposition method was formalized by University of Chicago researchers beginning in the late 1940s (Kitagawa, 1955) and has since been used by demographers and economists to quantify the components of rate differences in mortality, fertility and immigration. The method essentially separates the difference in rates between two time points (or two populations) into two additive components: the contribution of the changes in rate and the contribution of a compositional change in the population (Preston et al., 2001). Identifying contributing factors to population growth rates (Horiuchi, 1995), differences in educational attainment and wage earnings between immigrants in the U.S. and Canada (Borjas, 1991), and the influence of educational attainment on fertility (Castro Martin, 1995) are but a few examples of the application of decomposition in the social sciences found in the literature.

Some researchers have extended the decomposition method beyond its origins in economics and other social sciences to applications in public health and epidemiology, although its use as an epidemiologic method has been relatively infrequent. Demographers and epidemiologists have used decomposition to assess the impact of changing prevalences of chronic disease on declining trends in late-life disability (Freedman et al., 2007); differences in immigrant groups' health insurance coverage by length of residence and occupational category (Kao et al., 2010); gender and age contributions to differences in traffic fatality rates (Li et al., 1998); and trends in perinatal and infant mortality (Williams & Chen, 1982; MacDorman et al., 2005), low birth weight (Yang et al., 2006), and obesity (Hoque et al., 2010). One of the main advantages of decomposition is its economy and expositional clarity (Preston et al., 2001). The combination of a straightforward conceptual framework with quantifiable results makes decomposition a useful and desirable method to address public health issues that need to be stated succinctly and clearly. The influence of changes in the age and recentness of arrival of immigrant cohorts on the incidence of TB disease in California is one area in which this approach may shed light.

I performed the decomposition analysis as described in a classic textbook in the field of demography (Preston et al., 2001). Let R^A and R^B be the crude incidence rates of TB in the foreign-born population in California in 2000 and 2010, respectively. Let R_{ij}^A and R_{ij}^B be the age- and length of residence- specific TB rates in 2000 and 2010, where *i* = the age categories 0 to 4, 5 to 14, 15 to 24, 25 to 44, 45 to 64, and 65 years or over; and *j* = length of residence 0 to 2, 3 to 5, 6 to 10, 11 to 15, 16 to 20, 21 to 25, 26 to 30, 31 to 35, 36 to 40, and greater than 40 years. Similarly, let C_{ij}^A and C_{ij}^B be the population compositions of each age- and length of residence subgroup in California in 2000 and 2010, respectively.

The total contribution of age- and length of residence- compositional differences to the change in TB incidence between the two years was calculated as shown in Equation 1.

Equation 1:

$$\sum_{ij} (C_{ij}{}^{B} - C_{ij}{}^{A}) \times [\frac{R_{ij}{}^{A} + R_{ij}{}^{B}}{2}]$$

Similarly, the contribution of age- and length-of-residence specific TB *rate* differences to the change in TB incidence was computed according to Equation 2.

Equation 2:

$$\sum_{ij} (R_{ij}{}^{B} - R_{ij}{}^{A}) \times [\frac{C_{ij}{}^{A} + C_{ij}{}^{B}}{2}]$$

The sum of equations 1 and 2 equals the difference between the crude TB incidence rates in the foreign-born population in 2000 and 2010. The proportion of the difference in these rates attributable to differences in the age- and length of residence- composition of the foreign-born was then expressed as shown in Equation 3. Analogously, the proportion of the crude rate difference attributable to differences in the TB rate schedule in the age- and length of residence groups was calculated according to Equation 4.

Equation 3:

$$\frac{\sum_{ij} (C_{ij}{}^{B} - C_{ij}{}^{A}) \times [\frac{R_{ij}{}^{A} + R_{ij}{}^{B}}{2}]}{\sum_{ij} (C_{ij}{}^{B} - C_{ij}{}^{A}) \times [\frac{R_{ij}{}^{A} + R_{ij}{}^{B}}{2}] + \sum_{ij} (R_{ij}{}^{B} - R_{ij}{}^{A}) \times [\frac{C_{ij}{}^{A} + C_{ij}{}^{B}}{2}]}$$

Equation 4:

$$\frac{\sum_{ij} (R_{ij}{}^{B} - R_{ij}{}^{A}) \times [\frac{C_{ij}{}^{A} + C_{ij}{}^{B}}{2}]}{\sum_{ij} (C_{ij}{}^{B} - C_{ij}{}^{A}) \times [\frac{R_{ij}{}^{A} + R_{ij}{}^{B}}{2}] + \sum_{ij} (R_{ij}{}^{B} - R_{ij}{}^{A}) \times [\frac{C_{ij}{}^{A} + C_{ij}{}^{B}}{2}]}$$

The analysis was done for all foreign-born persons, and then separately for Latino and Asian immigrants. IPUMS datasets of California population estimates and demographic characteristics were accessed online and managed using SAS 9.2 (Cary, NC, U.S.A.). TB surveillance data were also queried and analyzed using SAS. Data management and decomposition calculations were done in Microsoft Excel (Redmond, WA, U.S.A.).

This project was reviewed by the University of California Committee for Protection of Human Subjects and deemed exempt due to the publicly available nature of the denominator data (i.e., population estimates) and the de-identified nature of the numerator data (i.e., TB cases).

Results

The analysis included 8.9 million foreign-born persons in California in 2000 and 10.4 million in 2010. The 2,268 foreign-born TB case patients in 2000 and the 1,744 in 2010 yielded incidence rates of 25.3 per 100,000 and 16.8 per 100,000 population, respectively- an absolute decrease of 8.5 per 100,000. Decomposition by age group alone showed that 126.8% of the decline was attributable to decreases in age group-specific rates, and −26.8% to changes in the age structure of the foreign-born population (Table 1a). The value exceeding 100% means that, in the absence of changes in the composition, the incidence decrease would have been even greater than what was observed. The negative value indicates that age compositional factors worked in the opposite direction of the rate distribution factors, i.e., they tended toward *increasing* the TB incidence rate. The rate decreases in the 45-64 and 65+ year age groups were substantial and contributed 3.9 and 3.2 per 100,000, respectively, to the crude rate difference of 8.5 per 100,000. However, these rate contributions were in large part offset by the remarkable population growth of these groups, reflected by the negative values of the composition contributions (-2.32 and -1.89). The group with the largest combined (rate and composition) contribution to the change in foreign-born TB incidence was the age 25-44 years stratum. Decomposing the crude incidence decline by duration of residence alone (Table 1b) showed that from this perspective, 67.4% of the incidence decline among all foreign-born persons was attributable to changes in the rate distribution, and 32.6% to changes in the duration of residence composition of the immigrant population. The subgroup with the single largest contribution to the TB incidence rate decline were the most recently arrived immigrants who developed TB disease within two years of U.S. arrival.

Decomposition of the simultaneous effects of age- and duration of residence attributed 92.2% of the decline in the crude rate of TB in the foreign-born population to changes in the age- and duration of residence-specific TB rate distribution, and 7.8% to changes in the population composition of the immigrant population in these factors (Table 1c). If the age- and duration of residence- distribution in the foreign-born population in 2010 had remained the same as in 2000, the expected absolute decline in the TB incidence rate would have been 7.9 instead of 8.5, to a level of 17.5 instead of the observed 16.8. Within the group of most recent arrivers (≤2 years' duration of residence in the U.S. at the time of TB diagnosis), it was the adults of prime working age 25-44 years who contributed the most to the rate decline, by virtue of both falling TB rates and contraction of their share of the population. Most of the population contribution to the declining TB incidence among the foreign-born was concentrated in the group of most recent arrivers with ≤2 years' duration of residence.

The incidence rate of TB in the foreign-born Hispanic/Latino group declined by 36% from 17.5 to 11.2 between 2000 and 2010- an absolute decline of 6.3. The results of the analysis restricted to the foreign-born Hispanic/Latino population are shown in Table 2. Decomposition by age group factors alone yielded a 128.7% contribution of age group-specific rate distribution changes and a -28.7% contribution of age structure changes (Table 2a). Once again, the value exceeding 100% means that, in the absence of changes in the composition, the incidence decrease would have been even more pronounced than was observed. As in the "all foreign-born" analysis, the contributions of the substantial rate decreases in the 45-64 and 65+ year age categories were in large part offset by the population expansion of these groups, reflected by the negative values of their composition contributions. Young adults age 25-44 years were the group with the largest contribution to the TB incidence decline among foreign-born Hispanics/Latinos. Decomposition by only duration of residence factors attributed 70.4% of the incidence decline to changes in the duration-specific rates and 29.6% to compositional changes (Table 2b). The subgroup with the highest contribution was that composed of the most recent immigrants, who developed TB disease within two years of U.S. arrival. As in the "all foreign-born" analysis, the dominant contribution to the incidence decline within this subgroup was made by the population composition, i.e., the impact of the severely shrinking population share (from 10.1% to 3.6%) was stronger than the impact due to the substantial decline in group-specific incidence (from 50.1 to 39.8).

In the decomposition analysis of both factors simultaneously in the Hispanic/Latino immigrant population, 92.0% of the rate decline was attributed to rate distribution changes and 8.0% to population composition changes (Table 2c). In the subgroup of most recent arrivers (0-2 years), stratified by age group, composition changes remained the predominant contributor to the incidence decline compared to rate changes. The population composition contribution to the crude incidence reduction made by these newest arrivers was not uniformly distributed by age group, but was concentrated among young adults 15 to 24 years old and prime working age adults 25 to 44 years of age. Furthermore, of these most recent arrivers, the only age group in which the incidence did not show a marked decline was the young adults ages 15 to 24 years, in which the rate increased slightly (hence the only negative sign in the rate contribution column in the first six rows of Table 2c). Beyond approximately 15 years of residence in the U.S., the population composition of Hispanic/Latino immigrants consistently contributed toward TB rate *increases* by virtue of population growth across all age groups (represented by the preponderance of negative signs in the values listed in the right-most column of the lower portion of Table 2c). However, these compositional contributions toward rate increases among the more established immigrants were outweighed by the rate declines in most age groups.

The incidence of TB in the foreign-born Asian/Pacific Islander group declined by 35%, from 44.0 in 2000 to 28.5 in 2010- an absolute decline of 15.5 per 100,000. Table 3 displays the results of the analysis restricted to this group. Decomposition by age category alone attributed 123.0% of the decline to changing age group-specific TB rates and -23.0% to a changing population age structure (Table 3a). As in the "all foreign-born" and Hispanic/Latino analyses, a remarkable growth in the share of the foreign-born Asian population age 45 and older counteracted the decreasing rates in this group, reflected by the negative values of composition contributions. The group with the largest combined contribution was adults 25-44 years of age. The duration of residence analysis resulted in a 78.8% share of the crude incidence decline being attributed to changing rate distributions, and 21.2% to population composition changes (Table 3b). The largest contribution toward the rate decline in the foreign-born Asian/Pacific Islander population was the made by the recently arrived group (0-2 years). The contribution to the incidence decline of this group was marked by the predominance of the rate contribution (3.9 per 100,000) compared to the composition contribution (1.6 per 100,000), in contrast to the analogous Hispanic/Latino group, in which the composition contribution was stronger.

The analysis of the Asian/Pacific Islander group on both decomposition factors simultaneously yielded a group-specific rate change contribution of 99.2% and a composition change contribution of 0.8% (Table 3c). The predominance of the rate contribution among the newest arrivers (≤2 years' duration of residence in the U.S. at the time of TB diagnosis) was even more pronounced than in the analysis considering only duration of residence. In the group of most recent arrivers (≤2 years) stratified by age group, changes in the population composition made a very small contribution to the incidence decline compared to specific rate changes, i.e., the population size of new immigrants of Asian/Pacific Islander origin did not contract as dramatically as it did in the Hispanic/Latino analysis. In further contrast to the findings in the Hispanic/Latino analysis, in which a 15 year duration of residence threshold was observed at which increases in the population share consistently offset the gains made by decreasing rates, the Asian/Pacific Islander analysis suggested that the change in population composition consistently contributed to increases in the incidence of TB only after ~25 years' residence in the U.S. (represented by the preponderance of negative signs in the values listed in the right-most column of the lower portion of Table 3c).

Discussion

This analysis of the relationships between age, duration of residence in the U.S., and the decline in TB incidence among the foreign-born over the course of the first decade of the 21st century adds new information to our understanding of the changing epidemiologic characteristics of TB in California. Using a simple –but in epidemiology, underutilized- tool, I showed that changes in age- and duration of residence- specific TB incidence rates were the main contributors (92.2%) to the overall decline in the immigrant population, with a lesser but notable contribution (7.8%) made by the changing age- and duration-specific "composition" (i.e., "structure" or "distribution") of the immigrant population over the course of the decade. Crucially, this aggregate finding masked an important difference by race/ethnicity. While the incidence rates of TB in the foreign-born Hispanic/Latino population and in the foreign-born Asian/Pacific Islander population both declined at a similar pace between 2000 and 2010 (by 36% and 35%, respectively), among Asian/Pacific Islanders the changing population composition contributed a small portion of the rate decline (0.8%), whereas among Hispanics/Latinos, population composition represented a sizeable proportion of the decline in that group (8.0%). These findings bring to light important differences between the two most influential race/ethnicity groups in TB among the foreign-born in California, and show that changes in immigration patterns have had a marked impact on the decline of TB among Hispanic/Latino immigrants, but less so among Asian/Pacific Islander immigrants. This report suggests that while substantial group-specific rate decreases have played an important role in the decline of the incidence of TB in the state, population changes such as differential shifts in the volume of recent immigration and the increasing share of immigrants that have been in the U.S. for a longer duration are placing counteracting pressures on the decline in the incidence of TB. These findings have important resource planning implications for health clinics and public health departments serving immigrant populations. Finally, these results may have implications for the projection of future TB incidence trends, and provide new insights into the differential roles of population aging in the Hispanic/Latino versus the Asian/Pacific Islander population.

To my knowledge, the epidemiology of TB in immigrants has not previously been analyzed using the decomposition method and assessing simultaneous changes in age and duration of residence. Previous studies of trends in the incidence of TB either do not address the impact of population changes or only hypothesized the influence of possible changes in immigration (e.g., Winston et al., 2011). If the age- and duration- specific incidence rates of TB remain similarly distributed within the population over time, a changing incidence trend would primarily reflect changes in the structure of the immigrant population in age and duration of residence in the U.S. (e.g., due to a sudden reduction in the volume of recent immigrant arrivers of young age, or a larger volume of immigrants of retirement age). This scenario of population composition changes having greater influence than group-specific rate changes would yield few leverage points for additional public health interventions in the post-immigration arrival period, although it would highlight specific targets and needs for resource planning and allocation. On the other hand, if age- and duration-specific changes in the incidence of TB predominate over population composition factors, this scenario would reflect shifts in TB control measures, prevalence of infection with *Mycobacterium tuberculosis*, and socioeconomic and other factors related to the risk of TB (e.g., co-morbid medical conditions such as diabetes). The finding that, at the end of a decade of substantial immigration shifts, the decline in the incidence of TB among immigrants was in large part due to subgroup-specific incidence declines and to a lesser degree due to population shifts is encouraging. It suggests that immigration changes during the first decade of the 21st century have had only a modest impact on the decline of TB among immigrants, and that the majority of the impact may be attributable to the success of public health interventions efforts and declining TB prevalence in the sending countries.

However, the difference observed between Asian/Pacific Islander and Hispanic/Latino groups highlights demographic groups that may warrant tailored approaches to TB control aimed at reducing the incidence of TB toward the goal of elimination, 1 case per 1 million population. The closer inspection of the 8% composition contribution to the incidence decline in the foreign-born Hispanic/Latino group highlights several sources of variation within that summary measure. Most strikingly, the population composition contribution to the declining incidence was by far the greatest in the stratum of most recent arrivers with up to 2 years' residence in the U.S. at the time of TB diagnosis. Both the lower numbers of these most recent immigrants and the sharp group-specific incidence declines in most age categories conspired to substantially contribute to the decrease in the crude TB incidence but the population factor was much more influential than the rate drop factor, as this analysis was able to quantify for the first time. The observation that the population composition contribution among the newest Hispanic/Latino immigrant arrivers (0 to 2 years' duration) was concentrated among young adults age 15 to 24 and adults of prime working age 25-44 years old likely reflects the impact of selective migration decisions on the epidemiology of TB in California. Others have speculated that economic recession toward the end of the decade under analysis may have contributed to a decline in immigration and a concomitant decline in TB morbidity (Winston et al., 2011), and the present study provides additional evidence that this may well be the case. Further evidence of a strong period effect due to economic and/or other factors is suggested by the finding that the next most recent group of immigrant arrivers (with 3 to 5 years' duration of residence), the population composition contribution to the TB incidence decline was comparatively much weaker. In addition to period effects, possible cohort effects were also suggested by the evidence in the present study. Cohort effects refer to differences in a health outcome that are stronger in a particular age group within a particular time period (Keyes et al., 2012). In the Hispanic/Latino analysis of the simultaneous impact of age and duration of residence on factors, the only age group that did not experience a substantial decline in incidence (of recent arrivers with up to 5 years of residence in the U.S.) was the group of 15 to 24 year-old young adults. It is unclear why the incidence in this age group did not drop as sharply as it did in the others. One possibility is that undocumented immigrants had disproportionately high representation in this age group among recent Hispanic/Latino arrivers, and as a result, pre-immigration screening interventions (restricted only to documented immigrants and refugees) were not able to prevent these cases from occurring. Another, related possibility is that this young adult immigrant cohort is disproportionately coming from regions and/or socioeconomic strata characterized by continuing high TB endemicity and transmission, whereas the other age groups draw from more socioeconomically advantaged strata characterized by lower levels of TB exposure.

The analysis of Asian/Pacific Islander immigrants yielded a strikingly contrasting pattern to that observed among Hispanics/Latinos. Most notably, the population composition among the newest arrivers (in the country for ≤2 years) that were middle age adults (45 to 64 years) *increased* among Asians/Pacific Islanders, partially offsetting the sharp incidence decreases in these groups. In the Hispanic/Latino analysis, this age group among the newest arrivers saw a population decline and only a modest decrease in TB incidence. In additional contrast to Hispanic/Latino new immigration, which declined across all age groups, Asian/Pacific Islander immigration actually increased among older adults, with a measurable impact on TB epidemiology on California, as demonstrated in this analysis. The one age stratum among the newest arrivers that does appear to have been negatively impacted by selective migration pressures is the prime working age category 25 to 44 years old, which saw a substantial decrease among Asian/Pacific Islander immigrants as it did in the Hispanic/Latino analysis. However, in contrast to Hispanics/Latinos, the impact of the rate decrease in the Asian/Pacific Islander group was greater than the impact of the population reduction, because of precipitous decline in the incidence immigrants in this age stratum. This suggests that TB endemicity, TB exposure, and/or case identification improvements have been relatively more successful for Asian/Pacific Islander immigrants of prime working age than for Hispanic/Latino immigrants, revealing a potential health disparity that has not been appreciated prior to this analysis. Furthermore, one resource implication of these findings among newly arrived Asian/Pacific Islander immigrants is that despite the greatly improved TB incidence findings among older persons over age 45, the observed increase in migration volume may be placing added demands on health care providers such as ethnic community clinics for TB testing and treatment services.

The observation of small but consistent upward pressures on the TB incidence attributable to the absolute and relative population composition of immigrants with longer duration of residence in the U.S. also has important implications for the future of TB control in California. Some leading TB epidemiologists in the U.S. have concluded that extending the current TB testing and treatment guidelines to include immigrants who have been in the U.S. for more than 5 years is probably warranted (Cain & Mac Kenzie, 2008), based on a mounting body of evidence that suggests that immigrants who have been residing in the country for well past this threshold continue to have an elevated risk of TB (Walter et al., 2014). The present study adds to that body of evidence not only by corroborating that TB incidence remains high long after immigration arrival, but also by showing that Hispanic/Latino immigrants with 15 or more years' residence and Asian/Pacific Islander immigrants with 25 or more years' residence consistently contribute an upward pressure on the foreign-born TB incidence trend. To have a chance of eliminating TB in California in the foreseeable future, TB testing and treatment resources must reach this growing sector of the aging immigrant population.

I estimate that, had the composition of the foreign-born population in 2000 remained constant throughout the decade, the decline in the foreign-born TB rate would have been slower, yielding a rate of 17.5 in 2010 instead of the observed 16.8 (i.e., amounting to approximately 70 additional cases reported). This finding is consistent with demographic observations of slowing and selective growth of the immigrant population in the decade under analysis. An increase of aging-in-place of the immigrant population already residing in California was accompanied by proportional increases in the number of newly arrived immigrants of retirement age, with economic migrants of prime working age (25 to 44 years) comprising a proportionally lower share of the population by decade's end. Immigration patterns (and population aging) are beyond the scope of direct public health interventions to combat TB, but understanding the demographic and epidemiologic changes that they bring about creates opportunities to more effectively target limited resources to diagnose and treat latent TB infection.

The differing results of decomposition by one factor at a time (by age group, and by duration of residence) compared to those of the analysis of simultaneous changes in age- and duration of residence- rate and composition reveal important recent shifts in the epidemiology of TB in the foreign-born in California, and serve as a caution against relying on duration of residence factors only, which is suggested by national TB guidelines that currently recommend actions such as prioritizing testing and treatment for those who" immigrated ≤5 years ago" (CDC, 2005). The age-only analyses attributed the entire magnitude of the decrease in foreign-born TB to decreasing stratum-specific rates and attributed an opposite pressure (toward increasing rates) to the age composition, driven exclusively by the substantial growth in the absolute and relative size of the population age 45 and older. Rates in the population age 24 and younger declined in every analyzed stratum except in the Asian group age 15 to 24 years, but a concomitant reduction in the absolute and relative size of this young population by 2010 meant that population structure changes were more influential than the age-specific rate declines in the foreign-born population under 24. Even though declines in duration of residence-specific TB rates contributed two thirds of the overall decline between 2000 and 2010, the magnitude of their contributions was offset by the markedly shrinking size of recently arrived immigrant groups, particularly new arrivers in the country less than 2 years at the time TB was diagnosed.

The age group-only analysis, however, does not address variations in an important effect modifier of the relationship between age and TB risk: duration of residence in the receiving country. It is well documented that recently arrived immigrants in the U.S. and Canada from countries with high TB burdens display higher rates of TB, and annual rates decline thereafter (McKenna et al., 1995; Cain et al., 2008; Langlois-Klassen et al., 2011). In contrast to the age-only analysis, decomposition by the duration of residence factor alone attributed substantial portions of the decreases in TB incidence rate to changes in the population structure (32.6% in the "all foreign-born" analysis, 29.6% in the Hispanic/Latino analysis, and 21.2% in the Asian/Pacific Islander analysis). A major portion of the composition contribution to the rate decline in the "all foreign-born" and Hispanic/Latino analyses was the sharp decline in the proportion of new arrivers with 2 or fewer years' duration of residence, whereas in the Asian/Pacific Islander group the opposite was observed, i.e., the composition contribution was smaller than the rate contribution among recent arrivers. If proportionally fewer young immigrants (i.e., reflecting economic migration) and more older immigrants (i.e., reflecting family reunification) continue to characterize the immigration stream into California in the second decade of the 21st century, this changing composition of the foreign-born population will likely continue to have a modest impact on the rate of decline of TB morbidity in this state. These results also suggest that the aging of the immigrant population is being accelerated by the increasing magnitude of new immigrants of retirement age. TB screening efforts in this important and growing group should be prioritized to focus on recent arrivers.

Patterns of age- specific TB rates and to a lesser extent length of residence-specific rates in the U.S. have been investigated by other researchers. A study of TB in the foreign-born population based on national data from 2001 to 2006 corroborated findings from previous periods that most cases occurred among young and middle aged adults, rates were highest among recent entrants (defined by the authors as less 2 years between U.S. arrival and TB diagnosis), and rates were progressively higher at older ages at immigration (Cain et al., 2008). Additionally, the authors reported a pattern whereby the rates among younger immigrants (under 40 years old at the time of arrival) progressively and rapidly decreased over the duration of time in the U.S., but among immigrants 40 years or older at arrival, the high rates consistent with recent arrival persisted even after decades in the U.S., and in arrivers 60 years or older, the rates were higher among those older immigrants who have lived in the U.S. for longer periods of time (Cain et al., 2008). Based on the finding of increasing risk of TB disease at older ages, the authors caution TB care providers against de-emphasizing treatment for latent TB infection persons of advanced age simply because of a perceived low benefit-to-risk ratio. Furthermore, they state that population-level analyses of foreign born groups to identify which specific immigrant subgroups are most affected by latent TB infection and therefore would be the most effective targets for selective screening are lacking. The present study identifies age- and duration or residence-specific groups in the foreign-born Hispanic/Latino and Asian/Pacific Islander population according to their quantitative contributions to the crude TB incidence decline, and could be useful in the selection of demographic strata to targeted testing and treatment of TB.

A limitation of the study is that other risk factors for TB disease such as co-morbid medical conditions and socio-behavioral characteristics were unmeasured. Such factors may have differentially increased the risk of TB disease and could have helped explain some of the variation in the observed group-specific TB incidence rates. For example, recent transmission of TB via exposure to an infectious person shedding bacteria substantially increases the short-term risk of becoming ill with TB. The present study does not distinguish between TB disease due to such recent transmission, and disease due to reactivation of a long-latent infection acquired in the distant past. However, molecular epidemiologic studies in California have suggested that the majority of cases of active TB disease in the foreign-born are due to reactivation of infection acquired remotely in time, rather than recent transmission and rapid breakdown to disease (Chin et al., 1998). The current study took the perspective of exposure to TB transmission effectively ending upon arrival in the U.S. (Cain et al., 2008), which is probably an oversimplification but a reasonable framework given the narrow objective of this study, which was to elucidate population-level differences and changes in TB incidence on two demographic factors used in the prioritization of population-based TB screening. Another limitation is the uncertainty of the representation of undocumented immigrants in population estimates used in the calculations. The ACS – like all other U.S. Census Bureau surveys – does not directly enumerate undocumented immigrants. It does however collect information about entry to the U.S., regardless of the respondent’s legal status. Some researchers suggest that undocumented immigrants are underrepresented in the ACS enumerations (e.g., Massey, 2010). If this was the case, some of the TB rates reported here are underestimates. On the other hand, the numerator data used in the present analysis (i.e., TB case counts) likely include undocumented immigrants, based on the studies that suggest that TB case finding efforts in the U.S. successfully reach undocumented migrants (Davidow et al., 2009).

Finding and treating latent TB infection among immigrants is one of the recommended strategies of current TB control efforts in the U.S. (Cain et al., 2008). The results of this study can inform efforts in California to selectively target Hispanic/Latino and Asian/Pacific Islander immigrant subgroups for screening and treatment, to help speed progress toward the elimination of TB. The presented methodology offers a novel, quantitative, computationally straightforward alternative to traditional incidence trend analyses of TB in the U.S. that may be useful in future assessments of the impact of population changes on the epidemiology of TB in the state that remains the nation's leading immigration destination, despite recent slowing trends in the growth of new immigration. Policy analyses of future TB control guidelines could benefit from this methodological intersection between epidemiology and demography.

Table 1. Decomposition of the contributions of changes in (a) age-specific TB incidence rates and population composition, (b) duration of residence-specific rates and composition, and (c) age- and duration of residence-specific rates and composition to the change in TB incidence in the **foreign-born** population in California, 2000-2010.

(a)	2000				2010				Contribution	
Age	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-4	122,265	26	21.3	1.4%	62,884	4	6.4	0.6%	0.15	0.11
5-14	534,711	39	7.3	6.0%	381,324	14	3.7	3.7%	0.17	0.13
15-24	1,298,929	250	19.2	14.5%	989,282	148	15.0	9.5%	0.52	0.85
25-44	4,144,384	789	19.0	46.3%	4,254,339	528	12.4	41.0%	2.89	0.84
45-64	2,046,192	633	30.9	22.9%	3,376,511	572	16.9	32.5%	3.88	-2.32
65+	802,040	531	66.2	9.0%	1,312,926	478	36.4	12.7%	3.22	-1.89
	8,948,521	2,268	25.3	100.0%	10,377,266	1,744	16.8	100.0%	10.83	-2.29
									126.8%	-26.8%

(b)	2000				2010				Contribution	
y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-2	849,240	623	73.4	9.5%	541,564	307	56.7	5.2%	1.23	2.78
3-5	882,505	249	28.2	9.9%	851,818	188	22.1	8.2%	0.56	0.42
6-10	1,579,893	377	23.9	17.7%	1,480,765	235	15.9	14.3%	1.28	0.67
11-15	1,600,228	289	18.1	17.9%	1,316,002	201	15.3	12.7%	0.43	0.87
16-20	1,295,101	297	22.9	14.5%	1,412,336	210	14.9	13.6%	1.13	0.16
21-25	999,415	180	18.0	11.2%	1,343,968	173	12.9	13.0%	0.62	-0.28
26-30	644,382	75	11.6	7.2%	1,105,884	170	15.4	10.7%	-0.33	-0.47
31-35	374,326	46	12.3	4.2%	867,236	94	10.8	8.4%	0.09	-0.48
36-40	281,224	55	19.6	3.1%	567,991	72	12.7	5.5%	0.30	-0.38
>40	442,207	77	17.4	4.9%	889,702	94	10.6	8.6%	0.46	-0.51
	8,948,521	2,268	25.3	100.0%	10,377,266	1,744	16.8	100.0%	5.75	2.79
									67.4%	32.6%

Notes on the tables: Years in the U.S. defined as the number of years between arrival in the U.S. and the report date of the TB diagnosis. Rates are expressed as TB cases per 100,000 population. “Comp.” is an abbreviation of “composition”. Positive values in the “contribution” columns indicate a positive contribution to the decline in TB incidence [e.g., in 1(a), specific rate changes contributed to a decline of 10.83 in the overall incidence rate].

1(c)		2000				2010				Contribution	
Age	y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-4	0-2	101,961	26	25.5	1.1%	47,717	4	8.4	0.5%	0.14	0.12
5-14	0-2	109,235	28	25.6	1.2%	56,758	9	15.9	0.5%	0.09	0.14
15-24	0-2	248,118	127	51.2	2.8%	128,815	76	59.0	1.2%	-0.16	0.84
25-44	0-2	295,501	219	74.1	3.3%	195,178	100	51.2	1.9%	0.59	0.89
45-64	0-2	65,970	134	203.1	0.7%	77,392	80	103.4	0.7%	0.74	-0.01
65+	0-2	28,455	89	312.8	0.3%	35,704	38	106.4	0.3%	0.68	-0.05
0-4	3-5	20,304	0	0.0	0.2%	15,167	0	0.0	0.1%	0.00	0.00
5-14	3-5	154,566	4	2.6	1.7%	110,587	1	0.9	1.1%	0.02	0.01
15-24	3-5	246,987	46	18.6	2.8%	197,601	40	20.2	1.9%	-0.04	0.17
25-44	3-5	352,145	113	32.1	3.9%	378,180	96	25.4	3.6%	0.25	0.08
45-64	3-5	80,350	53	66.0	0.9%	101,865	32	31.4	1.0%	0.32	-0.04
65+	3-5	28,153	33	117.2	0.3%	48,418	19	39.2	0.5%	0.30	-0.12
5-14	6-10	196,199	6	3.1	2.2%	165,771	4	2.4	1.6%	0.01	0.02
15-24	6-10	336,657	45	13.4	3.8%	252,325	18	7.1	2.4%	0.19	0.14
25-44	6-10	779,534	169	21.7	8.7%	780,515	115	14.7	7.5%	0.56	0.22
45-64	6-10	190,972	84	44.0	2.1%	220,038	58	26.4	2.1%	0.37	0.00
65+	6-10	76,531	73	95.4	0.9%	62,116	40	64.4	0.6%	0.23	0.21
5-14	11-15	74,711	1	1.3	0.8%	48,208	0	0.0	0.5%	0.01	0.00
15-24	11-15	263,385	11	4.2	2.9%	188,952	10	5.3	1.8%	-0.03	0.05
25-44	11-15	960,721	125	13.0	10.7%	730,946	73	10.0	7.0%	0.27	0.42
45-64	11-15	231,198	83	35.9	2.6%	272,427	71	26.1	2.6%	0.26	-0.01
65+	11-15	70,213	69	98.3	0.8%	75,469	47	62.3	0.7%	0.27	0.05
15-24	16-20	154,179	18	11.7	1.7%	159,337	4	2.5	1.5%	0.15	0.01
25-44	16-20	777,338	90	11.6	8.7%	764,603	67	8.8	7.4%	0.23	0.13
45-64	16-20	288,244	108	37.5	3.2%	377,954	78	20.6	3.6%	0.58	-0.12
65+	16-20	75,340	81	107.5	0.8%	110,442	61	55.2	1.1%	0.50	-0.18
15-24	21-25	49,603	3	6.0	0.6%	62,252	0	0.0	0.6%	0.03	0.00
25-44	21-25	535,985	55	10.3	6.0%	656,249	49	7.5	6.3%	0.17	-0.03
45-64	21-25	336,880	67	19.9	3.8%	518,073	60	11.6	5.0%	0.36	-0.19
65+	21-25	76,947	55	71.5	0.9%	107,394	64	59.6	1.0%	0.11	-0.11
25-44	26-30	256,296	14	5.5	2.9%	390,087	20	5.1	3.8%	0.01	-0.05
45-64	26-30	329,612	30	9.1	3.7%	587,084	80	13.6	5.7%	-0.21	-0.22
65+	26-30	58,474	31	53.0	0.7%	128,713	70	54.4	1.2%	-0.01	-0.32
25-44	31-35	108,264	2	1.8	1.2%	229,002	4	1.7	2.2%	0.00	-0.02
45-64	31-35	211,592	24	11.3	2.4%	508,521	51	10.0	4.9%	0.05	-0.27
65+	31-35	54,470	20	36.7	0.6%	129,713	39	30.1	1.2%	0.06	-0.21
	…										
		8,948,521	2,268	25.3	100%	10,377,266	1,744	16.8	100%	7.88	0.66
										92.2%	7.8%

Note: Data for persons with >35 years' duration of residence redacted, to fit the table on a single page.

Table 2. Decomposition of the contributions of changes in (a) age-specific TB incidence rates and population composition, (b) duration of residence-specific rates and composition, and (c) age- and duration of residence-specific rates and composition to the change in TB incidence in the **foreign-born Hispanic/Latino** population in California, 2000-2010.

(a)	2000				2010				Contribution	
Age	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp	Rate	Comp.
0-4	85,143	18	21.1	1.7%	30,612	1	3.3	0.5%	0.20	0.14
5-14	343,611	19	5.5	6.9%	217,789	3	1.4	3.9%	0.22	0.10
15-24	864,389	139	16.1	17.4%	599,496	58	9.7	10.7%	0.90	0.85
25-44	2,513,207	350	13.9	50.5%	2,583,281	237	9.2	46.3%	2.30	0.49
45-64	917,281	216	23.5	18.4%	1,671,624	192	11.5	29.9%	2.92	-2.02
65+	253,348	128	50.5	5.1%	479,806	134	27.9	8.6%	1.55	-1.37
	4,976,979	870	17.5	100.0%	5,582,608	625	11.2	100.0%	8.09	-1.80
									128.7%	-28.7%

(b)	2000				2010				Contribution	
y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp	Rate	Comp.
0-2	503,136	252	50.1	10.1%	198,564	79	39.8	3.6%	0.70	2.94
3-5	493,378	94	19.1	9.9%	437,578	73	16.7	7.8%	0.21	0.37
6-10	900,328	130	14.4	18.1%	862,857	80	9.3	15.5%	0.87	0.31
11-15	998,322	109	10.9	20.1%	736,162	63	8.6	13.2%	0.39	0.67
16-20	669,493	85	12.7	13.5%	772,642	75	9.7	13.8%	0.41	-0.04
21-25	519,268	69	13.3	10.4%	812,036	67	8.3	14.5%	0.63	-0.44
26-30	386,842	38	9.8	7.8%	563,608	54	9.6	10.1%	0.02	-0.23
31-35	201,991	23	11.4	4.1%	439,840	44	10.0	7.9%	0.08	-0.41
36-40	144,504	32	22.1	2.9%	337,897	32	9.5	6.1%	0.57	-0.50
>40	159,717	38	23.8	3.2%	421,424	58	13.8	7.5%	0.54	-0.81
	4,976,979	870	17.48	100.0%	5,582,608	625	11.2	100.0%	4.42	1.86
									70.4%	29.6%

2(c)		2000				2010				Contribution	
Age	y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-4	0-2	74,094	18	24.3	1.5%	22,008	1	4.5	0.4%	0.19	0.16
5-14	0-2	65,593	13	19.8	1.3%	24,146	1	4.1	0.4%	0.14	0.11
15-24	0-2	184,016	73	39.7	3.7%	51,367	21	40.9	0.9%	-0.03	1.12
25-44	0-2	139,602	80	57.3	2.8%	67,226	33	49.1	1.2%	0.16	0.85
45-64	0-2	29,108	34	116.8	0.6%	23,083	11	47.7	0.4%	0.35	0.14
65+	0-2	10,723	34	317.1	0.2%	10,734	12	111.8	0.2%	0.42	0.05
0-4	3-5	11,049	0	0.0	0.2%	8,604	0	0.0	0.2%	0.00	0.00
5-14	3-5	97,928	1	1.0	2.0%	60,067	0	0.0	1.1%	0.02	0.00
15-24	3-5	177,669	27	15.2	3.6%	126,899	22	17.3	2.3%	-0.06	0.21
25-44	3-5	174,820	43	24.6	3.5%	191,210	40	20.9	3.4%	0.13	0.02
45-64	3-5	23,065	18	78.0	0.5%	32,642	7	21.4	0.6%	0.30	-0.06
65+	3-5	8,847	5	56.5	0.2%	18,156	4	22.0	0.3%	0.09	-0.06
5-14	6-10	127,416	4	3.1	2.6%	104,705	2	1.9	1.9%	0.03	0.02
15-24	6-10	228,802	21	9.2	4.6%	164,141	8	4.9	2.9%	0.16	0.12
25-44	6-10	471,747	73	15.5	9.5%	487,182	50	10.3	8.7%	0.47	0.10
45-64	6-10	61,388	25	40.7	1.2%	84,117	9	10.7	1.5%	0.41	-0.07
65+	6-10	10,975	7	63.8	0.2%	22,712	11	48.4	0.4%	0.05	-0.10
5-14	11-15	52,674	1	1.9	1.1%	28,871	0	0.0	0.5%	0.01	0.01
15-24	11-15	168,425	4	2.4	3.4%	115,473	4	3.5	2.1%	-0.03	0.04
25-44	11-15	666,669	69	10.3	13.4%	466,628	32	6.9	8.4%	0.38	0.43
45-64	11-15	93,762	26	27.7	1.9%	104,377	11	10.5	1.9%	0.32	0.00
65+	11-15	16,792	9	53.6	0.3%	20,813	16	76.9	0.4%	-0.08	-0.02
15-24	16-20	77,382	12	15.5	1.6%	98,009	3	3.1	1.8%	0.21	-0.02
25-44	16-20	469,399	36	7.7	9.4%	497,192	40	8.0	8.9%	-0.03	0.04
45-64	16-20	105,735	28	26.5	2.1%	156,722	26	16.6	2.8%	0.24	-0.15
65+	16-20	16,977	9	53.0	0.3%	20,719	6	29.0	0.4%	0.09	-0.01
15-24	21-25	28,095	2	7.1	0.6%	43,607	0	0.0	0.8%	0.05	-0.01
25-44	21-25	327,751	36	11.0	6.6%	462,131	29	6.3	8.3%	0.35	-0.15
45-64	21-25	142,876	23	16.1	2.9%	276,522	28	10.1	5.0%	0.23	-0.27
65+	21-25	20,546	8	38.9	0.4%	29,776	10	33.6	0.5%	0.03	-0.04
25-44	26-30	167,239	10	6.0	3.4%	223,343	8	3.6	4.0%	0.09	-0.03
45-64	26-30	194,544	18	9.3	3.9%	302,254	33	10.9	5.4%	-0.08	-0.15
65+	26-30	25,059	10	39.9	0.5%	38,011	13	34.2	0.7%	0.03	-0.07
25-44	31-35	57,792	2	3.5	1.2%	115,427	1	0.9	2.1%	0.04	-0.02
45-64	31-35	118,350	11	9.3	2.4%	281,377	28	10.0	5.0%	-0.02	-0.26
65+	31-35	25,849	10	38.7	0.5%	43,036	15	34.9	0.8%	0.02	-0.09
	…										
		4,976,979	870	17.5	100.0%	5,582,608	625	11.2	100.0%	5.78	0.50
										92.0%	8.0%

Note: Data for persons with >35 years' duration of residence redacted, to fit the table on a single page.

Table 3. Decomposition of the contributions of changes in (a) age-specific TB incidence rates and population composition, (b) duration of residence-specific rates and composition, and (c) age- and duration of residence-specific rates and composition to the change in TB incidence in the **foreign-born Asian/Pacific Islander** population in California, 2000-2010.

(a)	2000				2010				Contribution	
Age	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-4	23,702	7	29.5	0.8%	23,478	1	4.3	0.7%	0.19	0.03
5-14	128,510	10	7.8	4.5%	115,369	8	6.9	3.2%	0.03	0.10
15-24	334,392	89	26.6	11.8%	276,354	75	27.1	7.8%	-0.05	1.08
25-44	1,213,179	394	32.5	42.8%	1,284,220	257	20.0	36.1%	4.92	1.77
45-64	804,992	389	48.3	28.4%	1,294,057	360	27.8	36.4%	6.64	-3.03
65+	328,532	359	109.3	11.6%	565,289	313	55.4	15.9%	7.41	-3.53
	2,833,307	1,248	44.0	100.0%	3,558,767	1,014	28.5	100.0%	19.14	-3.58
									123.0%	-23.0%

(b)	2000				2010				Contribution	
y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-2	237,098	312	131.6	8.4%	242,538	193	79.6	6.8%	3.9	1.6
3-5	284,518	135	47.4	10.0%	321,582	99	30.8	9.0%	1.6	0.4
6-10	508,182	234	46.0	17.9%	474,709	139	29.3	13.3%	2.6	1.7
11-15	474,883	168	35.4	16.8%	422,548	121	28.6	11.9%	1.0	1.6
16-20	517,774	196	37.9	18.3%	491,048	131	26.7	13.8%	1.8	1.4
21-25	386,162	102	26.4	13.6%	436,228	103	23.6	12.3%	0.4	0.3
26-30	186,427	35	18.8	6.6%	453,862	112	24.7	12.8%	-0.6	-1.3
31-35	95,533	21	22.0	3.4%	340,060	49	14.4	9.6%	0.5	-1.1
36-40	57,680	15	26.0	2.0%	171,213	37	21.6	4.8%	0.2	-0.7
>40	85,050	30	35.3	3.0%	204,979	30	14.6	5.8%	0.9	-0.7
	2,833,307	1,248	44.0	100.0%	3,558,767	1,014	28.5	100.0%	12.3	3.3
									78.8%	21.2%

3(c)		2000				2010				Contribution	
Age	y in U.S.	Population	Cases	Rate	Comp.	Population	Cases	Rate	Comp.	Rate	Comp.
0-4	0-2	18,168	7	38.5	0.6%	18,237	1	5.5	0.5%	0.19	0.03
5-14	0-2	28,245	6	21.2	1.0%	20,599	6	29.1	0.6%	-0.06	0.11
15-24	0-2	44,171	41	92.8	1.6%	53,409	46	86.1	1.5%	0.10	0.05
25-44	0-2	106,509	120	112.7	3.8%	87,503	53	60.6	2.5%	1.62	1.13
45-64	0-2	26,680	95	356.1	0.9%	43,338	64	147.7	1.2%	2.25	-0.70
65+	0-2	13,325	43	322.7	0.5%	19,452	23	118.2	0.5%	1.04	-0.17
0-4	3-5	5,534	0	0.0	0.2%	5,241	0	0.0	0.1%	0.00	0.00
5-14	3-5	40,470	3	7.4	1.4%	38,924	1	2.6	1.1%	0.06	0.02
15-24	3-5	53,747	15	27.9	1.9%	53,518	13	24.3	1.5%	0.06	0.10
25-44	3-5	123,727	57	46.1	4.4%	144,679	48	33.2	4.1%	0.54	0.12
45-64	3-5	45,858	34	74.1	1.6%	55,007	23	41.8	1.5%	0.51	0.04
65+	3-5	15,182	26	171.3	0.5%	24,213	14	57.8	0.7%	0.69	-0.17
5-14	6-10	47,042	1	2.1	1.7%	44,183	1	2.3	1.2%	0.00	0.01
15-24	6-10	82,403	22	26.7	2.9%	70,193	9	12.8	2.0%	0.34	0.18
25-44	6-10	228,255	91	39.9	8.1%	222,444	60	27.0	6.3%	0.92	0.60
45-64	6-10	99,323	57	57.4	3.5%	106,504	44	41.3	3.0%	0.52	0.25
65+	6-10	51,159	63	123.1	1.8%	31,385	25	79.7	0.9%	0.58	0.94
5-14	11-15	12,753	0	0.0	0.5%	11,663	0	0.0	0.3%	0.00	0.00
15-24	11-15	75,519	5	6.6	2.7%	47,855	6	12.5	1.3%	-0.12	0.13
25-44	11-15	234,657	53	22.6	8.3%	196,679	34	17.3	5.5%	0.37	0.55
45-64	11-15	108,746	52	47.8	3.8%	123,846	53	42.8	3.5%	0.18	0.16
65+	11-15	43,208	58	134.2	1.5%	42,505	28	65.9	1.2%	0.93	0.33
15-24	16-20	61,507	5	8.1	2.2%	39,371	1	2.5	1.1%	0.09	0.06
25-44	16-20	252,674	51	20.2	8.9%	207,613	27	13.0	5.8%	0.53	0.51
45-64	16-20	153,173	74	48.3	5.4%	169,886	51	30.0	4.8%	0.93	0.25
65+	16-20	50,420	66	130.9	1.8%	74,178	52	70.1	2.1%	1.17	-0.31
15-24	21-25	17,045	1	5.9	0.6%	12,008	0	0.0	0.3%	0.03	0.01
25-44	21-25	167,465	19	11.3	5.9%	160,022	20	12.5	4.5%	-0.06	0.17
45-64	21-25	154,586	39	25.2	5.5%	197,695	35	17.7	5.6%	0.41	-0.02
65+	21-25	47,066	43	91.4	1.7%	66,503	48	72.2	1.9%	0.34	-0.17
25-44	26-30	59,620	3	5.0	2.1%	141,096	12	8.5	4.0%	-0.11	-0.13
45-64	26-30	101,615	12	11.8	3.6%	237,037	45	19.0	6.7%	-0.37	-0.47
65+	26-30	25,192	20	79.4	0.9%	75,729	55	72.6	2.1%	0.10	-0.94
25-44	31-35	25,215	0	0.0	0.9%	88,988	3	3.4	2.5%	-0.06	-0.03
45-64	31-35	54,358	12	22.1	1.9%	183,729	23	12.5	5.2%	0.34	-0.56
65+	31-35	15,960	9	56.4	0.6%	67,343	23	34.2	1.9%	0.27	-0.60
	…										
		2,833,307	1,248	44.0	100.0%	3,558,767	1,014	28.5	100.0%	15.42	0.13
										99.2%	0.8%

Note: Data for persons with >35 years' duration of residence redacted, to fit the table on a single page.

Paper 2

Immigration entry cohort effects on tuberculosis incidence in the foreign-born population of California, 2000-2011

An application of the median polish method of cohort analysis

Abstract

Background TB incidence rates are declining in California but remain elevated in the foreign-born population - nearly 10 times higher than among the U.S.-born. Forces driving the decline among immigrants operate in three areas: declining TB morbidity in sending countries, immigrant selectivity, and effectiveness of TB control measures in the receiving country. California has experienced substantial and selective changes in immigration in 1990s and 2000s. Recentness of arrival is known to be associated with a higher risk of TB disease, but the relationships between immigration arrival cohorts and TB incidence have not been investigated. The objective of this study was to identify immigration cohort effects on TB rates in the foreign-born, and to determine the magnitude of these effects.

Methods Annual estimates of the foreign-born population from 2000 to 2011 drawn from the U.S. Census Bureau American Community Survey, and data on TB cases reported to the California TB registry were used in a cohort analysis. An immigration cohort effect was defined as a partial multiplicative interaction between duration of residence (from U.S. arrival to TB diagnosis) and period (year of TB case report). Its presence was estimated by applying a median polish to duration of residence-specific TB rates over the period 2000 to 2010 to generate residual values. The magnitude and significance of the effect was estimated by linear regression of the residuals and calculating rate ratios compared to a reference cohort.

Results The analysis revealed immigration cohort effects that influenced the TB incidence in California during the period from 2000 to 2010. The trend of the effects changed markedly over time. During most of the 1990's, the cohort effect declined (R^2=0.97). Its peak in 1992-93 was significantly higher than the reference cohort [rate ratio 1.18 (95% CI 1.10 – 1.26)], and the 1998-99 cohort was lower [0.91 (0.83 – 0.98)]. Through the first seven years of the first decade of the 2000's, the cohort effect increased (R^2=0.99). The 2004-05 and 2006-07 immigration cohorts showed significant cohort effects [1.10 (1.04 – 1.16) and 1.16 (1.09 – 1.22), respectively]. A sharp decline in the cohort effect after 2007 appears to coincide with a slowing immigration near the end of the decade attributed to unfavorable economic conditions.

Conclusions Changes in the pattern of immigration to California over the last two decades have had lasting effects on the decline of TB incidence in California. Periods of slowing or reverse of the decline in TB incidence among the foreign-born are likely due to cohort effects. Fluctuations in immigration cohort size and composition, and declines in TB morbidity in sending countries are likely contributors to the observed cohort effects. Identifying cohorts with elevated risk of TB can help develop and test hypotheses on the epidemiologic reasons for the observed effects, and can provide an evidence base for selecting demographic subgroup candidates for prioritizing TB screening.

Background

Immigration has indelibly shaped the epidemiology of tuberculosis (TB) in California. In 2011, 77 percent of the 2,325 cases reported in the state were in foreign-born persons (Westenhouse et al., 2012). In the U.S., this proportion was 62 percent (CDC, 2013). Between 2000 and 2011, the TB morbidity among the foreign-born in California has slowly declined but shows sign of having plateaued (Figure 1). The incidence rate of 17.6 cases per 100,000 among the foreign-born is many times higher than the rate of 1.9 observed among the native-born population in the state (Westenhouse et al., 2012) and both rates are still far from the stated target of the elimination of TB- 1 case per one million (Stop TB USA, 2010). The influence of immigration changes on the declining but stalling trend in the incidence of TB among the foreign-born has not previously been reported.

Changes in immigration can occur over a variety of dimensions. First, the volume of immigration can undergo changes, and the origins of immigration streams can shift from one sending country or regions another, based on changing immigration policies, socioeconomic, and political conditions. Changes can also be characterized by differential migration by age. For example, economic or skilled migration is usually concentrated in the young and middle age adult years of prime working age. In contrast, migration for family unification reasons also draws from older adults as well as children, while refugee migration affects migrants across the age spectrum. (Smith & Edmonston, 1997; Preston et al., 2001; Fairchild, 2004; Bollinger, 2008). The impact of migration change has been a topic of extensive research in the social sciences. Changes in immigration flows and their influences on population aging (Preston et al., 1989) and economic and fiscal outcomes (Smith & Edmonston, 1997) are just two active areas of inquiry. However, the public health literature has had very little to say about the impacts of population changes on a disease that in the U.S. is so strongly influenced by immigration factors.

The relationships between immigration changes and TB incidence in the U.S. are not well characterized. Most studies on the "impact" of immigration on TB epidemiology are limited to analyses of the proportion of the total TB burden that affects the immigrant population, and do not investigate relationships between *changes* in immigration and TB incidence (e.g., Svensson et al., 2011). A few additional studies did attempt to quantify the actual impact of immigration on TB epidemiology, but their scopes were limited. In one study, age at immigration to the U.S. and time between arrival and TB diagnosis were examined jointly for TB cases in the U.S. between 2001 and 2006 in a descriptive epidemiologic analysis of TB among the foreign-born (Cain et al., 2008). Investigation of trends in the proportions of the TB burden in the immigrant population and trends of rates are also common in the literature. These studies were often cross-sectional analyses of cases diagnosed in a given time period (e.g., the year in which the disease was reported). However, because cross- sectional investigations of cases identified in a particular period comprise numerous cohorts (e.g., birth cohorts of persons born at around the same time), important changes in the contributions to the case loads in successive cohorts may not be apparent in these types of analyses (Tarone & Chu, 1996).

In epidemiology, the term "cohort effect" (or "generation effect") has traditionally considered birth cohorts (i.e., groups of persons born at around the same time), and defined as a

> *Variation in health status that arises from the different causal factors to which each birth cohort in the population is exposed as the environment and society change. Each consecutive birth cohort is exposed to a unique environment that coincides with its life span.* (Porta, 2008).

Cohort effects have been demonstrated for a wide range of diseases and health conditions such as tuberculosis (Frost, 1939; Winston & Navin, 2010), lung cancer, prostate cancer, Parkinson's disease (Selvin & Stacks, 1979), peptic ulcers (Westbrook et al., 1993), substance abuse (O'Malley et al., 1984) and autism (Keyes et al., 2012). Cohort analysis is not entirely new to tuberculosis research. Arguably one of the most famous cohort studies in the history of infectious disease epidemiology was Frost's investigation of the decrease in age-specific TB mortality rates in Massachusetts in the pre-antibiotic era of the 1930s (Frost, 1939). In this landmark analysis [informed by even earlier research in Norway (Blomberg et al., 2002)], Frost cautions against relying on period estimates to analyze substantial influences such as differential TB exposure by birth cohort, which manifest themselves later in life and may be masked by a period perspective (i.e., the year in which the patient died of TB). More recently, the authors of a study of birth cohort effects on the prevalence of LTBI in the U.S. in 1972 compared to in 2000 restricted cohorts to those born no later than 1946, and did not specifically address nativity or immigration factors (Winston & Navin, 2010). Cohort effects and differences in TB incidence in cohorts of immigrants (i.e., immigrants arriving at approximately the same time) have gone largely uninvestigated. One Canadian study did describe differences in TB incidence in two broad groups of arrival cohorts (pre-1986 and 1986-2002) but this analysis did not address more recent changes in immigration patterns, and was restricted to Canada, yielding findings likely not generalizable to California or the United States (Langlois-Klassen et al., 2011).

Recent immigration data in the U.S. suggest that the opening decade of the new century offers a timely opportunity to study the impact of immigration on the epidemiology of TB. Of the 40 million immigrants living in the country in 2010, nearly 14 million arrived in or after 2000, making it "the highest decade of immigration in American history" (Camarota, 2011). However, a subtle yet important subtext of this enormous volume of immigration to the U.S. is a recent trend beginning in the late 1990's in which increasing proportions of new immigrants are choosing to settle in parts of the U.S. other than the traditional immigrant magnets of California, New York, Illinois, Texas, Florida and New Jersey. The age structure of new immigrant arrivers in California has also changed in recent years. Whereas in the 1980s, California's working-age immigrant population (age 23 to 64) grew 9.5 percent per year, this growth slowed to 4.4 percent per year in the 1990s and further decelerated to 2 percent per year in the 2000s (Bohn, 2009). Demographic shifts in the immigrant population in California are also occurring along lines of regions of origin and race and ethnicity. Compared to the 1990s, proportionally fewer newly arriving Latino immigrants chose to settle in California in the first half of the opening decade of the 2000s (Bohn, 2009).

Current public health guidelines in the U.S. aimed at reducing TB in immigrant communities recommend using information on the duration of time since immigration as a way to assess the risk of TB disease and to guide decisions about targeted testing efforts to identify and treat latent TB infection (CDC, 2005b). The objective of this study is to identify the presence of any cohort effects of immigration arrival cohorts that have contributed to significantly higher (or lower) TB incidence rates in California's foreign-born population during the surveillance period 2000 to 2010, and to quantify the magnitude of these effects. The study explored the possibility of differential cohort effects in immigrants entering the U.S. in the 1990s compared to those entering in the first decade of the 2000s.

Methods

Data sources and measures

Individual-level demographic characteristics of cases of active TB disease reported in California between the years 2000 and 2011 were queried from a de-identified electronic database of the Reports of Verified Case of Tuberculosis (RVCT, the standard TB surveillance tool in the U.S.) in the TB case registry of the California Department of Public Health. Annual population estimates in California were queried from the U.S. Census Bureau American Community Survey (ACS) 1-year estimates for the years 2000 to 2011. I accessed the ACS data on the Integrated Public Use Microdata Series (IPUMS) online database of the Minnesota Population Center, University of Minnesota (Ruggles et al., 2010). The analysis was limited to foreign-born persons. For TB case patients, the duration of residence in the U.S. at the time of the TB case report was calculated by subtracting the month and year of self-reported arrival in the U.S. from the month and year of the TB case report. For the California population, the duration of residence was calculated using the IPUMS variable "yrsusa1"- which ascertained "when did this person come to live in the United States?" These values were used in reference to each year of analysis and were categorized into these groups: in the U.S. for 0 to 1 year, 2 to 3, 4 to 5, 6 to 7, 8 to 9, 10 to 11, 12 to 13, 14 to 15, 16 to 17, 18 to 19, and 20 or more years. Using these numerators and denominators, I calculated duration of residence-specific TB incidence rates per 100,000 population. Periods of TB case reports were collapsed into two-year intervals (e.g., 2000-2001, 2002-2003, etc.) to match the length of the two-year duration of residence categories. This was done to facilitate the tracing of immigration cohorts (also known as entry cohorts) over time.

Cohort analysis

I carried out the immigration cohort analysis according to a recently published three-phase methodology for estimating cohort effects in contingency table data (Keyes & Li, 2010). The three phases outlined by the authors were 1) graphical inspection of the data arranged by period, 2) a median polish procedure to remove the additive components of duration of residence and period, and 3) linear regression of residuals resulting from the median polish to quantify the magnitude of the cohort effects. Duration of residence-specific TB incidence rates over time were graphed and visually examined for evidence of possible immigration entry cohort effects. If rates for different duration of residence groups changed in parallel over the time period (2000-2011), this would be suggestive of period effects, such as improvements in case finding. If rate trends for certain duration of residence groups diverge from the trend seen in other groups, this would indicate the possibility of an immigration cohort effect. The application of the median polish technique to cohort analysis was developed by Selvin (Selvin, 1996). The procedure involves computing a residual value for each cell in a contingency table by removing from each observation the additive influence of the row variable (e.g., duration of residence) and the additive influence of the column variable (e.g., TB case report year). Adapting the methodology proposed by Keyes & Li , I log-transformed the rates prior to median polish, which allowed for the cohort effect to be conceptualized as a partial multiplicative interaction between duration of residence and period (TB case report year). The median polish was done using standard spreadsheet software, following a standard protocol (Selvin, 1996). I then calculated modeled incidence rate data that would have been observed in the absence of cohort effects. I did this by exponentiating the negative value of the residual and multiplying by the observed group-specific incidence rate. The last step of the median polish step was to plot the resulting residual values against immigration entry cohort categories. This step necessitated rearranging the contingency table to show rates by immigration entry cohort, rather than by duration of residence. A distribution of the residuals around zero was interpreted as an absence of a cohort effect, and a deviation from zero indicated the presence of a cohort effect (Keyes & Li, 2010). To quantify the cohort effect, I regressed the residuals on the immigration cohort category using linear regression. The regression was segmented into two pieces (1990s, 2000s), to represent the differential immigration growth that has marked the decade of the 1990s compared to the first decade of the 21st. The r-square values for both segments of the linear regression analysis were calculated to measure the goodness of fit. Exponentiation of the residual coefficients for each immigration cohort generated the estimated rates of the cohort effect. Rate ratios and 95% confidence intervals were then calculated based on a reference cohort.

Results

Between 2000 and 2011, the number of TB cases in foreign-born persons declined from 2,268 (25.3 per 100,000 population) to 1,787 (17.6 per 100,000) (Figure 1). The number of cases declined by 21.6%, while the incidence rate declined by 32.4%. The cross-tabulation of duration of residence-specific TB incidence rates by case report year is presented in contingency Table 1. Corroborating what has commonly been reported in the literature on TB in immigrants in the U.S. (e.g., Cain et al., 2008), the incidence of TB disease is extremely high in the immediate post- immigration entry period, and then drops off rapidly. The high rates immediately post-arrival were observed at each time period, but the magnitude of initial rate tended to decline over calendar time, bar the peak value observed in 2002-2003. A key feature of these tabulated data is that successive incidence rates of immigration cohorts can be traced diagonally. To illustrate this, rates in the cohort of immigrants entering the U.S. in 2000-2001 are shaded in gray in Table 1.

The stratum-specific rate data in Table 1 are graphically displayed in Figure 2a. TB incidence rates of the most recent immigrants who entered the U.S. 0-1 year prior to TB diagnosis peaked in 2002-2003 and then decreased dramatically. The decreasing trend over calendar time (period) is not parallel with the trends of the other groups, which suggests the possible presence of a cohort effect. The non-parallel nature of the trends is not as apparent among the immigrants with longer durations of residence, but close inspection of the graph does reveal some additional areas of divergent trends indicative of cohort effects. For example, the rate declines in the 2-3 and 4-5 year groups are not as steep as in the 6-7 and 8-9 groups, at least in the first half of the decade. Another illustrative comparison is between the 10-11 and the 14-15 groups. The former is characterized by higher incidence rates at the beginning of the time period, but the trends cross over in mid-decade when the rates in the latter group become higher.

Table 2 summarizes the residual values that resulted from the median polish procedure on the log transformed group-specific TB incidence rates. Three iterations of the median polish were necessary in order to get the median row and column values to consistently result in "0" values. Exponentiation and multiplication by the observed incidence rates resulted in the modeled TB incidence data which were expected in the absence of cohort effects, summarized in Table 3. These rates were then graphically plotted, to highlight the time trends of the modeled data (Figure 2b).

Plotting the average residuals for each immigration entry cohort category yielded the plot graph shown in Figure 3. This figure shows systematic deviation of the residuals from zero, indicating the presence of positive cohort effects in the early 1990s and early 2000s (i.e., higher rates than expected, given the log-additive effects of duration of residence and calendar time). The r-square for the linear regression model for the years 1992-1998 was 0.97. For the years 2000-2007, the r-square value was 0.998. Hence, multiplicative cohort effects during the modeled time periods explain nearly all of the variance in the duration of residence-period interaction, with virtually no variance attributable to error (Keyes & Li, 2010). The statistical quantification of these observed immigration entry cohort effects is summarized in Table 4.
In the 1990s, a modest but statistically significant positive cohort effect on the TB incidence rate among immigrants in California was found for the entry cohort 1992-1993, and a significant negative cohort effect was found for the entry cohort 1998-1999. In the first decade of the 2000s, statistically significant positive cohort effects were identified in the entry cohorts 2004-2005, and 2006-2007.

Discussion

To my knowledge, this report is the first systematic, quantitative assessment of immigration entry cohort effects on the incidence rate of tuberculosis in the foreign-born population in the U.S. This was achieved by the novel adaptation of the median polish method of age-period-cohort analysis, replacing the age term with the duration of residence of immigrants- the "age", so to speak, of the immigration experience. The main findings of this investigation were that modest but statistically significant, positive immigration entry cohort effects were found for immigrants arriving in 1992-1993, 2004-2005, and 2006-2007. These cohort effects represented subtle but measurable increases in TB incidence during the period 2000-2011, which were masked by the overall TB incidence trend among the foreign-born- a declining trend that has slowed (Figure 1; Cain et al., 2008). These results provide evidence that some immigration entry cohort effects add subtle upward pressures on the otherwise declining TB incidence trend among the foreign-born, and that this could partly explain the slowing of the declining trend.
The finding that an immigration entry cohort in the early 1990s exhibited significant cohort effects on TB incidence well into the first decade of the 2000s is a stark reminder of the long-lasting impacts of immigration cohorts on the epidemiology of TB in an immigration-rich, low TB burden setting such as the U.S.

The cohort effects described in this analysis provide new insights into the dynamic and lasting influences of waves of immigration on the TB incidence trend in California. The dynamism of changing cohort effects was reflected by a pattern of decreasing cohort effects throughout most of the 1990s (even yielding statistically significant negative effects for the

1998-1999 entry cohort), followed by increasing effects at the beginning of the 2000s that continued the climb well into the decade. While the objective of this study was to identify the presence of and to quantify cohort effects rather than adjudicate on the *causes* of these effects, this observation of shifting directions is evidence of temporal changes in the composition of the immigrant arriver population along lines of TB disease risk. One tantalizing hypothesis that these data suggest is that immigration policies have sufficiently altered the composition of immigrant streams such that population-level excess TB risk noticeably ebbs and flows over the course of decades. For example, the federal Immigration Act of 1990 increased legal immigration ceilings, favored more employment-based immigration, and initiated a diversity program that drew from previously underrepresented sending countries (e.g., Ireland) (Smith & Edmonston, 1997). Employment-based immigrants are predominantly in executive, administrative and managerial occupations (Smith & Edmonston, 1997) reflecting higher socioeconomic position. They also tend to have better health measures than persons in other immigration admission classifications (Jasso et al., 2004), so it is reasonably follows that their TB risk as a group would also be relatively low compared to fellow nationals from the sending country with lower socioeconomic status- even if that country has a high TB burden.

The recognition of temporal trends in tuberculosis epidemiology directly impacts the funding and prioritization of national and state-level control efforts. The swift resurgence of TB in the late 1980s led to the rapid escalation of categorical TB funding. More recently, the increasing preponderance of foreign-born case patients has led to recommendations to focus targeted testing efforts at specific high-risk subpopulations such as recently arrived immigrants from high-tuberculosis burden sending countries.

The traditional approach in surveillance and epidemiology to measure TB rates by the calendar time of TB notifications (i.e., period analysis) is useful for some applications such as descriptive studies of the magnitude or trends of TB in the population, and assessments of resource needs to deal with the size of the TB burden. However, such cross- sectional investigations do not account for the important detail that persons who became ill with TB in a particular year immigrated to the U.S. at different times, and differential morbidity contributions in successive entry cohorts may not be apparent in these types of period analyses. The topic of cohort effects related to immigration has not been seriously considered in the TB literature, and only occasionally brought up as a possibility (e.g., Creatore et al., 2005). This report is the first to report such immigration entry cohort effects.

This study had several limitations. First, as with any analysis of two-factor contingency table data, the estimates of cohort effects incorporated neither the impact of possible overlaps of adjacent cohorts, nor the precision of the underlying TB incidence data (Keyes & Li, 2010). The cohort intervals in the present study were defined according to convention (Keyes & Li, 2010) such that the lowest duration of residence value was subtracted from the earliest and the latest case report year in the interval. Thus, immigrants in the country for 4 to 5 years during the TB case count period 2010-2011 were assigned to the immigration entry cohort “2006 to 2007”. This introduces some misclassification, because some of the patients in this category (i.e., those who entered 5 years ago) arrived in the U.S. between 2005 and 2006. Although this possibility of misclassification warrants some caution in the interpretation of the magnitude of the cohort effects presented here, the primary purpose of this cohort analysis was to identify the presence of effects and estimate the strengths of the effects relative to reference groups, and the pattern of relative strengths is unlikely to have been affected, since it was likely that misclassification was distributed evenly and not differentially. The issue of the precision of the underlying incidence data was most likely allayed by the large population sample sized represented in the study. The smallest cell in the analysis contained more than 300,000 persons, therefore the rate calculations were likely to have yielded reasonably precise estimates, and uncertainty around these estimates was unlikely to have significantly changed the cohort effect results. In addition to these general limitations inherent to this type of age-period-cohort analysis, the broad “foreign-born” perspective taken in this particular analysis may have hidden important variations in cohort effects by race/ethnicity and/or country of origin. Future analyses using this methodology might consider stratifying the population data to determine if cohort effects vary across race or sending country groups.

Despite the limitations of this study, it is the first to offer evidence of distinct and long-lasting impacts of immigration pattern changes on TB incidence in the U.S. from a previously unexplored perspective, and has the potential to add value to current and future epidemiologic analyses of TB among the foreign-born in the U.S. Published studies predicting future TB morbidity trends- for the purposes of setting priorities among interventions competing for the same resources as well as projecting future public health expenditures- have generally ignored immigration patterns despite the recognition of their importance (e.g., Woodruff et al., 2013). The findings of the present study and those of further investigations it hopes to stimulate and inform could yield inputs that allow for more accurate and nuanced mathematical modeling of future TB incidence trends among immigrants. Furthermore, the attention that the present findings call to cohort effects will hopefully motivate mathematical modelers to go beyond relying on current trends in immigration. Immigration is a dynamic process that can be punctuated by major surges in immigration along the dimensions of volume, composition and country of origin (Smith & Edmonston, 1997). An unforeseen change in immigration from one of more new countries of high TB incidence could significantly impact the short- and long-term epidemiologic picture of TB among the foreign-born in California, and this study provides a framework to analyze entry cohort effects that will hopefully inform efforts by the California Department of Health and the California Tuberculosis Controllers Association to lead statewide efforts to eliminate TB in the state in the near future.

Figure 1. Annual magnitude of new TB cases in foreign-born persons reported in California, 2000 – 2011.

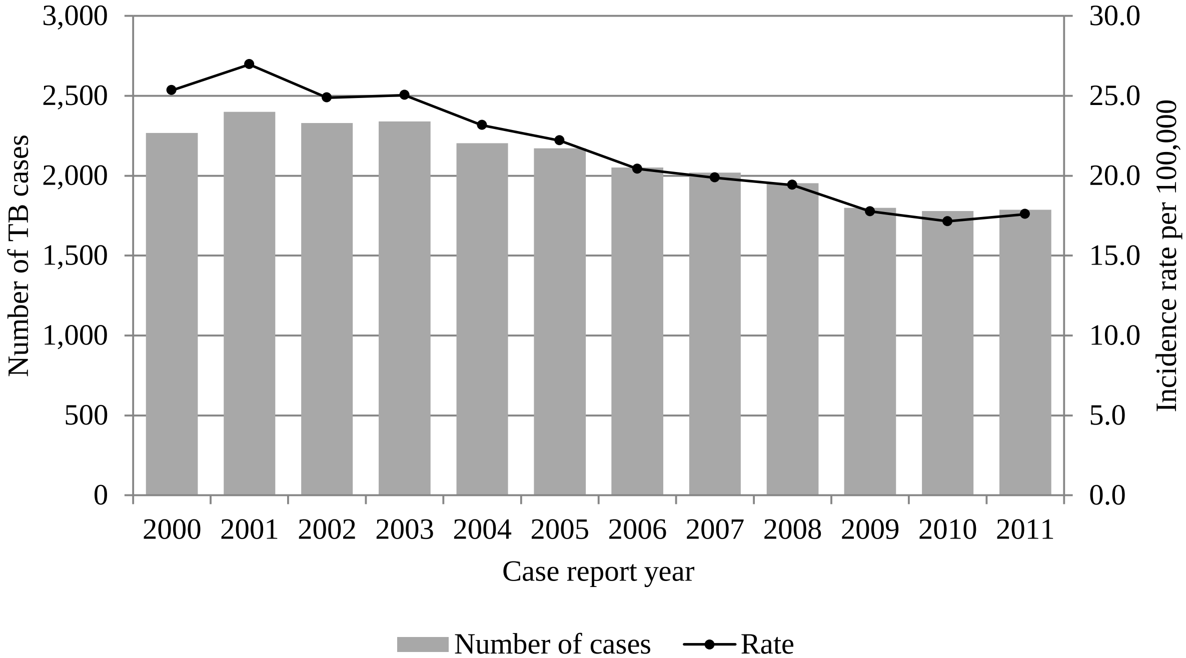

Table 1. Duration of residence-specific TB incidence rates in the foreign-born population of California, 2000 – 2011. To illustrate how to trace the incidence rates of an immigration cohort, the shaded cells indicate the 2000-2001 immigration cohort over time.

	TB case report year period					
Duration of residence in the U.S. at the time of TB diagnosis, years	**2000-01**	**2002-2003**	**2004-05**	**2006-07**	**2008-09**	**2010-11**
0-1	108.2	140.3	128.3	110.6	89.1	74.0
2-3	32.1	33.3	31.1	31.6	32.5	24.1
4-5	27.2	24.1	24.7	21.9	22.9	23.4
6-7	25.8	22.6	18.8	19.9	19.2	17.8
8-9	28.9	22.7	18.3	14.7	16.6	15.4
10-11	21.3	22.9	17.8	16.2	14.5	14.7
12-13	18.8	20.1	19.8	15.8	16.4	13.8
14-15	20.3	14.3	16.0	18.6	16.6	14.8
16-17	18.8	17.3	15.8	14.6	15.9	14.0
18-19	23.7	16.8	15.4	15.5	14.5	15.5
20+	16.2	16.1	15.6	13.3	13.7	13.6
All foreign-born	*26.2*	*25.0*	*22.7*	*20.2*	*18.6*	*17.0*

Figure 2. Duration of residence-specific TB incidence rates by case report year, California, 2000 – 2010. (a) Observed data and (b) modeled additive data, i.e., with the cohort effect removed.
(a)

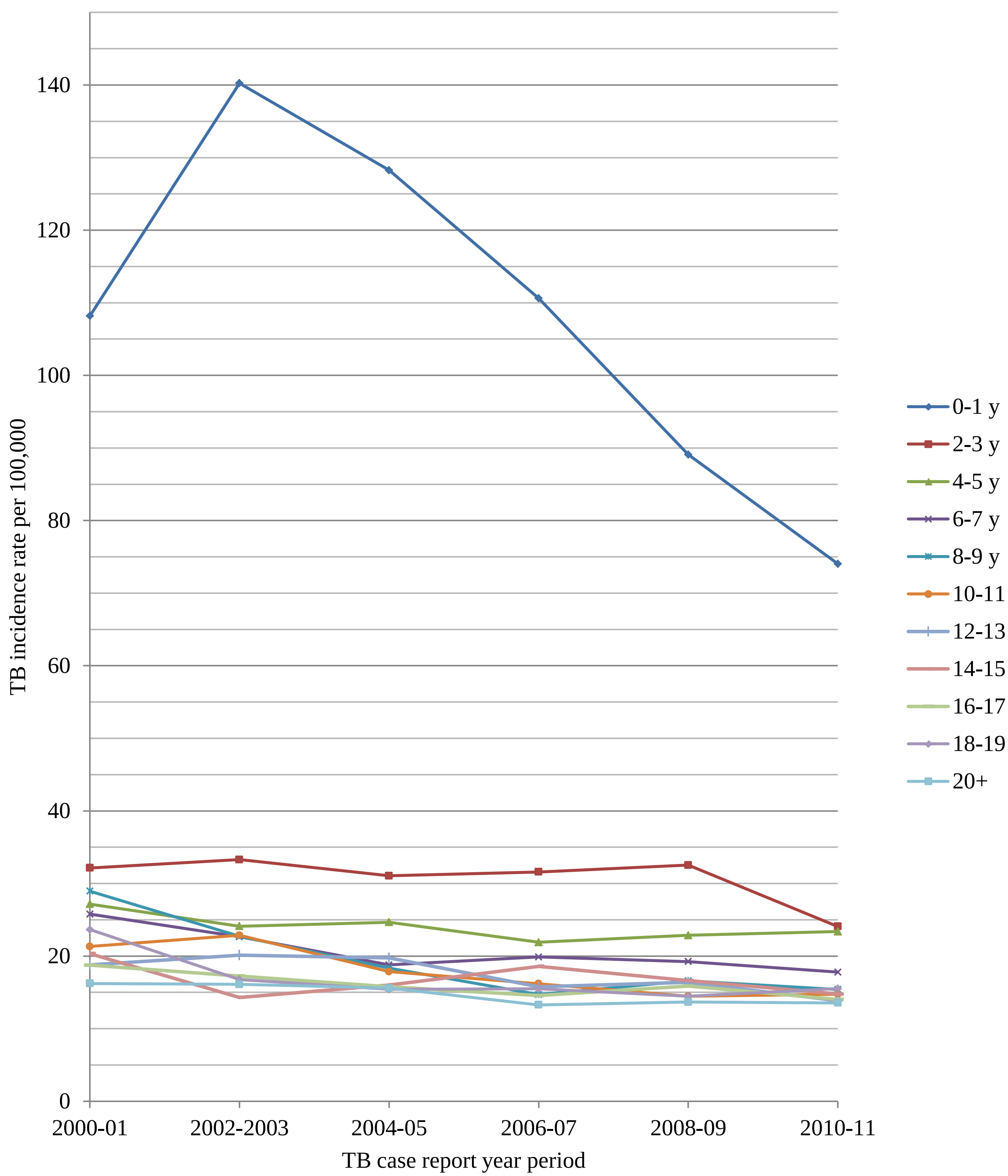

Figure 2(b)

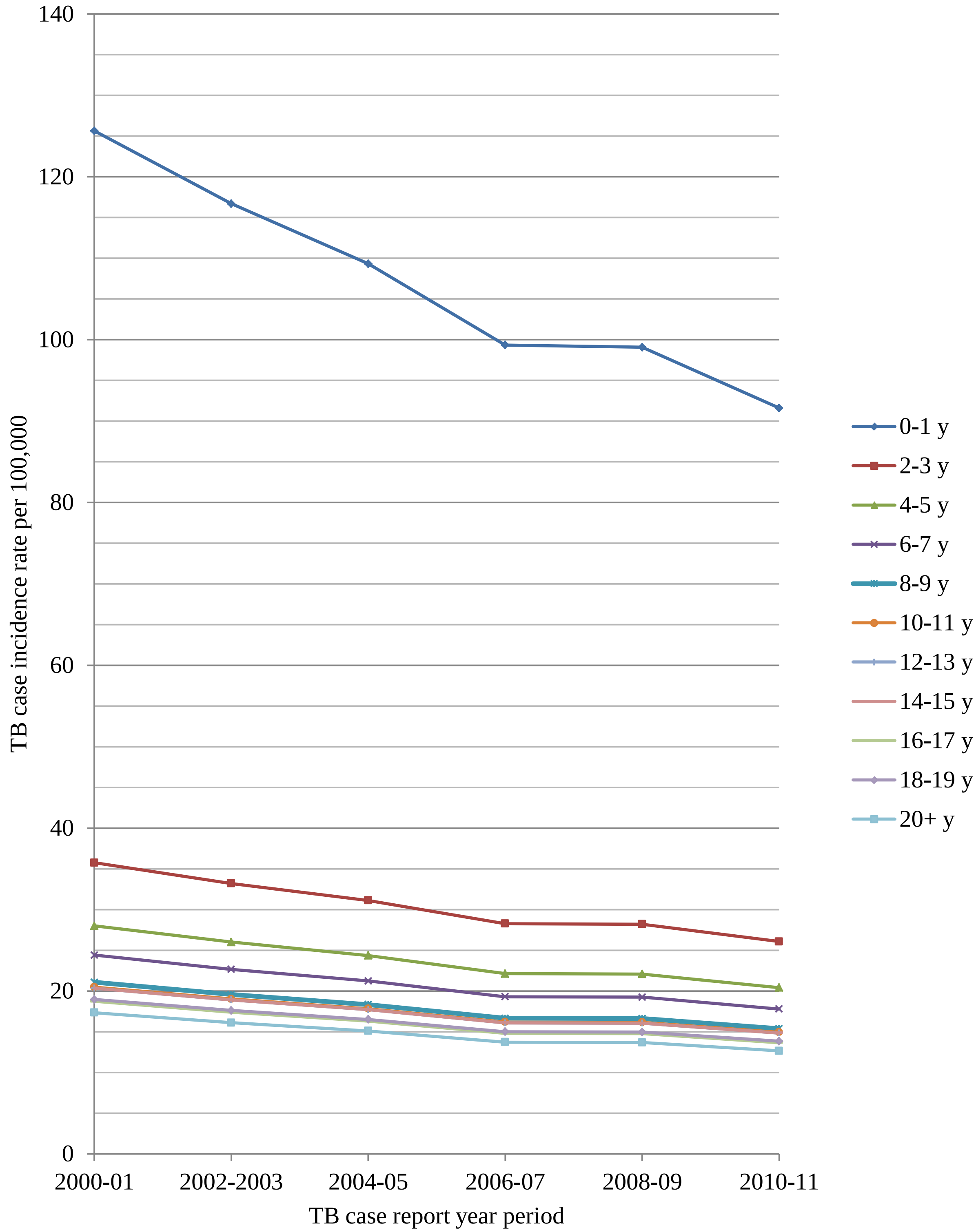
140
120
100
80
60
40
20
0
TB case incidence rate per 100,000
2000-01
2002-2003
2004-05
2006-07
2008-09
2010-11
TB case report year period
0-1 y
2-3 y
4-5 y
6-7 y
8-9 y
10-11 y
12-13 y
14-15 y
16-17 y
18-19 y
20+ y

Table 2. Residual values resulting from the median polish procedure. (Rates were log transformed prior to median polish).

	TB case report year period					
Time in U.S., y	2000-01	2002-2003	2004-05	2006-07	2008-09	2010-11
0-1	-0.15	0.18	0.16	0.11	-0.11	-0.21
2-3	-0.11	0.00	0.00	0.11	0.14	-0.08
4-5	-0.03	-0.08	0.01	-0.01	0.03	0.14
6-7	0.05	0.00	-0.12	0.03	0.00	0.00
8-9	0.32	0.15	0.00	-0.12	0.00	0.00
10-11	0.04	0.18	0.00	0.00	-0.11	-0.01
12-13	-0.08	0.06	0.11	-0.02	0.02	-0.07
14-15	0.00	-0.28	-0.10	0.15	0.04	0.00
16-17	0.00	-0.01	-0.03	-0.02	0.07	0.03
18-19	0.22	-0.05	-0.07	0.03	-0.03	0.12
20+	-0.07	0.00	0.03	-0.03	0.00	0.07

Table 3. Modeled TB incidence data of additive values (on a log scale).

	TB case report year period					
Time in U.S., y	2000-01	2002-2003	2004-05	2006-07	2008-09	2010-11
0-1 y	125.6	116.7	109.3	99.3	99.1	91.6
2-3 y	35.8	33.2	31.1	28.3	28.2	26.1
4-5 y	28.0	26.0	24.4	22.1	22.1	20.4
6-7 y	24.4	22.7	21.2	19.3	19.2	17.8
8-9 y	21.1	19.6	18.3	16.7	16.6	15.4
10-11 y	20.5	19.0	17.8	16.2	16.1	14.9
12-13 y	20.4	18.9	17.7	16.1	16.0	14.8
14-15 y	20.3	18.9	17.7	16.1	16.0	14.8
16-17 y	18.7	17.4	16.3	14.8	14.8	13.7
18-19 y	19.0	17.6	16.5	15.0	14.9	13.8
20+ y	17.3	16.1	15.1	13.7	13.7	12.6

Figure 3. Mean residual values resulting from median polish of TB incidence rates by immigration arrival cohort, foreign-born persons in California.

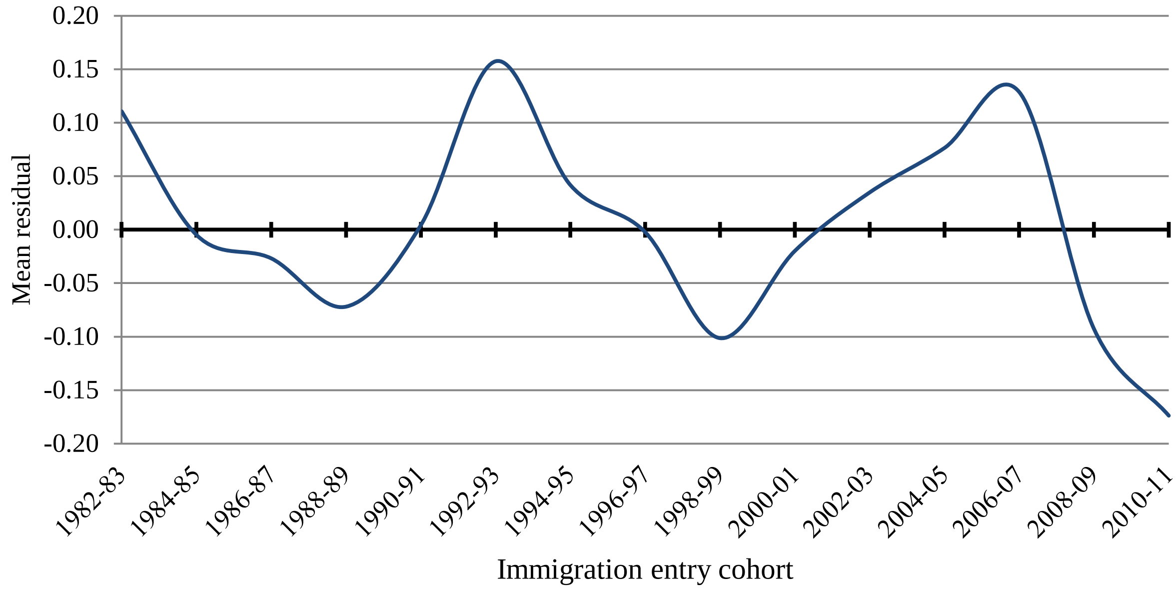

Table 4. Estimated rate ratios for the immigration cohort effect on tuberculosis incidence rate per 100,000, California, 2000-2011

Decade of immigration	Immigration entry cohort	Rate ratio	95% confidence interval	
1990s	1992-93	1.18	1.10	1.26
	1994-95	1.09	1.00	1.17
	1996-97	1.00	Reference	
	1998-99	0.91	0.83	0.98
2000s	2000-01	1.00	Reference	
	2002-03	1.05	0.99	1.11
	2004-05	1.10	1.04	1.16
	2006-07	1.16	1.09	1.22

Paper Three

Associations of demographic, socioeconomic, immigration and health factors with tuberculosis screening and infection among immigrants to the United States

Abstract

Background Identifying associations of demographic and socioeconomic factors with 1) tuberculosis (TB) screening uptake and 2) prevalence of latent TB infection (LTBI) is useful in informing efforts in the United States to efficiently target TB screening interventions necessary to speed the decline of TB incidence rates. The majority of TB cases in the U.S. occur in the foreign-born population. Data from the New Immigrant Survey (NIS) - the first and only nationally representative survey sample of immigrants, i.e., foreign-born persons adjusting to permanent residence in 2003, included questions about respondents' TB history, providing a unique opportunity to assess such associations while adjusting for important immigration-, and health- related factors, which previous studies have not been able to do.

Methods In the TB screening uptake analysis, the outcome variable was a self-report of "not tested" for TB. Predictors under consideration were gender, age, race/ethnicity, immigration sending country/region, arrival period and admission classification; health care occupation, diabetes history, educational attainment, health insurance status, and health care utilization. In the TB infection analysis, the sample was limited to respondents with a history of TB testing, with a positive test as the outcome. Predictors in the infection analysis were the same as in the screening analysis, with the addition of tobacco smoking history, underweight status, and self-reported childhood health status. Odds ratios (OR) were calculated and adjusted using multivariate logistic regression. Predictor variables with p values <.2 in the univariate analysis were considered for inclusion in the multivariate models.

Results The screening uptake analysis (n=7,770) showed that 28.1% of the immigrant sample had not been tested for TB. Black race, white race and Hispanic ethnicity were independently and negatively associated with an absence of TB screening (aOR 0.68, 95% CI 0.47-0.97; aOR 0.52, 0.36-0.75; and aOR 0.42, 0.29-0.62; respectively]. Origin in the following sending countries/regions was associated with no TB screening: Middle East/North Africa (aOR 2.41, 1.58-3.69), China (aOR 2.40, 1.79-3.22), India (aOR 2.17, 1.64-2.68), "other" Asia (aOR 1.82, 1.39-2.40), and Latin America other than Mexico (aOR 1.60, 1.06-2.43). The immigration arrival cohorts of 2003 (i.e., with 0-1 years' residence in the U.S.) and 1993-1997 (i.e., 6-10 years) were more likely to not have been tested (aOR 1.79, 1.47-2.19; and aOR 1.26, 1.01-1.59, respectively). The only immigration admission category with an independent and positive association was the "legalization" group (previously undocumented persons; aOR 1.74, 1.24-2.43). Fewer than 12 years of education was also positively associated with a lack of TB testing (aOR 1.33, 1.18-1.50), as was occupation outside of health care (aOR 2.34, 1.64-3.34) and lack of health insurance (aOR 1.21, 1.08-1.36).

The infection prevalence analysis (n=5,359) revealed that 8.0% of the sample reported a positive TB test. Men were less likely to report a positive test result than women (aOR 0.75, 0.61-0.93). Countries/regions independently associated with a positive result were the Philippines (aOR 2.18, 1.32-3.59), Mexico (aOR 1.82, 1.22-2.72) and "other" Asia (aOR 1.68, 1.04-2.73). The arrival cohorts "1982 and earlier", 1983-1992, and 1993-1997 were predicted positive TB test results (aOR 4.22, 2.47-7.20; aOR 2.65, 1.88-3.74; aOR 1.92, 1.34-2.75; respectively). Immigrants with a family preference admission classification were negatively associated with having a positive TB test (aOR 0.67, 0.46-0.96). An occupational history in health care also predicted a positive test (aOR 2.12, 1.44-3.11). Fair or poor health while growing up was also positively associated (aOR 1.73, 1.14-2.62), while lack of health insurance was negatively associated (aOR 0.56, 0.46-0.70).

Conclusions The finding of 72% screening uptake corroborates a published tuberculin skin test-based study that estimated one third of the foreign-born population in the U.S. as not being screened for TB infection, despite high-risk group status. Screening uptake varies substantially by subgroup. Screening among Chinese, Indian and other Asian immigrant groups significantly lags behind that of Filipino and

Vietnamese groups, suggesting opportunities for improving targeted TB screening efforts. Efforts to reach the undocumented population and persons without health insurance coverage to increase TB testing coverage need improvement. The overall prevalence of LTBI among the foreign-born suggested by the present study is lower than reported in the literature. The elevated risk of TB infection among Philippine-, Mexican- and Asian-born persons other than Vietnamese, Chinese and Indian reflects the high group-specific TB disease incidence rates in these strata. Refugees, previously undocumented persons and diversity visa immigrants had similar a risk of TB infection as economic migrants, suggesting similar TB exposure environments in the sending countries and less social stratification of TB risk than might be expected. Occupational exposure in the health care setting appears to be an important risk factor for LTBI among immigrants. The association between self-rated health status and LTBI has previously not been explored. The positive finding in this study may aid in further focusing targeted TB testing strategies. NIS follow-up interview data collected in 2007-2009 will allow for a longitudinal assessment of improvements in TB screening uptake and test results.

Background

As tuberculosis (TB) disease incidence rates decline in the U.S., the identification and treatment of persons with TB infection (TBI) who are at high risk for progression to active disease have become essential components of the national TB control strategy (CDC, 1999; Geiter, 2000; CDC, 2005a; Stop TB USA, 2010). The risk of progression from infection to active disease has been documented to significantly increase in the presence of conditions such as co-infection with the human immunodeficiency virus (HIV), silicosis, low body mass index (BMI) (CDC, 2000). Other clinical conditions that have been shown to increase the risk of developing active TB disease are diabetes mellitus, renal failure and/or hemodialysis, gastrectomy, jejunoileal bypass surgery, solid organ transplantation, and cancers of the head and neck- although participants in these studies were not stratified by TBI status (CDC, 2000). In addition to these clinical factors that influence the likelihood of progression to active TB disease, immigration-related demographic characteristics are associated with an elevated risk of infection. In immigrant groups originating in regions of the world with high TB morbidity, incidence rates approach those in the sending countries for the first several years after arrival in the U.S. (McKenna et al., 1995; Cain et al., 2008). This pattern of high incidence in the early post-immigration arrival period followed by declining incidence in subsequent years is viewed as evidence that the risk of progression from infection to disease is greatest shortly after infection has occurred. Hence, national TB control guidelines in the U.S. specifically recommend that targeted testing programs include recent immigrants (within the last 5 years) among the risk groups to prioritize for TB screening (CDC, 2000). The Institute of Medicine also concluded that identifying and targeting groups with high levels of TBI are required components of a successful TB control strategy in the U.S. (Geiter et al., 2000).

Population-level analyses of foreign born groups to identify which specific immigrant subgroups are most affected by LTBI and therefore would be the most effective targets for selective screening are lacking (Cain et al, 2008). Few studies in the U.S. have produced group-specific estimates of the prevalence of TB infection or have adjusted the risk of infection for important clinical, socio-economic and immigration-related co-factors. Improved knowledge of the variations of TB screening history and infection is needed to help identify immigrant population sub-groups with key markers such as low rates of TB testing history and high rates of LTBI, to whom TB control efforts such as targeted screening might be aimed to better make use of increasingly scarce public health resources. The present study utilizes TB data in the first and only nationally representative sample survey of immigrants in the U.S. to identify factors associated with TB screening and TB infection.

Methods

Data source

The New Immigrant Survey (NIS) is the first and only survey in the U.S. of a nationally representative sample of immigrants. It was administered in 2003, at the time the immigrants were granted permanent resident status (Jasso et al., 2000; Jasso et al., 2005; Jasso et al., 2006). The sampling frame was based on U.S. Citizenship and Immigration Services administrative records of immigrants admitted to legal permanent residence (i.e., granted a “green card”), and the timeframe specified as those persons admitted between May and November 2003 for a total sampling frame of 12,500 persons. The cohort of “new” immigrants surveyed included both recently arrived immigrants and those who had been residing in the U.S. for a longer time and were admitted to legal permanent residence at the time of the implementation of the survey. The full 2003 baseline cohort consisted of the 8,573 respondents (representing a 69% survey response rate) who were interviewed by telephone or in person (See Appendix for a summary table of selected characteristics of the 2003 NIS cohort). The cohort of new immigrants includes both the newly arrived (those with immigration documentation acquired abroad) and those adjusting their status (who were already in the U.S. with a temporary visa- or no visa at all- and met requirements to adjust to legal permanent residence). It is a longitudinal survey- a follow-up interview of respondents was conducted between 2007 and 2009. The data from the follow-up interview recently became available in the spring of 2014. The present cross-sectional analysis focuses on the baseline survey data collected in 2003.

The NIS queried respondents on a range of social, economic and health topics. Health measures consisted of health care utilization, health insurance, and self-reported information on medical conditions including history of TB screening, diagnosis and treatment completion. (The two questions about TB that were considered in this analysis were “Have you ever been tested for TB?” and “Did you ever test positive for TB?”). Other queried medical conditions and health behavior and history measures relevant to TB infection and screening included diabetes and history of tobacco smoking. Relevant socioeconomic measures included educational attainment, migration history and the type of immigrant visa, health care occupation, and childhood health status. Published articles investigating health conditions using NIS data include studies of urban health (Jasso et al., 2005), chronic disease among refugees (Yun et al., 2012), the relationship between health insurance and self-reported health status (Lee et al., 2012), obesity (Roshania et al., 2008), prostate cancer screening among the elderly (Kagotho & Tan, 2008), and health service utilization (Akresh, 2009). No studies investigating the TB data collected in the NIS have been published.

Study sample and measures

In the screening uptake analysis, the NIS dataset of all study respondents (n=8,573) was restricted to adult respondents 18 years and older with complete data on all of the analytic variables, and sampling weights applied (weighted n=7,770). The outcome evaluated was a binary “not tested for TB” versus “tested for TB” variable. Predictor variables were gender, age category (18-24, 25-44, 45-64, 65 years and older), race/ethnicity (white, Hispanic/Latino, black, Asian/Pacific Islander, American Indian), country/region of origin (Mexico, other Latin America, India, Philippines, China, Vietnam, other Asia, Europe/Central Asia, Middle East/North Africa, Sub-Saharan Africa, North America), immigration arrival cohort (2003, 2001-2002, 1998-2000, 1993-1997, 1983-1992, 1982 and earlier), immigration admission classification (family preference, employment preference, diversity lottery, legalization, refugee), years of education completed (fewer than 12 years, 12 or more years), health care worker (yes or no), diabetes history (yes or no), health insurance status (uninsured, insured), and health care utilization (accessed health care in the past year, did not access health care). Health care worker status was determined from the response to the question about respondents’ current job(s), and encompassed those persons working as “health diagnosis and treating practitioners” or in “health care technical and support” positions.

In the infection analysis, the dataset was restricted to those respondents who reported a history of having been tested for TB, and had complete data on the analytic variables (weighted n=5,359). The outcome measure was a binary yes/no variable based on the answer to the question "Did you ever test positive for TB?" The covariates under consideration were the same as in the screening uptake analysis, with the addition of three variables: tobacco smoking history, binary underweight variable [body mass index (BMI) < 18.5 or ≥ 18.5], and self-rated health status during childhood (from birth to age 16, binary fair/poor versus good/very good/excellent).

Statistical analysis

In the bivariate analysis, the strength of the association between each categorical predictor variable and the outcome variable was measured by calculating the odds ratio (with 95% confidence interval) and a P value using the chi-square test (all variables under consideration were categorical variables). Associations of $P < 0.05$ were considered statistically significant. Predictor variables associated with the outcome variable at the level of $P < 0.20$ were then considered for inclusion in three sequential multivariate logistic regression models for each analysis (screening uptake, and infection). The base model included only gender, age, and the country/region of origin terms. The second model added the immigration arrival cohort and the immigration visa classification terms. The third model (full model) further added the health insurance, educational attainment and health care occupation terms for the screening uptake analysis, while in the infection analysis, the added terms were the health insurance, educational attainment and self-rated health variables. Several variables were not included in the multivariate analysis despite significant results in the bivariate analysis, due to collinearity. While both the "race/ethnicity" and the "country/region of origin" variables were significantly associated with the outcomes in the screening and infection analyses, only the country/region of origin was entered into the multivariate model. Similarly, both the "health insurance status" and "health care utilization" variables were considered in the bivariate analysis, but only the latter variable was included in the multivariate step. Multivariate analyses were performed using the *surveylogistic* procedure in SAS, version 9.3 (Cary, NC).

This study was based on the public-use version of the NIS dataset, with personal identifiers removed. The University of California, Berkeley Committee for Protection of Human Subjects reviewed the study protocol and deemed it exempt from human subjects research approval.

Results

Of the total sample of 8,537 participants in the NIS, a weighted subset of 7,770 adults age 18 and older with complete data on all analytic variables comprised the study sample for the screening uptake analysis. Table 1 summarizes the geographic distribution of the participants' state of residence of at the time of interview. Immigrants in California represented 29% of the national sample under analysis. Together with the other traditional immigration magnets of New York, Texas, Florida and New Jersey, the top five states comprised more than 62% of the study population. The demographic characteristics of the sample are shown in Table 2. The male-to-female ratio of the sample was 0.78:1, the median age 36 years, and the distribution of race/ethnicity was 35% Hispanic/Latino, 31% Asian/Pacific Islander, 20% white, 12% black, and 3% American Indian/Native Alaskan. The most common sending countries were Mexico (16.8%), India (7.2%), El Salvador (6.1%), the Philippines (5.7%) and China (5.3%). Table 3 displays key immigration-related characteristics of the study sample. The majority of the participants were admitted to permanent residence via a family preference immigration classification (67%). The other classifications represented were employment-related (10%), diversity lottery winners (8.2%), those undergoing legalization (8.1%), and refugees (6.9%). A little under half of the sample (46%) arrived in the U.S. within the year prior to interview. Those in the U.S. for over one year but no more than 10 years represented 36% of the dataset, and the remaining 19% had been in the country for 11 years or more before being granted permanent residence.

Screening analysis

Overall, 28.1% of participants were not screened for TB. The results of the bivariate screening uptake analysis are summarized in Table 4. The proportion unscreened was higher among men than women, but the difference was not significant (P=.41). All age groups had lower unscreened proportions than the reference group (65 years and older), but only for the 25 to 44 year age group was the difference significant (P<.0001). All race/ethnicity groups were significantly more likely to be screened than the Asian/Pacific Islander reference group (P<.0001). At the country/region level, the lowest likelihoods of TB screening were observed among immigrants from China, India, Vietnam, other Asian countries, and the Middle Eastern/North African region. In contrast, immigrants with origins in Canada, Europe/Central Asia, and Mexico had higher likelihoods of a TB screening history. Persons arriving from Sub-Saharan Africa and Latin American countries other than Mexico had statistically similar screening proportions as the reference group. Of the immigration arrival cohort categories evaluated in the bivariate analysis, only the newly-arrived 2003 cohort had a significantly lower likelihood of screening history (compared to the reference group of arrival between 1983 and 1992), while the immigrants who arrived before 1983 were more significantly more likely to have been screened. All immigration admission classification groups were associated with lower screening uptake than the refugee comparison group. Furthermore, lower educational attainment significantly predicted lower levels of screening. Persons employed as health care workers were significantly more likely to be screened than other occupational classes. A history of diabetes did not significantly impact the likelihood of being screened for TB. A lack of health insurance was associated with lower screening uptake, while the group of respondents that did not utilize health care within the 12 months prior to the survey interview was more likely to be unscreened.

Table 5 shows the results of the three sequential logistic regression models for the screening analysis. In the simplest model, only the country/region of origin was included, in addition to the adjustment for gender and age group. In this Model 1, immigrants from China, India, Vietnam and other Asian countries had significantly greater odds of not having been screened for TB than immigrants from the Philippines. In contrast, several groups were independently associated with significantly higher proportions screened. Immigrants from Canada, Mexico, and Europe/Central Asia were each screened at significantly higher proportions. Also, adults age 25 to 44 were more likely to have a TB screening history. In Model 2, immigration arrival cohort and admission classification were added, and both yielded significant results. The most recent arrival cohort (2003) was associated with a significantly higher unscreened proportion, while the preceding cohorts were statistically similar to the reference group of those arriving between 1983 and 1992. Compared to the refugee group, the legalization group (i.e., persons who were undocumented residents in the U.S. and successfully applied for legalization) had significantly higher odds of remaining unscreened for TB. The addition of the immigration variables to the model resulted in the loss of significance for the association between the 25 to 44 year age group and greater likelihood of screening. Additionally, Mexican and Canadian origin no longer resulted in significant associations with a higher proportion screened as they did in Model 1. The significance of the associations of the other countries/regions of origin did not change in Model 2, but the magnitudes of the effects were slightly elevated compared to Model 1. In Model 3, the health insurance, health care occupation and educational attainment terms were added. All three of these terms were significantly associated with lower screening proportions, with health care occupation yielding the strongest association. The addition of these terms in Model 3 led to one association in Model 2 gaining statistical significance: Mexican origin significantly lowered the odds of being unscreened (i.e., screening uptake was higher). On the other hand, the addition of the insurance, occupation and educational attainment terms led to two statistically significant associations in Model 2 dropping out of significance in Model 3: immigration from Vietnam and from the Middle East/North Africa was no longer associated with significantly higher proportions of unscreened persons. The other demographic and immigration-related effects were reduced in magnitude but did not change their statistical significance. Effect modification of the association between country/region of origin and TB screening uptake outcome by history of diabetes was explored. An analysis of interaction terms combining diabetes and region of origin yielded no evidence of diabetes acting as an effect modifier (data not shown).

Infection analysis

Of the participants with a history of TB screening, 8.0% reported having had a positive TB test. Table 6 summarizes the results of the bivariate analysis of TB infection. Men were significantly less likely than women to report a positive TB test. Age groups were not significantly associated with a positive test. Compared to whites, Hispanics/Latinos, Asians/Pacific Islanders and American Indians were more likely to report a positive test, while blacks were statistically similar to the reference group. Immigration from Mexico and from the Philippines was associated with a higher likelihood of a positive test. Compared to the reference cohort of new immigrants arriving in 2003, the 2001-2002 cohort had statistically similar odds of infection, but starting with the 1998-2000 cohort and going further back in time, there were progressively more significant associations with a positive TB test. The group undergoing legalization had a higher likelihood of a positive TB test compared to the reference group of persons with an employment preference visa. In contrast, diversity lottery winners and family preference visa holders had lower odds of a positive test, and refugees as a group were statistically similar to the reference. Current employment (at the time of interview) in the health care industry significantly predicted a positive TB test. None of the tested health conditions (diabetes, tobacco smoking, and being underweight) was significantly associated with the outcome measure. However, fair or poor self-rated health during childhood was significantly associated with TB infection. The health insurance status variable yielded an unexpected finding: the uninsured group had a significantly lower proportion with a positive test than the comparison group with health insurance. Lower educational attainment was not significantly associated with a higher likelihood of a positive TB test.

The three logistic regression models comprising the multivariate analysis of factors associated with TB are shown in Table 7. In the basic model of only the demographic terms (Model 1), men had a lower likelihood of positive TB test than women, while immigration from Mexico and from the Philippines had significantly higher odds of a positive test. Model 2 added the immigration arrival cohort and the visa classification terms to the basic model. Here, the four immigration arrival cohort categories with significant results in the bivariate analysis (1998 – 2000, 1993 – 1997, 1983 – 1992 and 1982 and earlier) preserved their significant associations, although the magnitudes of the strength of association were slightly reduced. The family preference and the diversity lottery classifications significantly predicted a lower likelihood of a positive TB test, whereas the legalization and refugee classifications were not significant in Model 2. (Note that the legalization group was significantly associated with TB infection in the bivariate model). Model 3 expanded the model to include the health care occupation, health insurance status and self-rated health variables. Health care employment remained a significant predictor of TB infection as in the bivariate analysis, as did fair or poor self-rated health. The health insurance term was also significantly associated in Model 3: being uninsured had a lower likelihood of TB infection. Effect modification of the association between country/region of origin and TB infection by educational attainment was investigated. No evidence of educational attainment acting as an effect modifier was found in an analysis of interaction terms combining the educational attainment variable and region of origin (data not shown).

Discussion

This analysis of the tuberculosis history data collected in the New Immigrant Survey (NIS)- the first and only nationally representative survey of immigrants adjusting to legal permanent residence in the U.S. – provides new information on population subgroups in which TB screening is lagging, and suggests specific targets for future screening and testing efforts in immigrant communities. NIS data offered a unique opportunity to conduct country of origin-specific analyses of TB screening uptake and infection prevalence, while controlling for potential confounding effects of immigration visa, immigration arrival cohort, socioeconomic and medical and social factors garnered in the survey. To my knowledge, the present study is the first to provide estimates of TB screening uptake and TB infection prevalence among immigrants to the U.S. at the sending country-specific level. The main findings of the screening analysis were 1) immigrants of Chinese, Indian, and other Asian origin (except the Philippines and Vietnam), 2) immigrants who were undocumented residents in the U.S., and 3) uninsured immigrants were significantly less likely to have been screened for TB. The principal findings of the infection analysis were 1) Filipino and Mexican immigrants were more likely to have a history of positive TB test, 2) immigration arrival prior to the late 1990's was associated with a higher likelihood of a positive test, and 3) family reunification visa holders were significantly less likely to report a positive test.

The observation that nearly 3 out of 10 new immigrants had no TB screening history is consistent with the finding in one of the few population-based studies in U.S. assessing TB infection prevalence, which concluded that approximately one-third of the foreign-born U.S. population had never had a tuberculin skin test (TST) administered to screen for TB infection (Bennett et al., 2008). In 2012, nearly one fifth of the 6,274 foreign-born TB cases reported in the U.S. occurred among immigrants from countries/regions associated with under-screening for TB in the present study- 17% from India, China or Korea (CDC, 2013). The fact that immigration from these regions of high TB incidence – e.g., 176 cases per 100,000 in India, 73 in China, 108 in Korea (WHO, 2013) - was associated with lower levels of TB screening is important information for public health departments and health care providers such as community clinics serving these communities. National TB control guidelines specify immigrants from high TB burden countries – particularly the recently arrived, within the past 5 years - as one of the priority groups for targeted testing and treatment of TB infection (CDC, 2000). The recommendations recognize that newly arrived immigrants pose challenges to public health systems and health care providers because they might not realize their TB risk, often lack ready access to health care services, and might have strong cultural conceptions about TB that could clash with approaches taken by American public health systems (CDC, 2005). The present study's sending country-specific finding that new arrivers from specific regions are at an elevated risk of under-screening adds to the evidence base for improving targeted TB testing coverage among immigrants from India, China, and other Asian countries outside of the Philippines and Vietnam.

A key dimension which this report adds to the understanding of TB testing success is the simultaneous adjustment for the covariates of immigration arrival cohort and immigrant visa classification. The finding that undocumented immigration status (immediately prior to adjustment to legal permanent residence) was a significant predictor of low TB screening uptake is a novel finding. While the literature has provided evidence that undocumented immigrants underutilize medical services for acute health needs requiring substantial financial cost (e.g., Chavez, 2012), it reveals very little about the utilization of relatively inexpensive preventive services such as TB testing at public health clinics. Estimates suggest that undocumented immigrants account for a sizeable proportion of the foreign-born TB case patients in the U.S. - approximately 20 percent (Davidow et al., 2009). Even with the expansion of health insurance coverage under the Affordable Care Act of 2010, undocumented persons continue to be excluded from programs that would provide services such as TB testing and treatment (Zuckerman et al., 2011). The present study's findings that undocumented status and lack of health insurance were both independent predictors of low TB screening uptake are timely reminders to health policy makers and public health departments that epidemiologically influential swathes of the U.S. immigrant population may remain unscreened for TB if preventive services do not become available to all persons who are recommended for TB testing. The immigration arrival cohort information included in the present study also provided novel findings. The observation that the newest arrivers (the cohort of immigrants arriving in 2003) had the highest likelihood of no screening history was perhaps not surprising, given that a short duration of residence could inherently produce relatively few opportunities for screening compared to a cohort resident in the country for a longer period of time. The additional finding, however, that the longer-resident arrival cohorts did not have significantly higher levels of screening suggests that testing coverage and/or testing opportunities do not necessarily increase with a longer duration of residence in the U.S.

The results of the infection analysis provide new information to help build on the sparse literature on TB infection prevalence estimates of at-risk populations in the U.S. A report on a prospective cohort study of heart disease in selected urban locales in the U.S. analyzed risk factors for TB infection while controlling for socioeconomic factors (Nahid et al., 2011). However, this study focused on U.S.-born populations of young black and white adults. A frequently cited source of population-based estimates the prevalence of TB infection using tuberculin skin test results in the National Health and Nutritional Examination Survey (NHANES) in 1999-2000 (Bennett et al., 2008; Khan et al., 2008). While the authors were able to assess prevalence at the level of nativity and race, the NHANES did not include country of origin information and therefore the analysis was limited to prevalence estimates among non-Hispanic whites, non-Hispanic blacks/African Americans, Mexican/Mexican-American. Importantly, the study of NHANES data did not have sufficient power to generate estimates among Asian immigrants due to sample limitations. Of the foreign-born TB cases reported in the U.S. in 2012, 46% occurred in immigrants from Asia (CDC, 2013). The present study adds to the literature by providing TB infection prevalence estimates for Asian immigrants, at the level of country of origin.

In general, the estimates of TB infection in the present study are lower than those that have been reported in the literature. The self-report-based 8.0% TB infection prevalence estimate among immigrants who have been screened for TB is markedly lower than the 14.6% found in the aforementioned study of NHANES data – the only other published source of national population-based TB infection prevalence estimates, including for the foreign-born population (described in the online supplement of Bennett et al., 2008). Disregarding TB screening history, 5.5% of the NIS sample had a history of TB infection, compared to 9.5% of the foreign-born sample in the NHANES study (Bennett et al., 2008).

The other U.S.-based foreign-born TB infection prevalence estimates reported in the literature are higher still. Contrary to the present analysis of a nationally representative sample of new immigrants, infection prevalence estimates in the literature are based on samples of subgroups such as undocumented immigrants, refugees or drug users. Such estimates, while useful in estimating the TB burden in narrow population pockets, probably do not reflect the infection prevalence among new immigrants as a whole. In Denver, Colorado, a study of primarily young adult, undocumented Mexican-born persons in the late 1980’s revealed a 42% TB infection prevalence based on tuberculin skin test results (Blum et al., 1993). The Denver study was conducted in the wake of the federal Immigration Reform and Control Act of 1986 (IRCA), which allowed undocumented immigrants to adjust to legal status provided that they underwent screening for illnesses including TB. The selection bias toward one particular slice of the immigrant population renders the finding of infection prevalence in excess of 40% most likely not generalizable to the general population of Mexican immigrants. Another study, which recruited persons voluntarily presenting at chest clinics in New York City between 2002 and 2004, also estimated the infection prevalence of Mexican-born immigrants at over 40% (Li et al., 2010). The authors conceded that the group of persons coming to a chest clinic for TB screening could be systematically different from persons tested elsewhere and that the findings could not be generalized to the larger Mexican immigrant population. The NHANES study estimated that 19.1% of Mexican-born immigrants had TB infection in 1999-2000. The present study estimated the prevalence in this group at 12.5%, and determined, after statistically controlling for undocumented immigration status, an elevated risk of TB infection.

The infection prevalence among U.S. immigrants from the Philippines has not been reported in the literature. The country of origin-specific incidence of active TB disease in this group of immigrants is among the highest in the U.S. (over 50 cases per 100,000 population; Manangan et al., 2011), and the infection prevalence in the Philippines appears to be greater than 60% (Tupasi et al., 2000). The present study estimated the TB infection prevalence of Filipino immigrants in the U.S. at 12.0%, and found that after controlling for immigration cohort factors, Filipino origin remained a significant predictor of TB infection among new immigrants. A study of California-bound Filipino immigrants evaluated for TB between 2001 and 2010 concluded that the risk of TB disease stemming from reactivation of latent TB infection remains high throughout the first post-arrival decade (Walter et al., 2014). The authors concluded that the current recommendations to focus TB screening on recently arrived immigrants (less than 5 years ago) should be expanded to include immigrants who have been in the U.S. for a longer period. The present study provides further evidence to support this recommendation.

Vietnamese immigrants comprise another important group of immigrants for whom published TB infection prevalence estimates are rare. Studies of visa applicants for immigration to the U.S. suggest that over 50% of Vietnamese immigrants have TB infection (Painter et al., 2013; Chuke et al., 2014). A literature review of TB screening efforts estimated that about 35% of Southeast Asian refugees in the U.S. have TB infection (Dasgupta & Menzies, 2005). In contrast, the TB infection prevalence suggested by the present study is much lower. The substantial gulf between the magnitudes of the reported estimates and the ones suggested by the present studies could be explained, in part, by sampling differences. The published two published studies in Vietnam (Painter et al., 2013; Chuke et al., 2014) drew their samples from the same urban hospital clinic performing pre-immigration TB screening and did not necessarily reflect the wider Vietnamese immigrant population sampled in the NIS. Vietnam is a high TB incidence country (147 cases per 100,000; WHO, 2013) with an unknown but presumably high prevalence of TB infection that would manifest itself in high rates of positive TB test results in the NIS. It is possible that the Vietnamese immigrants who actually completed the immigration process were systematically different in their TB exposure characteristics compared to the samples described in the published literature. Still, the magnitude of the gap between the published and presently reported prevalence estimates leaves open the possibility that the accuracy of self-reported of TB test history can vary from group to group, and that Vietnamese immigrants are more likely to under-report TB infection.

The finding that Mexican immigrants had high screening uptake for TB is encouraging. Even though the TB incidence rate in Mexico is relatively low (23 cases per 100,000 in 2012; WHO, 2013), Mexico is the most common country of origin among foreign-born TB cases in the U.S. In 2012, 21% of all foreign-born TB case patients in the U.S. were from Mexico (CDC, 2013). In California, the proportion is 34% (CDPH, 2013). Health selection research suggests that immigration from Mexico to the U.S. is characterized by weaker positive health selection than from other regions (Akresh & Frank, 2008). Given the substantial share of the TB case burden in the U.S. borne by the Mexican immigrant population, it is encouraging that TB screening appears to be well accepted and applied in this sizeable group. In comparison, screening among other Hispanic groups including Central Americans was lower which may reflect cultural or structural differences within Latino immigrant populations in the acceptance of TB screening. Immigrants from Guatemala, Haiti, Honduras, and El Salvador together account for 10% of the foreign-born TB cases in the U.S. (CDC, 2013). While the study did not find that Latin American immigrants had significantly lower screening uptake, the lag behind Mexican immigrants suggests opportunities for improvements in reaching Central American and other Latin American immigrants for TB screening, particularly in light of the evidence that TB incidence rates in Central America exceed that in Mexico (WHO, 2013).

That immigration arrival prior to the late 1990's was associated with a higher likelihood of a positive TB test compared to more recent arrival cohorts further adds to current knowledge of TB prevalence. Immigration arrival cohorts between 1998 and 2003 had statistically similar levels of TB infection in the full multivariate model, but retrograde cohorts before 1998 showed increasingly higher proportions of TB infection. This could represent a cohort-level impact on TB prevalence, whereby pre-1998 U.S. immigration policy and global migration pressures together selected for immigrant streams with more exposure to the TB organism at a time when the disease was more prevalent globally than it is today. The lower TB infection prevalence in the more recent arrival cohorts in the late 1990s could reflect a combination of lower TB prevalence in the sending countries, and changing immigrant selection pressures that resulted in different socioeconomic classes of migrants choosing to emigrate to the U.S. in the 2000s. The related finding that a family reunification visa classification was independently associated with lower TB infection prevalence compared to immigrants who had a work visa demonstrates the potential existence of heterogeneity in TB infection prevalence by immigration classification. In terms of exposure to TB in the sending country, it is reasonable to expect that within a country monolithically characterized by high TB prevalence, there would be variation in exposure to TB based on socioeconomic class stratifications. Social science research on immigration recognizes the importance of statistically controlling for visa status to avoid bias in models of assimilation and incorporation (Massey et al., 2010), and the present study applied a similar view to infectious disease epidemiology. The results suggest that targeting testing in a way that prioritizes family reunification visa holders may not be effective in identifying TB infection. While the legalization group (i.e., previously undocumented immigrants successfully adjusting to legal permanent residence) and the refugee group had elevated odds of TB infection, they were not statistically significant. This suggests that while the undocumented make up a substantial proportion of the foreign-born TB caseload as mentioned earlier, the infection prevalence in this group is not as high as might be expected. Consequently, the provision of TB testing and treatment services to undocumented immigrants, the extent of which remains unclear as the Affordable Care Act is implemented, is not likely to produce inordinate demands on the public health system. However, tempering these conclusions is the possibility that the sample of previously undocumented immigrants captured in the NIS was not representative of undocumented immigrants as a whole (i.e., including those who were not able to adjust to legal resident status). Surveillance data show that the incidence of TB disease among refugees in the U.S. greatly exceeds that in other immigrants, and this disparity has been attributed to both a higher prevalence of TB infection and having experienced crowded conditions associated with TB exposure (Greenaway et al., 2011). Furthermore, refugees' medical care utilization for TB-related symptoms has been shown to be markedly lower than other immigrants (DeRiemer et al., 1998). However, the present study did not find significantly elevated odds of TB infection among refugees after adjusting for other factors, challenging the notion that high TB infection prevalence is one of the main drivers of high disease incidence in this group.

It is well documented that a health care occupation poses an elevated risk of TB infection and disease in developing countries as well as in low TB incidence countries like the U.S. (Menzies et al., 2007; Horsburgh et al., 2011). The findings that current health care work was significantly associated with both a higher screening uptake and a higher likelihood of TB infection corroborate previously published studies and add to the literature in several important ways: First, population-based studies of the reach of TB screening in the U.S. immigrant population are virtually absent from the literature, and the present study is the first to quantify the levels of TB screening uptake among new immigrant health care workers. The observation that most (87%) of the health care workers in the present analysis were screened for TB is an encouraging finding, in line with what might be expected in a field of work more attuned to TB risks than others. Second, the finding that 17% of health care worker immigrants reported TB infection is generally in line with the few existing estimates of TB infection prevalence among health care workers in high-income countries, where the median prevalence estimate is approximately 24%, with a wide range between 4% and 46% (Menzies et al., 2007).

The finding that lower educational attainment independently predicted lower screening levels as well as a higher likelihood of TB infection among immigrants adds to a skeletal literature on the social determinants of TB in the U.S. The importance of drawing from social science theory to inform epidemiological investigations of the relationships between etiological agents such as *Mycobacterium tuberculosis* and infection and disease has long been recognized (e.g., Cassel, 1964; Farmer, 1997; Krieger, 1994; Krieger, 2000; Krieger, 2001), but few empirical studies of the effects socioeconomic factors on TB outcomes, particularly in developed countries with high levels of immigration, have been published. Even in a high-resource and low-incidence locale such as California in the early 21st century, social determinants of TB are a relevant but underappreciated topic. The evidence suggests that the current array of public health interventions in place to control and eliminate TB in California may not be sufficient to prevent new cases of TB among the foreign-born (Walter et al., 2008), and that the assessment of socioeconomic factors impacting the epidemiology of TB needs further attention. In the U.S., published studies on socioeconomic factors related to TB are limited to only a few reports, the majority of which were ecological studies: state-level correlations of social capital measures with TB incidence rates (Holtgrave & Crosby, 2004), the associations between zip code-level socioeconomic factors and racial disparities in TB incidence rates in New Jersey (Acevedo-Garcia, 2001), the association between poverty and crowding factors with TB incidence in Massachusetts (Mitnick et al., 1998), the impact of zip-code level socioeconomic status indicators on race/ethnicity-specific incidence rates nationwide (Cantwell et al., 1997), the associations between neighborhood-level poverty measures in TB incidence in New York City during the HIV epidemic in the 1980s and early 1990s (Barr et al., 2001), and the relationship between census tract-level socioeconomic factors on pediatric TB incidence- a proxy for disease transmission (Myers, et al., 2006). Still fewer studies examined individual-level associations such as the association between race/ethnicity as well as educational attainment and TB infection rates among school employees in New York City in the 1970s (Reichman & O'Day, 1978), the impact of unemployment and other social factors on delays in seeking care for TB symptoms (Asch et al., 1998), and the association between household-level poverty and TB infection

(Bennett et al., 2008). The present study is the first to report an independent association between lower educational attainment (as well as under-screening) and TB infection in the foreign-born population in the U.S. This finding is in contrast to Bennett and colleagues' analysis of educational attainment as an independent predictor of TB infection in their analysis of 1999-2000 NHANES data. In their stratified analysis considering only the foreign-born population, educational level did not independently predict a higher TB infection risk (Bennett et al., 2008).

Low education level is one of the recognized proximate determinants of TB (Lönnroth et al., 2009), and the finding in the screening study that lower educational attainment predicted lower levels of screening for TB underscores the concern that foreign-born persons encounter barriers to accessing services for addressing TB infection or disease (CDC, 2005b). More than one third of the new immigrants included in the infection analysis had low educational attainment, and this characteristic was associated with lower likelihood of TB screening. While immigrant populations vary widely in terms of socioeconomic position, groups characterized by lower educational levels such as laborers and service industry workers may need additional outreach by community health centers and public health departments to rectify what may be a socioeconomic disparity in the application of TB testing and treatment. Social epidemiologists and demographers consider level of education a useful and important indicator of socioeconomic position not only due to its relatively simple construction and ubiquitous applicability, but also due to its advantage of being less affected by negative adult health selection than other measures such as occupational status (Lynch & Kaplan, 1999; Elo & Preston, 1996).

To my knowledge, this study among the first to show evidence of childhood health acting as a social determinant of TB infection among adults U.S. immigrants. According to the life course approach to epidemiology, the long term effects on health or disease risk in adulthood by exposures during gestation, early childhood, and adolescence warrant investigation, not just the proximate risk factors usually associated with traditional epidemiology (Kuh et al., 2003). While the exploration of the proxy of the self-reported childhood health status variable in the present study is admittedly not the definitive word on the life course epidemiology of TB infection, it does highlight an unprecedented finding and suggests further exploration of poor childhood health as a marker of TB infection risk that may have practical utility in the primary care or public health clinic setting. In 2003, the CDC convened a national forum of TB researchers in public health and the behavioral and social sciences, in an attempt to synthesize what is known about social determinants of TB and to prioritize research directions (CDC, 2005b). At the forum, the director of the TB program of a major city in California emphasized the importance of framing TB data in its full demographic context, including social determinants of TB. I hope that the findings from the present study will contribute to the realization of this potential of social science tools to help improve our understanding of the epidemiology of TB.

This study also adds important new information about the association of health insurance status with TB screening and infection prevalence among immigrants. While TB control agencies in the U.S. recognize that a lack of health insurance creates an impediment to TB testing and treatment (CDC, 2005b), the extent to which this issue hampers TB control efforts in the U.S. has been infrequently reported in the literature. The present study showed that a lack of health insurance independently predicts lower TB screening rates. This information is useful to community health centers and clinics providing TB testing and treatment services to populations of immigrants and refugees, as these groups have higher uninsured proportions compared to the native-born population (Geiter, 2000; Ku & Matani, 2001). As local public health departments- traditionally the primary source of outpatient TB care services- begin to share the responsibilities of TB testing and treatment with primary care providers as the federal Affordable Care Act is implemented (California Tuberculosis Controllers Association, 2012), it will become increasingly important for these community-based health care providers to reach immigrants for TB testing, including those who are uninsured. The infection analysis, however, produced the unexpected finding that a lack of health insurance was independently associated with a *lower* likelihood of a positive TB test. An explanation for this unexpected finding may be found in the age distribution of the NIS sample and health selection. New immigrants adjusting to legal permanent residence tend to be concentrated in the 25 to 44 year age group, usually associated with peak economic productivity and potentially selected for good health, from the pool of similarly aged peers in their sending countries who did not emigrate. Respondents in this age group represented the majority of the sample in the infection analysis (64%), and it is possible that they were more likely to hold jobs in places where health insurance is not offered, influencing the significant association between uninsured status and a lower likelihood of a positive TB test. At the health policy level, this result suggests that an expansion of TB testing opportunities to include the insured among new immigrants should result in a manageable level of newly identified TB infections that will need to be assessed for treatment and follow-up, instead of a placing an inordinate burden on already stretched public health resources.

Several statistical relationships tested in the screening and infection analyses did not produce significant associations, warranting some consideration. The finding that diabetes history was not associated with screening uptake was unexpected. Although the biological basis of the associated between diabetes and TB remains unclear, an increased risk of TB disease among diabetics has been documented for decades- TB disease appears to be 2 to 4 times more prevalent among persons with diabetes than among those without this chronic condition (Restrepo, 2007). Therefore it was reasonable to hypothesize that a history of diabetes would predict an increased likelihood of screening for TB (Jeon et al., 2011). That diabetes had virtually no influence on screening uptake (P =.90) is useful baseline information for those public health policy makers considering systematic testing of sub-groups of the diabetic population for TB infection. In the infection analysis, diabetes history did result in an elevated likelihood of a positive test in the bivariate analysis, but not at a statistically significant level (P=.24) and was therefore excluded from the multivariate model.

The finding that men were less likely than women to report a positive TB test is counterintuitive at first. As in the rest of the world, the gender-specific TB disease incidence in the U.S. has consistently been higher among men than women (e.g., 6.9 vs. 4.7 in California in 2012) (California Department of Public Health, 2013). Previous studies based on tuberculin skin test results have found TB infection to be more prevalent among men than women in most situations (Hudelson, 1996; Bennett et al., 2008; Shea et al., 2014). Age- and gender- specific TB incidence data, however, point to one important exception: young and middle-aged adults between 15 and 44 years. In this age group, the incidence of TB disease is higher among women than among men (Hudelson, 1996; Westenhouse et al., 2012). This is precisely the age group that made up the majority of the NIS sample in the infection analysis- Nearly 3 out of 4 respondents were between 18 and 44 years old (Table 5). Given the young age of the study sample, the finding that women were more likely to report TB infection is less surprising, and is actually consistent with what is known about the age- and gender-specific incidence of TB disease. Some researchers have hypothesized the presence of a gender differential in the “breakdown rate” from TB infection to disease among young adults, based on the common joint observation of higher infection prevalence in men but lower disease incidence (e.g., Hudelson, 1996). The present study provides evidence against such a gender differential in the breakdown rate, suggesting instead a gender differential in infection prevalence among young adults.

This study had several limitations. Foremost was the self-reported nature of the TB screening and infection data. Recall bias could have resulted in lowered sensitivity of the screening outcome, because some participants may not have remembered that they had been tested for TB. The literature does provide evidence of good agreement between self-reports of health conditions such as diabetes and medical record data (Goldman et al., 2003; Okura et al., 2004). There are no population-based studies that assess the validity of self-reported TB screening and infection history, and the CDC has stated the need for such validation research (CDC, 2005b). One study of migrant farm workers in North Carolina found a high degree of agreement between self-reported TB history and tuberculin skin test results (Ciesielski et al., 1991). A few published epidemiological studies have used self-reports of TB infection and/or disease as the primary outcome variable (e.g., Harling et al., 2008; Nahid et al., 2011), and the present study takes a similar approach. Further evidence of the usefulness of self-reported data in epidemiological analyses of TB is provided by the finding that patient self-report was shown to accurately predict adherence to treatment for TB infection (Hirsch-Moverman et al., 2008). Another potential limitation is the possibility that a past Bacille Calmette-Guerin (BCG) vaccination could have led some participants to erroneously report that they were “tested” for TB. This is a concern because in most countries outside North America and Europe, the BCG vaccine is routinely administered at birth, and in some countries a booster vaccine is recommended in early childhood (Zwerling et al., 2011). BCG vaccination can increase the likelihood of a false positive result on a TB screening test, especially the tuberculin skin test (TST; also known as purified protein derivative, PPD) (Mazurek et al., 2010). Therefore, it is possible that for an unknown subset of respondents in the infection analysis who reported a positive TB test, that the result may have been due to BCG vaccine and not a result of exposure to TB. However, research suggests that tuberculin skin test reactions induced by BCG vaccine wane over time and become negligible approximately 10 years after vaccine administration (Wang et al., 2002). For these reasons it is reasonable to assume that the majority of the positive TB tests reported by NIS participants reflected exposure to TB rather than BCG vaccine. The NIS was implemented at around the same time that a new class of TB test – the interferon gamma release assay (IGRA) – came into use in the U.S., as a more specific method to diagnose TB infection (Mazurek et al., 2010). IGRAs have been found to produce fewer false-positive results than the tuberculin skin test because the antigens used in IGRAs are more specific to *Mycobacterium tuberculosis,* with little cross-reaction with BCG or non-tuberculous mycobacteria.

Despite the limitations, this study and the sample on which it is based offer several unique strengths. The NIS is the only nationally representative survey designed to specifically target the foreign-born population. Therefore the results can be considered generalizable to the population of U.S. immigrants adjusting to legal permanent residence. Importantly, the analysis includes previously undocumented persons, a group that comprises a substantial portion of the foreign-born TB caseload in the U.S. and about which little is known in terms of TB risk factors. The availability of individual-level data on important covariates such as health insurance, co-morbid conditions and socioeconomic measures provided a unique opportunity to conduct statistical adjustments for the tested associations. These important but infrequently investigated social and medical correlates of TB infection reported here are a reminder that it is not only the country or region of origin of the immigrant that determines his or her risk of TB infection, but also other factors such as educational attainment or health status. This information could be useful in efforts to tailor evidence-based strategies for targeted testing and treatment of TB in the foreign-born population in California. Finally, the sending country-specific estimates provided by this study are useful in disaggregating race/ethnicity categories (e.g.,"Asian" and "Hispanic/Latino") into more precise and practically useful categories that highlight the substantial variation within these monolithic grouping and provide public health policy makers with opportunities to inform more specifically targeted interventions.

Pre-immigration overseas screening of U.S.-bound adult immigrants (legal permanent residents) has been in place since 1991, under the oversight of the CDC Division of Global Migration and Quarantine. In 2007, this screening process was enhanced by the addition of sputum microscopy and sputum culture testing, to improve detection of active TB disease among immigration applications with chest radiograph abnormalities (Lowenthal et al., 2011). Importantly, the primary focus of the current immigration-related screening policy is active TB disease not TB infection, and current testing guidelines do not address post-arrival screening for TB among immigrants (Cain et al., 2007; Alvarez, et al., 2011; Ricks et al., 2011). Should current guidelines be updated to support screening for TB infection of immigrants beyond the five-year arrival mark as some studies have suggested (e.g., Cain & Mac Kenzie, 2008; Walter et al., 2014), the arrival cohort-specific findings of the present study provide evidence that the yield of such testing efforts prioritizing earlier immigrant arrival cohorts (i.e., those U.S. residence > 5 years) will likely be effective in identifying TB infection. This study provides further support for the Institute of Medicine's recommendation for improved outreach to the foreign-born population in the U.S. in order to more effectively and efficiently screen for and treat TB infection (Geiter et al., 2000). The availability of an effective and shorter treatment regimen for latent TB infection, reducing the therapy duration from 9 months to 3 months (Sterling et al., 2011), provides an exciting opportunity to overcome concerns about treatment adherence and to make substantial progress toward the elimination of TB in the U.S.

Table 1. Geographic distribution of the adult sample of the New Immigrant Survey (2003) included in the TB screening analysis.

	N=7,770 Weighted n	Weighted %
U.S. state / region of residence		
California	2,223	28.6
New York	941	12.1
Texas	614	7.9
Florida	592	7.6
New Jersey	466	6.0
New England region	449	5.8
Mountain region	421	5.4
South Atlantic region	420	5.4
Illinois	379	4.8
Middle Atlantic region	402	5.2
Pacific region (other than California)	310	4.0
East North Central region	292	3.8
West North Central region	178	2.3
East South Central region	52	0.7
West South Central region	37	0.5

Table 2. Demographic characteristics of the adult sample of the New Immigrant Survey (2003) included in the TB screening analysis.

	N=7,770 Weighted n	Weighted %
Male gender	3,401	43.8
Age- mean, median (interquartile range)	39, 36	IQR 29 – 46
Age group 18-24	832	10.7
25-44	4,774	61.5
45-64	1,668	21.5
65+	495	6.4
Race/ethnicity		
White, Non-Hispanic / non-Latino	1,531	19.7
White, Hispanic / Latino	2,695	34.7
Black	924	11.9
Asian/Pacific Islander	2,394	30.8
American Indian / Native Alaskan	225	2.9
Region / country of birth		
Latin America	3,404	43.8
Mexico	1,309	16.8
El Salvador	471	6.1
Guatemala	195	2.5
Dominican Republic	178	2.3
Colombia	163	2.1
Haiti	159	2.0
Cuba	140	1.8
Jamaica	133	1.7
Peru	111	1.4
Other Latin America / Caribbean	545	7.0
Asia (except Central Asia)	2,313	29.8
India	562	7.2
Philippines	442	5.7
China	412	5.3
Vietnam	255	3.3
Korea	111	1.4
Other Asia / Pacific Islands	531	6.8
Europe and Central Asia	1,083	13.9
Poland	121	1.6
Ukraine	107	1.4
Russia	101	1.3
United Kingdom	82	1.1
Other Europe and Central Asia	672	8.6
Middle East and North Africa	454	5.8
Ethiopia	109	1.4
Other Middle East and North Africa	345	4.4
Sub-Saharan Africa	412	5.3
Nigeria	112	1.4
Other Sub-Saharan Africa	300	3.9
North America	104	1.3

Notes: Sums of subgroups may not be exact due to rounding error.

Table 3. Immigration characteristics of the adult sample of the New Immigrant Survey (2003) included in the TB screening analysis.

	N=7,770 Weighted n	Weighted %
Immigration admission classification		
Family preference	5,201	66.9
Employment preference	775	10.0
Diversity lottery	634	8.2
Legalization	627	8.1
Refugee	533	6.9
Duration of residence* (Arrival year cohort**)		
< 1 year (2003)	3,546	45.6
1 to 2 years (2001-2002)	800	10.3
3 to 5 years (1998-2000)	990	12.8
6 to 10 years (1993-1997)	963	12.4
11 to 20 years (1983-1992)	1,318	17.0
>20 years (1982 and earlier)	152	2.0

*From first arrival in U.S. to interview. **First arrival in the U.S. Sums of subgroups may not be exact due to rounding error.

Table 4. Bivariate associations between demographic, socioeconomic and health factors and a history of no TB screening.

		Not screened n=2,182	Total n=7,770	Unadjusted OR [95% CI]	*P* value
Gender	Male	973 (28.6)	3,401	Reference	
	Female	1,208 (27.6)	4,369	0.95 [0.85 – 1.07]	.41
Age group	18 – 24	258 (31.0)	832	0.84 [0.64 – 1.09]	.19
	25 – 44	1,237 (25.9)	4,774	*0.65 [0.53 – 0.80]*	<.0001
	45 – 64	514 (30.8)	1,668	0.83 [0.67 – 1.04]	.11
	65 and older	173 (34.9)	495	Reference	
Race / ethnicity	White	312 (20.4)	2,695	*0.37 [0.31 – 0.44]*	<.0001
	Hispanic/Latino	541 (20.1)	1,531	*0.36 [0.32 – 0.42]*	<.0001
	Black	273 (29.5)	924	*0.60 [0.50 – 0.72]*	<.0001
	Asian/Pacific Islander	984 (41.1)	2,395	Reference	
	American Indian	72 (32.0)	225	0.68 [0.47 – 0.96]	.030
Country/region of origin	Mexico	237 (18.1)	1,309	*0.58 [0.44 – 0.78]*	.0003
	Other Latin America	522 (24.9)	2,094	0.88 [0.68 – 1.14]	.33
	India	262 (46.5)	562	*2.30 [1.72 – 3.08]*	<.0001
	Philippines	121 (27.4)	442	Reference	
	China	212 (51.5)	412	*2.81 [2.04 – 3.86]*	<.0001
	Vietnam	94 (36.8)	255	*1.54 [1.05 – 2.25]*	.026
	Other Asia	256 (39.8)	642	*1.75 [1.30 – 2.36]*	<.0001
	Europe/Central Asia	192 (17.8)	1,083	*0.57 [0.43 – 0.76]*	.0002
	Middle East/No. Africa	166 (36.7)	453	*1.53 [1.11 – 2.11]*	.0090
	Sub-Saharan Africa	108 (26.2)	412	0.94 [0.67 – 1.30]	.70
	North America	12 (11.5)	105	*0.34 [0.16 – 0.75]*	.075
Arrival cohort	2003	1,290 (36.4)	3,546	*2.21 [1.86 – 2.62]*	<.0001
	2001-2002	172 (21.5)	800	1.05 [0.81 – 1.38]	.70
	1998-2000	210 (21.2)	990	1.04 [0.81 – 1.33]	.76
	1993-1997	221 (22.9)	963	1.15 [0.90 – 1.46]	.26
	1983-1992	271 (20.6)	1,318	Reference	
	1982 and earlier	18 (11.7)	152	*0.51 [0.29 – 0.90]*	.020
Immigration class	Family preference	1,486 (28.6)	5,201	*1.60 [1.27 – 2.02]*	<.0001
	Employment preference	235 (30.3)	775	*1.74 [1.36 – 2.24]*	<.0001
	Diversity lottery	194 (30.5)	634	*1.76 [1.37 – 2.27]*	<.0001
	Legalization	160 (25.6)	628	*1.38 [1.04 – 1.83]*	.028
	Refugee	106 (20.0)	533	Reference	
Years of education	Fewer than 12	862 (31.1)	2,754	*1.28 [1.14 – 1.44]*	<.0001
	12 or more	1,319 (26.3)	5,016	Reference	
Health care worker	Yes	39 (12.9)	299	Reference	
	No	2,143 (28.7)	7,471	*2.72 [1.84 – 4.01]*	<.0001
Diabetes history	Yes	83 (27.7)	298	Reference	
	No	2,098 (28.1)	7,472	1.02 [0.77 – 1.34]	.90
Health insurance status	Uninsured	1,462 (31.2)	4,691	*1.49 [1.32 – 1.68]*	<.0001
	Insured	719 (23.4)	3,079	Reference	
Accessed health care	Yes	716 (23.0)	3,109	Reference	
	No	1,466 (31.5)	4,660	*1.53 [1.36 – 1.73]*	<.0001

OR: odds ratio, CI: confidence interval. Italics emphasize statistically significant independent associations.

Table 5. Multivariate associations between demographic, socioeconomic and health factors and a history of no TB screening.

	Model 1 aOR [95% CI]	Model 2 aOR [95% CI]	Model 3 aOR [95% CI]
Gender			
Male	1.08 [0.96 – 1.21]	1.08 [0.96 – 1.22]	1.05 [0.93 – 1.19]
Female	Reference	Reference	Reference
Age group			
18 – 24	0.96 [0.73 – 1.27]	1.02 [0.77 – 1.35]	1.14 [0.86 – 1.52]
25 – 44	*0.71 [0.56 – 0.88]*	0.81 [0.64 – 1.02]	0.92 [0.73 – 1.17]
45 – 64	0.84 [0.66 – 1.06]	0.90 [0.70 – 1.14]	0.95 [0.74 – 1.21]
65 and older	Reference	Reference	Reference
Country/region of origin			
Mexico	*0.58 [0.44 – 0.78]*	0.74 [0.54 – 1.01]	*0.57 [0.41 – 0.79]*
Other Latin America	0.88 [0.68 – 1.14]	0.95 [0.72 – 1.26]	0.81 [0.61 – 1.08]
India	*2.32 [1.73 – 3.11]*	*2.44 [1.82 – 3.29]*	*2.16 [1.59 – 2.95]*
Philippines	Reference	Reference	Reference
China	*2.74 [1.99 – 3.77]*	*2.86 [2.07 – 3.96]*	*2.40 [1.72 – 3.36]*
Vietnam	*1.58 [1.08 – 2.31]*	*1.55 [1.06 – 2.29]*	1.27 [0.86 – 1.89]
Other Asia	*1.78 [1.32 – 2.41]*	*1.98 [1.45 – 2.69]*	*1.78 [1.29 – 2.45]*
Europe/Central Asia	*0.58 [0.43 – 0.77]*	*0.66 [0.48 – 0.91]*	*0.61 [0.44 – 0.84]*
Middle East/North Africa	*1.53 [1.11 – 2.12]*	*1.59 [1.13 – 2.25]*	1.42 [0.99 – 2.02]
Sub-Saharan Africa	0.95 [0.68 – 1.32]	1.02 [0.72 – 1.46]	0.95 [0.66 – 1.36]
North America	*0.35 [0.16 – 0.77]*	0.48 [0.21 – 1.06]	0.48 [0.22 – 1.06]
Immigration arrival cohort			
2003		*1.95 [1.53 – 2.47]*	*1.81 [1.42 – 2.30]*
2001-2002		1.08 [0.79 – 1.47]	1.09 [0.80 – 1.50]
1998-2000		1.07 [0.80 – 1.43]	1.10 [0.82 – 1.47]
1993-1997		1.26 [0.96 – 1.65]	1.28 [0.98 – 1.89]
1983-1992		Reference	Reference
1982 and earlier		0.58 [0.33 – 1.04]	0.61 [0.34 – 1.08]
Immigration classification			
Family preference		1.10 [0.85 – 1.45]	1.10 [0.84 – 1.44]
Employment preference		0.87 [0.65 – 1.16]	1.02 [0.75 – 1.37]
Diversity lottery		1.08 [0.79 – 1.45]	1.08 [0.79 – 1.48]
Legalization		*1.75 [1.23 – 2.49]*	*1.56 [1.10 – 2.23]*
Refugee		Reference	Reference
Health insurance status			
Uninsured			*1.20 [1.04 – 1.38]*
Insured			Reference
Years of education			
Fewer than 12			*1.34 [1.16 – 1.54]*
12 or more			Reference
Health care worker			
Yes			Reference
No			*2.23 [1.50 – 3.34]*

aOR: adjusted odds ratio. Italics emphasize statistically significant independent associations.

† The race/ethnicity variable was not included in multivariate model due to collinearity with country/region of origin (data not shown).

‡ The health care access in the past year variable was not included in the multivariate model due to collinearity with the "uninsured" variable (data not shown).

Table 6. Bivariate associations between demographic, socioeconomic and health care utilization factors with a history of a positive TB test.

		Positive TB test n=428	Total n=5,359	Unadjusted OR [95% CI]	*P* value
Gender	Male	161 (6.8)	2,378	*0.74 [0.58 – 0.94]*	.013
	Female	267 (9.0)	2,981	Reference	
Age group	18 – 24	41 (7.3)	557	Reference	
	25 – 44	294 (8.6)	3,408	1.20 [0.78 – 1.85]	.40
	45 – 64	78 (7.0)	1,109	0.96 [0.60 – 1.56]	.88
	65 and older	15 (5.3)	284	0.71 [0.36 – 1.40]	.32
Race / ethnicity	White	61 (5.1)	1,189	Reference	
	Hispanic/Latino	211 (10.3)	2,044	*2.15 [1.51 – 3.05]*	<.0001
	Black	33 (5.4)	607	1.06 [0.65 – 1.75]	.81
	Asian/Pacific Islander	106 (7.8)	1,374	*1.57 [1.08 – 2.27]*	.018
	American Indian	17 (12.0)	145	*2.53 [1.27 – 5.03]*	.0082
Country/region of origin	Mexico	126 (12.5)	1,008	*2.35 [1.57 – 3.52]*	<.0001
	Other Latin America	118 (7.9)	1,483	1.42 [0.97 – 2.10]	.075
	India	18 (6.1)	295	1.06 [0.60 – 1.90]	.84
	Philippines	38 (12.0)	316	*2.26 [1.38 – 3.69]*	.0011
	China	7 (3.5)	196	0.61 [0.29 – 1.26]	.18
	Vietnam	12 (7.2)	160	1.28 [0.64 – 2.56]	.49
	Other Asia	33 (8.8)	372	1.59 [0.93 – 2.74]	.092
	Europe/Central Asia	50 (5.7)	866	Reference	
	Middle East/No. Africa	12 (4.2)	281	0.72 [0.31 – 1.66]	.44
	Sub-Saharan Africa	14 (5.0)	289	0.86 [0.46 – 1.64]	.66
	North America	2 (2.4)	93	0.41 [0.06 – 3.06]	.39
Arrival cohort	2003	96 (4.5)	2,150	Reference	
	2001-2002	38 (6.2)	612	1.41 [0.89 – 2.25]	.15
	1998-2000	55 (7.4)	746	*1.72 [1.15 – 2.56]*	.0084
	1993-1997	73 (10.1)	726	*2.41 [1.66 – 3.51]*	<.0001
	1983-1992	140 (14.1)	995	*3.51 [2.57 – 4.79]*	<.0001
	1982 and earlier	26 (20.1)	129	*5.40 [3.03 – 9.65]*	<.0001
Immigration class	Family preference	252 (7.1)	3,569	*0.68 [0.51 – 0.90]*	.0068
	Employment preference	53 (10.1)	527	Reference	
	Diversity lottery	13 (3.0)	426	*0.28 [0.16 – 0.47]*	<.0001
	Legalization	68 (15.6)	437	*1.65 [1.16 – 2.34]*	.0054
	Refugee	42 (10.5)	399	1.04 [0.70 – 1.56]	.83
Years of education	Fewer than 12	139 (7.9)	1,750	0.99 [0.77 – 1.27]	.91
	12 or more	289 (8.0)	3,608	Reference	
Health care worker	Yes	43 (17.1)	252	2.54 [1.74 – 3.70]	<.0001
	No	385 (7.5)	5,107	Reference	
Diabetes history	Yes	21 (10.4)	206	1.35 [0.82 – 2.23]	.24
	No	407 (7.9)	5,153	Reference	
Tobacco smoking history	Yes	117 (8.2)	1,417	1.04 [0.80 – 1.38]	.74
	No	311 (7.9)	3,942	Reference	
Underweight	Yes	17 (9.6)	179	1.23 [0.67 – 2.26]	.51
	No	411 (7.9)	5,179	Reference	
Health while growing up	Fair/Poor	30 (14.6)	209	*2.04 [1.24 – 3.36]*	.0050
	Good/Very good/Excellent	397 (7.7)	5,145	Reference	
Health insurance status					

		Positive TB test n=428	Total n=5,359	Unadjusted OR [95% CI]	*P* value
	Uninsured	179 (5.8)	3,070	*0.51 [0.40 – 0.64]*	<.0001
	Has health insurance	249 (10.9)	2,288	Reference	
Health care utilization	Did not access care	174 (5.7)	3,049	*0.49 [0.39 – 0.62]*	<.0001
	Accessed health care	254 (11.0)	2,310	Reference	

OR: odds ratio, CI: confidence interval. Italics emphasize statistically significant independent associations.

Table 7. Multivariate associations between demographic, socioeconomic and health factors and a history of a positive TB test.

	Model 1 aOR [95% CI]	Model 2 aOR [95% CI]	Model 3 aOR [95% CI]
Gender			
Male	*0.77 [0.61 – 0.99]*	*0.71 [0.56 – 0.91]*	*0.75 [0.59 – 0.97]*
Female	Reference	Reference	Reference
Age group			
18 – 24	Reference	Reference	Reference
25 – 44	1.23 [0.79 – 1.89]	1.01 [0.65 – 1.57]	0.94 [0.60 – 1.47]
45 – 64	1.00 [0.62 – 1.63]	0.80 [0.48 – 1.32]	0.81 [0.49 – 1.65]
65 and older	0.71 [0.36 – 1.42]	0.78 [0.39 – 1.58]	0.81 [0.40 – 1.65]
Country/region of origin			
Mexico	*2.31 [1.53 – 3.47]*	*1.64 [1.02 – 2.64]*	*1.78 [1.10 – 2.87]*
Other Latin America	1.42 [0.96 – 2.10]	1.01 [0.65 – 1.57]	1.05 [0.67 – 1.64]
India	1.07 [0.59 – 1.91]	1.06 [0.56 – 2.02]	1.11 [0.58 – 2.13]
Philippines	*2.22 [1.35 – 3.64]*	*2.54 [1.48 – 4.34]*	*2.17 [1.21 – 3.87]*
China	0.64 [0.30 – 1.34]	0.73 [0.34 – 1.56]	0.78 [0.36 – 1.70]
Vietnam	1.22 [0.60 – 2.46]	1.60 [0.77 – 3.33]	1.63 [0.78 – 3.45]
Other Asia	1.57 [0.91 – 2.70]	1.71 [0.96 – 3.03]	1.69 [0.94 – 3.02]
Europe/Central Asia	Reference	Reference	Reference
Middle East/North Africa	0.74 [0.32 – 1.70]	0.80 [0.34 – 1.87]	0.81 [0.35 – 1.91]
Sub-Saharan Africa	0.85 [0.45 – 1.62]	0.84 [0.44 – 1.58]	0.75 [0.39 – 1.44]
North America	0.40 [0.05 – 2.92]	0.35 [0.04 – 2.75]	0.28 [0.04 – 2.12]
Immigration arrival cohort			
2003		Reference	Reference
2001-2002		1.31 [0.81 – 2.13]	1.15 [0.71 – 1.88]
1998-2000		*1.56 [1.01 – 2.41]*	1.36 [0.87 – 2.12]
1993-1997		*2.15 [1.43 – 3.24]*	*1.89 [1.24 – 2.89]*
1983-1992		*2.91 [1.95 – 4.33]*	*2.63 [1.76 – 3.94]*
1982 and earlier		*5.38 [2.79 – 10.4]*	*4.47 [2.29 – 8.73]*
Immigration classification			
Family preference		*0.53 [0.38 – 0.75]*	*0.67 [0.47 – 0.97]*
Employment preference		Reference	Reference
Diversity lottery		*0.45 [0.24 – 0.85]*	0.63 [0.33 – 1.20]
Legalization		0.89 [0.54 – 1.46]	1.13 [0.67 – 1.89]
Refugee		1.04 [0.64 – 1.68]	1.21 [0.73 – 1.99]
Health insurance status			
Uninsured			*0.57 [0.44 – 0.74]*
Insured			Reference
Health care worker			
Yes			*2.13 [1.35 – 3.36]*
No			Reference
Health while growing up			
Fair/Poor			*1.73 [1.02 – 2.94]*
Good/Very Good /Excellent			Reference

† The race/ethnicity variable was not included in multivariate model due to collinearity with country/region of origin (data not shown).

‡ The health care access in the past year variable was not included in the multivariate model due to collinearity with the “uninsured” variable (data not shown).

Conclusion

This dissertation contributes several key findings that enhance the understanding of the current decline in the incidence of TB among the foreign-born in California. It found that changes in the composition of the immigrant population by age and duration of residence in the U.S. made a modest contribution to the decline in the incidence of TB in the first decade of the 21st century. Crucially, it revealed an important difference by race/ethnicity whereby the shift in immigration of Hispanics/Latinos made a sizeable contribution to the decline in incidence in that group, whereas shifts in immigration from Asia had a minimal contribution on the decline in incidence. This finding has practical implications for the evidence-based prioritization of targeted TB testing and treatment interventions targeted immigrant communities of specific ethnic backgrounds. The reductions in the volume of recent immigrants of prime working age observed in the Hispanic/Latino group may reverse with improving economic conditions.

The findings of the cohort analysis described in Paper Two suggest that changes in the pattern of immigration to California going back to the early 1990s have had lasting effects on the decline of TB incidence in the first decade of the 21st century. Periods of slowing or reverse of the decline in TB incidence among the foreign-born may be due to cohort effects. Fluctuations in immigration cohort size and composition, and declines in TB morbidity in sending countries are likely contributors to the observed cohort effects. Identifying cohorts with elevated risk of TB can help develop and test hypotheses on the epidemiologic reasons for the observed effects, and can provide an evidence base for selecting demographic subgroup candidates for prioritizing TB screening.

The findings of the analysis of New Immigrant Survey data suggest key gaps in the testing for TB among immigrants by country of origin. Screening among Chinese, Indian and other Asian immigrant groups significantly lags behind that of Filipino and Vietnamese groups, suggesting opportunities for improving targeted TB screening efforts in specific communities of immigrants in the U.S. Efforts to reach the undocumented population and persons without health insurance coverage to increase TB testing coverage need improvement. The overall prevalence of latent TB infection among the foreign-born suggested by the present study is lower than reported in the literature. The elevated risk of TB infection among Philippine-, Mexican- and Asian-born persons other than Vietnamese, Chinese and Indian reflects the high group-specific TB disease incidence rates in these strata. Refugees, previously undocumented persons and diversity visa immigrants had similar a risk of TB infection as economic migrants, suggesting similar TB exposure environments in the sending countries and less social stratification of TB risk than might be expected. Occupational exposure in the health care setting appears to be an important risk factor for LTBI among immigrants. The associations between educational level, poor self-rated health status, and LTBI has previously not been explored and the significant associations found in this study may aid in further focusing targeted TB testing strategies to fit socioeconomic characteristics in immigrant communities.

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