Foreign-born pulmonary tuberculosis in Washington State, 2009-2013: analysis of cases based on visa type and overseas screening status

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Abstract

Foreign-born pulmonary tuberculosis in Washington State, 2009-2013: analysis of cases based on visa type and overseas screening status

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Tuberculosis (TB) disproportionately affects foreign-born persons in Washington State in the US overall. While foreign-born persons entering the US with a refugee or immigrant visa are screened for active TB disease overseas, nonimmigrant visa holder's such as those entering temporarily as students, employees or tourists do not require an overseas TB screening. Little is known about the burden of TB specifically in foreign-born persons not receiving an overseas TB screening. This retrospective cohort study is the first to analyze characteristics and risk factors associated with pulmonary TB in foreign-born persons diagnosed in Washington State who did not receive an overseas TB screening.

Objective: This study sought to understand the burden of active TB disease among foreign-born persons in Washington State based on visa type and overseas screening status. It achieved this by determining the overseas TB screening status of TB cases among foreign-born individuals reported in Washington State, describing the characteristics of foreign-born cases of active TB reported in Washington State who did not receive a pre-travel overseas TB screening, and identifying opportunities for targeted interventions in the foreign-born population in Washington and the US that does not receive pre-travel overseas TB screening.

Methods: The overall study cohort consisted of 592 foreign-born pulmonary TB cases diagnosed in Washington State between January 1st, 2009-December 31st, 2013. The cohort was then stratified based on overseas screening status (not screened, screened, or unknown). The sub-cohort of cases who were not screened was further stratified based on nonimmigrant visa type (student, tourist, employment, other immigration status). Descriptive and analytic analyses were performed in order to describe characteristics of the study cohort based on overseas screening status and nonimmigrant visa type.

Results: Characteristics of TB among the overall study cohort include 90% being culture positive, 47% being sputum smear positive with 50% being linked to a genotyped cluster of cases, and 75% being sensitive to all TB medication. In terms of TB risk factors diabetes was found to be significantly more prevalent than other risk factors analyzed. When stratified by overseas screening status; 53% received an overseas TB screening, 22% did not have an overseas TB screening, and 25% had an unknown screening status.

Significant differences were noted amongst the stratified groups for race/ethnicity, country of origin, mean age at arrival, and mean age at diagnosis. Stratification based on nonimmigrant visa type showed significant differences amongst the stratified groups for race/ethnicity, country of origin, mean age at arrival, and years between arrival and diagnosis.

Conclusion: This study was able to describe the burden and characteristics of pulmonary TB disease among foreign-born persons in Washington State who did not receive overseas TB screening, as well as among the entire cohort of foreign-born pulmonary TB cases. This study contributed to knowledge of the burden and characteristics of foreign-born pulmonary TB cases in Washington State, especially those without an overseas TB screening. This information helped identify opportunities for targeted interventions and policy changes to address TB in the Washington State foreign-born population. These interventions and policy change recommendations are targeted to national, state, and local government agencies as well as other stakeholder's. Interventions involving all of these levels will be needed to reach the goal of TB elimination.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

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I. Introduction

Tuberculosis (TB) is one of the world's deadliest diseases with nearly 9 million people becoming sick with active TB disease and causing nearly 2 million TB-related deaths each year. In addition, it is estimated that approximately one third of the world's population are infected with TB, harboring a dormant infection that may progress to active TB disease at any time.[i] Despite these staggering statistics, many people in the US think that TB is a disease of the past and is no longer a threat. After all, the incidence of TB in the US has dropped dramatically over the past three decades. However, more than 11 million people in the US have a latent TB infection. About five to ten percent of these latent infections will progress to TB disease resulting in more than 550,000 cases of active TB disease.[i] In 2012, there were 9,951 new TB cases reported in the US.[ii]

TB is caused by the organism *Mycobacterium tuberculosis*. When someone with infectious active TB disease of the lungs or throat coughs, sneezes, speaks, or sings infected droplets are expelled into the air and can be breathed in by others. If inhaled, the droplets may then enter the lungs and cause TB infection. Most persons with TB infection are unaware they are harboring the bacteria.

TB bacteria are able to live in the human body in a dormant state. This is known as latent TB infection (LTBI) and the person does not feel sick and is not contagious. Antibiotics can be prescribed to eradicate TB while it is in this latent state. If antibiotics are not taken there is a five to ten percent chance that the LTBI may progress to active TB disease. If this were to occur, the person would most likely be symptomatic and possibly contagious.

There are well known risk factors associated with both acquiring TB infection and progressing to active TB disease. Factors which make a person at high risk for acquiring infection tend to include social and environmental factors such as being foreign-born, living or working in a congregate setting, or having been around someone with infectious TB disease. Risk factors for progressing from LTBI to active disease tend to be associated with medical issues such as having a weakened immune system due to a medical condition or being on immunosuppressive medications.

The US has been successful in decreasing the incidence of TB throughout the country. Much of the credit for this decline is attributed to rapid case finding, investigation of contacts to infectious cases, strong treatment standards, and the ability to screen and offer treatment for LTBI. Yet despite the progress, the rate of decline in TB incidence is slowing and foreign-born persons and racial/ethnic minorities bear a disproportionate burden of TB disease in the US.[ii] Since 2000 the rate of TB in US-born persons declined by 57.6%, while the rate of TB in foreign-born persons in the US only declined by 18.1%.[ii] In cities that are home to many newly arriving immigrants and refugees rates of TB are often well above the national average.[iii] Washington State data reflects this trend with 75-80% of cases being in foreign-born individuals, and the incidence rate in King County, where the largest proportion of foreign-born residents live, is nearly double the Washington State overall case rate.[iv]

The Centers for Disease Control and Prevention (CDC), recognizes the burden of TB disease in the foreign-born population and has included recommendations to address this problem in published TB elimination strategies. Specifically, one of the

strategies is to engage in global TB prevention and control by providing leadership, technical support, and forming international partnerships. It goes on to say that worldwide control of TB is in the nation's best interest.[i]

One way the US government attempts to mitigate the effects of global TB within the country is by requiring a TB screening prior to arrival in the US for persons seeking permanent residency in the US as a refugee or immigrant.[v,vi] An overseas TB screening is not required for persons entering the US with a non-immigrant visa such as a student, tourist or work visa[vi] (see table 2).

This study seeks to answer the question: **What is the burden of active TB disease among foreign-born persons in Washington State who did not receive overseas TB screening prior to their arrivals in the US?**

Objectives and Outcomes of the Study

The objectives of this study are to:

a. determine the overseas TB screening status of TB cases among foreign-born individuals reported in Washington State
b. describe the characteristics of foreign-born cases of active TB reported in Washington State who did not receive a pre-travel overseas TB screening, and
c. identify opportunities for targeted interventions in the foreign-born population in Washington and the US that does not receive pre-travel overseas TB screening

Upon completion of this project, Washington State and CDC will be better able to determine the burden of active TB disease among foreign-born persons in the US who did not receive an overseas medical exam prior to their arrivals in the US.

The desired outcomes of this study are to:

a. gain knowledge of the burden of active TB among foreign-born who did not receive an overseas TB screening
b. gain knowledge of demographic characteristics and risk factors for TB among foreign-born who did not receive an overseas TB screening, and
c. recommend changes in policy for targeted interventions among foreign-born who did not receive an overseas TB screening

II. Background and Significance

TB is imported into the US through foreign-born persons by one of two ways; either persons with active TB disease cross the US border, or persons with LTBI convert to active TB disease after arrival in the US.[vii] Screening persons for TB before they arrive in the US has been shown effective in diagnosing hundreds of TB cases and saving millions of dollars in healthcare expenses. At this time, overseas TB screening is only completed on persons applying for specific US visas.[xi]

Foreign-born persons arriving in the US are classified based on their visa status at the time of arrival. Those who intend to permanently reside in the US are granted an immigrant or refugee visa, and those who are in the US temporarily are granted a nonimmigrant visa such as a student, work, or tourist visa. Approximately 163.5 million foreign-born persons are admitted to the US each year. About 500,000 are immigrant or refugee visa holders, and 163 million are nonimmigrant visa holders.[viii] In addition, approximately 11.5 million undocumented immigrants were living in the US in 2011.[ix] While millions of nonimmigrant visa holders and undocumented persons enter the US each year, research on the health status of these populations is limited[x] partly because they do not receive overseas medical examinations to gain entry to the US.

Overseas TB screening is required for immigrants and refugees entering the US. TB screenings are conducted by panel physicians according to technical instructions developed and overseen by the Centers for Disease Control and Prevention (CDC). The most recent update to the technical instructions in 2007 requires all US-bound

immigrants and refugees ≥15 years of age to be screened for TB using chest radiograph, followed by sputum culture for those with an abnormal chest radiograph suggestive of tuberculosis. Drug susceptibility testing is conducted on positive cultures and directly observed therapy (DOT) is provided for the entire treatment course.[xi] The overseas TB screening aims to prevent the importation of TB into the US and identify immigrants and refugees with suspected TB for expedited follow-up evaluations in the US.[viii] Those identified as having TB disease or those needing an expedited domestic follow-up evaluation are assigned a TB classification status such as class A or class B (see table 1). This begins a notification process so that the jurisdiction receiving the class B refugee or immigrant can initiate a domestic follow-up evaluation within 30 days of the immigrant or refugee's arrival in the US.[xii] Domestic TB screening includes a physical exam and medical history, TB test if not completed overseas, chest radiograph if indicated, and laboratory diagnostics if indicated.[xiii] Refugees without a TB classification still undergo domestic TB screening as part of their adjustment of status requirements, however, they are not held to the same "within 30 days of arrival" timeline as those with a TB classification.[xiv]

While immigrant and refugee visa holders receive one or more TB screenings during the migration process, overseas TB screening is not required for individuals entering the US under a nonimmigrant visa. Domestic TB screening is only required for nonimmigrant visa holders if they adjust their status and stay in the US as a permanent resident.[vi] Countries which screen refugees and immigrants for active TB prior to arrival

have been shown to be less likely to have a high incidence of TB[xv], and overseas screening for TB with follow-up evaluation after arrival in the US has been shown to be a high-yield intervention for identifying TB in US-bound immigrants and refugees.[xvi] For nonimmigrant visitors to the US, screening all of these visa holders has been considered infeasible and of low-yield due to the large volume of annual admissions and the overall low TB rate.[xvii,xviii] However, a recent study showed that between 2001-2008, nonimmigrant visa holders in the US made up approximately 58% of TB cases among newly arrived foreign-born persons, while immigrants and refugees made up approximately 42%. Of the newly arrived nonimmigrant cases, approximately 95% were from a country considered to have a medium or high-incidence of TB suggesting that screening nonimmigrant visa holders from medium and high-incidence countries, with extended stays in the US, may be an effective intervention. [viii]

Other countries, including Canada and the United Kingdom require TB screening for nonimmigrant visa holders from medium and high-incidence countries who will be in the country for an extended period of time.[xviii,xix] Australia requires overseas TB screening for student and tourist visa holders. One study showed that over 45 % of TB cases detected in Australia's overseas screening program were intending students and tourists.[xx]

In the US, from 2001-2008, 230,673,431 persons entered under a tourist visa and 22,328,345 entered with a student or work visa. While student and work visa holders had far fewer arrivals then tourist visa holders, they contributed to the TB case rates much more. During this same time period, over 4200 cases of TB were diagnosed in

persons with a student or work visa, compared to approximately 1500 in tourist visa holders.[viii]

Domestic TB screening for student visa holders has been considered especially for those attending a college or university. Despite recommendation from the American College Health Association to perform TB testing in all incoming international students from medium and high-incidence countries,[xxi] higher education TB policies vary throughout the country. Kansas is one of the first states to put into law that high-risk incoming college students be evaluated for TB. This comes after finding that 15-20% of active TB cases each year were among international college students.[xxii] A review of Washington State colleges and university's suggested that most TB screening requirements are based on the program the student is entering, for example a healthcare program, and not on the student's individual risk factors. For work visa holder's, it is unlikely that any domestic TB screening is performed unless their place of employment requires it. In Washington State, only facilities that provide healthcare or childcare are required to have employees undergo a TB screening.

Like nonimmigrants, undocumented immigrants do not receive overseas TB screenings. They are more elusive to the US healthcare system compared to other populations. Fear of immigration authorities, uncertainty about where to go for care and lack of a primary care provider contribute to the difficulty in preventing and diagnosing TB in this population.[xxiii] Interestingly, it is estimated that 40% of undocumented immigrants arrived legally with a nonimmigrant visa and overstayed their periods of authorized admission.[xxiv] An estimate of the percentage of TB cases in

undocumented immigrants is difficult to determine due to the lack of this data in the US National TB Surveillance System.[viii] However, undocumented immigrants are coming from many countries with high rates of TB such as Guatemala, Philippines, India, and Vietnam.[viii]

Screening for, identifying, and preventing TB in high-risk, foreign-born individuals is important from both a financial and public health perspective. Treatment regimens are expensive and if not treated successfully, it can lead to transmission in the community resulting in subsequent cases of TB and additional cost. Each case of non-drug resistant TB costs approximately $17,000 to treat.[xxv] These costs include laboratory and radiology diagnostics, medications, directly observed therapy, and other case management activities. In Washington State, county health departments are responsible for assuring the person with TB is treated which includes bearing the financial burden for TB cases that do not have the means to pay.[xxvi] This can create a difficult financial situation for health departments which are primarily funded through local tax dollars, especially if the TB case has a multi-drug resistant (MDR) strain.

MDR TB disproportionately affects the foreign-born population who make up 82.7 percent of MDR cases in the US[xxvii]MDR TB is defined as TB that is resistant to at least Isoniazid and Rifampin, two of the most effective anti-TB drugs. MDR TB is significantly more expensive to treat than drug sensitive strains costing $134,000 on average in direct costs.[xxv] One case of MDR TB has the potential to bankrupt a health department. Overseas tuberculosis screening of immigrants and refugees identified

hundreds of TB cases, including many MDR cases that would have otherwise gone undetected until after arrival in the US. This saved taxpayers roughly $15 million dollars.[xxviii]

Not only is treatment for TB cases costly, a significant amount of resources are spent on finding, screening, and potentially treating those who were exposed to an infectious case. For each case of TB, approximately 20-30% of people identified as contacts to the case have LTBI, and 1% have TB disease. Those who are infected are at highest risk for progressing to active disease within the first two years after infection.[xxix] The more advanced a person's TB disease is, the more infectious they are likely to be. Early identification of infectious cases is key in order to decrease transmission. For foreign-born differences in insurance coverage, health beliefs, and health seeking behavior may contribute to delay in seeking treatment and subsequent delay in diagnosis.[xxx] Delay in diagnosis correlates with more advanced disease and higher infectivity.[xxxi] One study showed that undocumented immigrants tended to be more symptomatic then documented immigrants[xxxii] making them more at risk for being infectious.

Nonimmigrants and undocumented immigrants may represent a percentage of the foreign-born population at increased risk for TB due to lack of overseas screening and domestic follow-up TB screening. This risk not only affects the individual, but also the health and wellness of the community in which they live. This study retrospectively reviews foreign-born cases of TB in Washington State who did not receive an overseas

TB screening, in order to describe the characteristics of the cases and the impact they have on TB incidence in the state.

III. Methods

This project retrospectively describes active pulmonary tuberculosis in foreign-born persons diagnosed between 2009-2013 in Washington State based on visa type and overseas screening status. The CDC, Washington State Department of Health (DOH), and the University of Washington Institutional Review Boards reviewed and approved all study procedures giving this project an exempt status.

Study Setting

This descriptive retrospective study evaluates foreign-born TB cases without an overseas TB screening who were diagnosed with TB in Washington State from 2009-2013. Washington State is considered a medium TB incidence state with 209 TB cases being reported in 2013.[iv] In 2012, an estimated 918,491 foreign born persons were residing in Washington.[xxxiii] Also since 2009, Washington's percentage of TB cases among foreign-born has been greater than 70 percent.[xxxiv] All TB cases diagnosed in Washington are reported through a database which contains health information and patient demographics. DOH is then responsible for aggregating the data and reporting the information to CDC.

Cohort Selection

The study cohort consisted of all verified cases of active pulmonary TB, reported in Washington State, from January 1, 2009 through December 31st,2013 among persons born to non-US citizen parents in a country other than the US or any US territory. Cases

of TB diagnosed in foreign-born individuals with a site other than pulmonary were excluded from this study because extra pulmonary sites of disease are not considered a public health threat and are not routinely screened for during an overseas medical exam. Persons with pulmonary TB were defined as laboratory confirmed, clinical confirmed, or provider diagnosed case of TB with a site of disease in the lungs (see table 3).

Data Sources

Data collection for the entire time period was consistent for the variables used in this study. The CDC established standardized reporting of certain variables outlined in the Report of Verified Case of TB (RVCT) requirements. These requirements were initiated in 1985, and remain in use with the most recent update being in 2009.[xxxv]

The project used three databases to extract data to be analyzed. The information from each database was provided by the Washington State DOH TB Program. The primary database was the Public Health Information Management System-TB (PHIMS-TB). PHIMS-TB is an electronic database containing information on all reported TB cases from 1993 to the present. Local health jurisdictions (LHJs) report patient demographics and health information through this system. Data entered into PHIMS-TB is closely monitored by Washington State DOH and quality assurance checks are performed quarterly at minimum.

The second database used was CDC's Electronic Disease Notification System (EDN). EDN contains demographic and health information on all refugees and immigrants with a class B TB status, who had an overseas TB evaluation prior to arriving in the US from 2009 to the present. The database also documents and tracks medical evaluation and medical care follow-up among refugees and immigrants entering the US with a TB classification.

The third database used was the CDC's Tuberculosis Genotyping Information Management System (TBGIMS) which collects, catalogues and associates by genetic profile, specimens collected from culture-confirmed cases of TB throughout the US. Specimens sharing an identical genetic profile are considered to be of the same mycobacterium strain and are assigned a unique strain identity. Cases within Washington State that share the same strain identity represent a cluster and are assigned a state-specific cluster number.

Analysis Plan

1. Stratify by overseas screening status

In order to determine the overseas TB screening status of TB cases among foreign-born individuals diagnosed in Washington State, all foreign-born cases of pulmonary TB diagnosed in Washington State from 2009-2013, were categorized based on their visa status upon US arrival. Using the available visa status information and knowledge of overseas screening practices according to visa type, the cohort was stratified by the

following statuses: received overseas TB screening, no overseas TB screening, and overseas screening unknown.

2. Analyze characteristics of cohort based on overseas TB screening status

In order to describe the characteristics of foreign-born cases with active TB in Washington State who did and did not receive a pre-travel overseas TB screening, cases stratified by overseas screening status were summarized on characteristics such as age, sex, country of birth, age at arrival, age at diagnosis, time between arrival and diagnosis drug susceptibility results (pan-sensitive, mono- and multidrug-resistant TB), and other co-factors such as HIV/AIDS, diabetes, and other immunosuppression, as well as history of TB, likelihood to transmit, and genotype/cluster data.

3. Stratify cohort of foreign-born cases who did not receive an overseas TB screening by nonimmigrant visa status

In order to further investigate groups not receiving overseas TB screening, those with a nonimmigrant or "other" visa status were stratified by nonimmigrant visa types including work visa, student visa, tourist visa, and other.

4. Analyze characteristics of nonimmigrant visa type cohort

In order to describe the characteristics of foreign-born cases of active TB reported in Washington State by nonimmigrant visa type, cases stratified by nonimmigrant visa type were summarized on characteristics as mentioned above in number two.

Data Preparation

All data management and analyses were performed using the SAS statistical software package, version 9.3 (SAS Institute Inc.; Cary, NC USA). Before the analysis began data were cleaned and reconciled as needed. Data cleaning began by pulling all foreign-born pulmonary TB cases diagnosed 2009-2013 from PHIMS-TB. The Washington State DOH TB program ran study data through quality assurance (QA) programming to identify records showing inconsistency or absence of key data elements to be used in analyses. As much as possible data were obtained and corrected to provide the most accurate data set.

Stratification by overseas TB screening status:

In order to most accurately stratify by overseas TB screening status, cases of TB within the study cohort captured in PHIMS-TB were matched to data records obtained from EDN. The purpose of the match was to confirm that the immigration status for refugees and class B TB immigrants, as well as the date of arrival to the US, was accurate.

Matching was performed using the probabilistic record linkage software program Link Plus version 2.0, as developed by CDC. Study cohort records were matched to those from EDN using first name, last name, and date of birth as matching variables. Matched pairs assigned a match-score of six or above were manually reviewed to visually evaluate, resolve and confirm matches.

Once the match was complete the cohort was stratified into the following groups:

1. No overseas TB screening- which includes persons having arrived in the US with an employment, student, tourist visa or other immigration status. Because PHIMS-TB does not explicitly elicit undocumented immigration status, persons with this status are reported as having "other" immigration status (see table 2).

2. Received overseas TB screening- which includes those having arrived in the US with an immigrant or refugee visa (see table 2).

3. Overseas screening unknown- which includes persons having arrived in the US with an asylee, parolee, family, or fiancé visa, or unknown or unreported immigration status.

Stratification by specific visa status at first entry to US:

The sub cohort that did not receive an overseas TB screening was further stratified by visa status at first entry to the US. These stratification groups included:

1. Work visa, which includes persons who obtained a visa to work for a specific period of time including migrant work.

2. Student visa, which includes persons who obtained a visa for a specific period of time to pursue a full course of study in an approved institution.

3. Tourist visa, which includes persons who obtained a visa for a specific period for business or pleasure.

4. Other, which includes those who entered with no official immigration status and those entering the US for <= 90 days from a country that is part of the US visa waiver program (e.g. Canada).

Calculation of age at TB diagnosis:

Dates of diagnosis were assigned consistent with the time when case-verifying evidence, as outlined in a CDC-defined schema for determining case verification (see table 3), was available. For example, in this schema positive culture results are ranked as the most definitive evidence for verifying a case of active TB. For culture confirmed cases within the study cohort, the date of diagnosis was defined as the earliest collection date for culture-positive specimen(s) on record. Assignment of diagnosis dates for clinically confirmed cases proceeded similarly, using the earliest date of specimen collection (or antigen placement date in the case of skin test). For those cases without any positive biological evidence on record (e.g. provider diagnosed), the date of diagnosis was set equal to the date of first case report to public health authorities. Once dates of diagnosis were assigned as described above, age in years at diagnosis was calculated from the date of birth on record, dividing elapsed days by 365.25 to account for leap year events.

Classification of country of birth:

Country of birth was categorized to best describe the unique demographic of this study cohort, while also preserving the distinct identity of cultures that have seen

notable shifts in representation due to global events (e.g. influx of persons fleeing civil strife or natural disaster). The country of birth profile of this study cohort represents a frequency-ordered tabulation of countries of birth on record, including all countries accounting for 2 percent or more of the total. In addition, select countries that have seen notable shifts in their representation due to contemporary world events (e.g. Burma) were also included among distinct entries. All other countries of birth were aggregated into the classification of "other."

Medical risk factors:

Select data from PHIMS-TB regarding additional TB disease risk factors present at the time of diagnosis were stratified into those representing principal medical-related risks for TB. Classification of medical risk included diabetes, HIV, other immunosuppression, history of TB disease, and any comorbidity among these individual risks.

Genotyping data:

Data from TBGIMS were used to examine the extent of state-specific clustering and the role that any clustered case may have played within the given chain of transmission in Washington. TBGIMS data were linked to all Washington TB case records verified from January 1st, 2000 to March 31, 2014, using the case's unique state case identification number for linkage. Cases were ordered by assigned cluster and then in ascending order of collection date of the genotyped specimen as recorded in TBGIMS. In

cases for which these TBGIMS date data were missing or otherwise invalid the earliest specimen collection date recorded from the TB case record was imputed.

Once the cases were chronologically ordered they were then numbered sequentially with the case having the earliest specimen collection date being assigned the number one. Cases assigned the value of one in this sequential numbering represented the first known case within the Washington cluster.

Data Analysis

Descriptive analyses:

Analyses were performed separately for both the entire study cohort (n=562), and a sub-cohort of cases who did not receive overseas medical examination as per visa status upon entry to the US (n=126). For each group these analyses were performed both overall and by select stratification (overseas medical exam status, and specific visa status at first entry to the US). Continuous study variables (age at arrival to US, age at diagnosis, and time from arrival to diagnosis) were analyzed both in raw form, and as classified by select, mutually-exclusive categories. Means, medians and standard deviations were calculated for continuous study variables. Frequencies and proportions were calculated for all categorical and nominal study variables.

Analytic analyses:

One-way analyses of variance was used to investigate differences in means of continuous variables overall across strata defined for analyses, and in pair-wise

comparisons between individual strata. Tests for homogeneity of variance were simultaneously performed, with variance-weighted p-values reported when the assumption of equal variance was not present. Pearson chi-square tests were performed to investigate unadjusted association between categorical or nominal study variables and defined analytic strata. When tabular data were sparse (cell counts less than five), p-values were reported as estimates of exact statistics generated using Monte Carlo methods. Under the assumption of an underlying Poisson distribution, 95% confidence intervals for proportions were calculated to investigate differences in overall prevalence of defined medical risks as well as confirmed treatment completion within the entire study cohort.

IV. Results

There were 562 foreign-born active pulmonary TB cases reported in Washington State between 2009 and 2013. This represented 73.1% of all pulmonary TB cases reported in Washington State during that time period.

The overall study cohort (see table 4) was 57% (n=321) male and 43% (n=241) female; 39% (n=218) arrived in the US between the ages of 25-44 with the average age at arrival being 34.8 years (SD=17.7). Overall, 60% (n=336) were reported as being of Asian race/ethnicity, 17% (n=98) were reported as Hispanic, and 15% (n=85) were reported as black (see figure 1). The top three countries of birth reported in the cohort were The Philippines (19%, n=105), Mexico (14%, n=80) and Vietnam (13 %, n=73).

The average age at TB diagnosis was 47.8 (SD=21.2), with 38% (n=216) being diagnosed between the ages of 25-44 years. The average time from arrival to the US to TB diagnosis was 12.6 years (SD=12.7); 28% (n=155) had 20 or more years between arrival and TB diagnosis.

Characteristics of TB disease in this cohort included 90% (n=505) being culture positive, 7% diagnosed as a clinical case, 2% provider diagnosed, and 1% diagnosed based on a positive NAAT result (see table 3). The majority, 75% (n=424) were sensitive to the first four-line drugs Isoniazid, Rifampin, Pyrazinamide, and Ethambutol. No significant difference was observed when classified by select levels of drug-resistance (p=0.8137). However, 8 (1.4%) of cases were found to have multi-drug resistant disease strains (MDR-TB) resistant to both key first-line drugs isoniazid and rifampin which

accounted for 67% of all MDR-TB cases counted in Washington during the same time period. Whether reported in isolation, or together with another of the select medical risk factors analyzed (see figure 2), diabetes was significantly more prevalent among the study cohort (95% CI= 16.7%-24.4%), as compared to other medical risk factors—History of TB (5.4%-10.1%); Other immunosuppression (5.1%-9.7%); and HIV (1.8%-4.8%). Analyses of treatment completion for the study cohort showed that 456 (81%) cases were confirmed as having completed treatment.

In terms of likelihood to transmit TB, the cohort was analyzed based on a hierarchy of laboratory and radiology findings with sputum smear positivity *and* a cavitary radiology finding being the highest transmission risk, followed by sputum smear positive without a cavitary radiology finding, and the lowest transmission risk being sputum smear negative. In the study cohort, 24% (n=137) were sputum smear positive with a cavitary radiology finding, 23% (n=129) were sputum smear positive without a cavitary radiology finding, and 48% (n=270) were sputum smear negative. Based on genotyping data, 50% (n=278) were linked to a cluster of TB cases in Washington State, and 23% (n=65) were the first case reported in a cluster.

Based on the medical examination requirements for visas and self-reported visa status upon first entry into the US the study cohort was stratified by overseas screening status (see table 4); 53% (n=297) had received an overseas TB screening, 22% (n=126) had not received a TB screening overseas, and for 25% (n=139) it was unknown whether or not they had received an overseas TB screening. Distribution of race and ethnicity differed significantly across the study cohort (p=<0.0001). Notable differences include,

of those with no overseas TB screening, 51% (n=64) reported being of Hispanic ethnicity, 70% (n=207) of those who received an overseas TB screening and 58% (n=81) of those with an unknown overseas screening status 58% (n=81) were reported as being of Asian race. Distribution by countries of origin also differed significantly (*p*=<0.0001). The countries most frequently represented were The Philippines (19%), Mexico (14%), and Vietnam (13%).

Significant differences in the mean age at arrival (p=0.0004) were found amongst stratified groups (see figure 3) with the highest average age being in those that received an overseas TB screening (37.3 years) compared to those with no overseas TB screening (30.1 years) and those whose overseas screening status was unknown (33.6 years). The average age at diagnosis also showed significant differences (*p*=0.0003) amongst the stratified groups (see figure 4). Those who received an overseas TB screening were older (50.4 years) compared to those who did not receive and overseas TB screening (41.3 years) and those whose overseas screening status was unknown (48 years). No significant differences were found when analyzing the time between arrival in the US to TB diagnosis. The average time from arrival to diagnosis for those whose overseas screening status was unknown was 14 years, for those with no overseas TB screening, 11 years, and for those that received an overseas TB screening, 13 years.

Cases who did not receive an overseas TB screening were further stratified by visa type at entry into the US (see table 5); 18% (n=23) were student visa holders, 16% (n=20) were tourist visa holders, 11% (n=14) were work visa holders, and 55% (n=69)

had an “other” immigration status such as undocumented or those entering the US for less than 90 days from a visa waiver country.

Of those who entered the US with a student visa, 87% (n=20) were reported as being Asian, 65% (n=13) of those who entered with a tourist visa were reported as being Asian, 79% (n=11) of those who entered with a work visa were reported as Asian and of those with an other immigration status, 86% (n=59) were reported as being Hispanic (p=<0.0001, see figure 5). For country of birth, 26% (n=6) of those who entered with a student visa reported Vietnam as their country of birth, 15% (n=3) of those who entered with a tourist visa reported Ethiopia as their country of birth, 36% (n=5) of those who entered with a work visa reported India as their country of birth and 71% (n=49) of those who entered with an other immigration status reported Mexico as their country of birth (p=<0.0001).

The average age at arrival in the US (see table 6) for tourist visa holders (45.3 years) was significantly higher than student visa holders (23.9 years), those with an other immigration status (27.2 years), and work visa holders (32.2 years; p=0.0008). No significance was found in the average age at diagnosis which was 50.9 years for tourist visa holders, 41.2 years for work visa holders, 39.9 years for those with an other immigration status, and 37.4 years for student visa holders. Significant differences in the mean time from arrival to diagnosis (p=0.0208) were found amongst stratified groups (see figure 7) with student visa holders having the longest time (13.1 years), followed by those with an other immigration status (11.6 years), work visa holders (8.6 years), and

tourist visa holders (5.3 years). Over 20% of those who entered with a work visa, student visa, or other immigration had 20+ years between arrival and diagnosis.

When analyzing confirmed treatment completion data by nonimmigrant visa type it was found that 86% (n=12) of work visa holder's, 85% (n=17) of tourist visa holder's, 74% (n=17) of student visa holder's, and 68% (n=46) of those with an other immigration status had confirmed treatment completion reported. Confidence intervals calculated on this analysis did not show these findings to be significant.

V. Discussion

This study reinforced that, as also throughout the US, foreign-born persons from TB endemic countries represent a disproportionate burden of TB in Washington State. Despite current interventions, such as overseas TB medical exams for immigrants and refugees, and CDC recommendations for targeted TB screening of foreign-born persons from TB endemic countries, the proportion of foreign-born TB cases remains high. Over half of foreign-born TB cases in Washington State received an overseas medical exam and nearly a quarter of foreign-born cases are not required to have an overseas medical exam. These TB cases may be the effect of gaps in the current system. In order to identify the gaps and develop effective interventions, an understanding of this population in terms of their TB risk and characteristics is necessary. This study helped develop this understanding of foreign-born cases in Washington State.

Demographic characteristics of cases

According to national surveillance data, foreign-born persons of Asian, Black, and Hispanic race/ethnicity make up the majority of TB cases within the US [xxxvi] . This study found this same trend to be true among the study cohort with significant association found among these same racial/ethnic groups. National surveillance data also shows the top 5 countries of origin for foreign-born cases as being Mexico, Philippines, India, Vietnam and China. [xxxvii] This study was similar in that The Philippines, Mexico, Vietnam and India were in the top 5 countries of origin reported. While Asian race and having an Asian country of birth was most frequently reported for the overall study cohort,

Hispanic ethnicity with Mexico as country of birth was most often reported for those with no overseas medical exam and more specifically those with an other immigration status. Because Mexico is not part of the visa waiver program (see table 2), it is likely that these cases arrived with an undocumented status. Unscreened upon entry, and ineligible for subsidized medical insurance, undocumented persons with active disease may not be detected until later stages of disease which may increase the likelihood of transmission to others, as well as poor treatment outcomes.[xxx,xxxi,xxxii] The impact of the cost to county health departments to treat persons who are uninsured is also a concern and adds to the necessity of preventing TB disease in this population.

Among this study's cohort, those diagnosed between 25 and 44 years of age accounted for the largest proportion of this study's cohort which is consistent with national surveillance data. [xxxviii] Due to the fact that this age group is the most productive in terms of work and childbearing, TB disease can lead to loss of productivity. Loss of productivity may be due to a variety of reasons such as fatigue, medication side effects, and need for isolation. Globally, loss of productivity due to TB approaches 7% of GDP.[xxxix] Active TB can also negatively impact maternal health by contributing to perinatal deaths, premature birth, low birth-weight for age and infertility.[xl]

In addition, because 25-44 year olds are young, viable, and mobile the opportunity to transmit may be more frequent. This age group may have children in the home, attend social activities frequently, and spend time in a workplace setting. All of these settings are potential areas for transmission to occur.

Washington State DOH should ensure that TB programs as well as medical providers are made aware of key demographic statistics associated with active TB disease. Based on this study, recommendations for targeted screening and treatment of persons from The Philippines, Mexico, Vietnam and India, especially those in the 25-44 year old age group, should be promoted. As LHJs may lack resources for implementation of targeted screening programs, Washington State DOH should make the availability of assisting with resources a priority.

Gaps in overseas and domestic TB screening practices

The most recent national guidelines state that recent immigration (i.e., within the last 2-5 years) from high prevalence countries increase the risk of developing active TB disease.[xli,xlii] However, according to national guidelines specific for domestic screening for TB infection and disease in refugees, it mentions that risk of TB disease may remain high for many years after immigration.[iii] This study supports this statement and further research should be done to determine if an update to the most recent national guidelines is needed. While 35% of cases did develop active disease within the first 5 years of arrival, 63% did not develop active disease until they had been in the US for 5 years or more. Over a quarter of the cases had been in the US for 20+ years before being diagnosed with active TB. This indicates that either they had a latent infection when they migrated to the US, which studies have shown to be a likely possibility[xliii], or they were infected after arrival in the US. With LTBI treatment the risk that TB infection will progress to disease is substantially reduce.[xliv] Many of these cases could have been

prevented if they had been offered and completed LTBI therapy. It is essential that TB programs and medical provider's seek out opportunities to identify and screen foreign-born persons for LTBI regardless of how many years they have lived in the US. Primary care providers should routinely screen new patients who are high-risk for TB, obstetricians should screen foreign-born women especially if infertility issues are present, and TB programs should make priority and implement targeted testing outreach to high-risk foreign-born persons.

Unfortunately, adults who receive a medical exam overseas are only screened for active disease and not LTBI; however, domestic TB screenings offer an opportunity to identify persons who would benefit from LTBI therapy. For those who receive an overseas medical exam and are given a class B status, every reasonable effort should be made to assure follow-up with a domestic TB screening initiated within 30 days of arrival in the US. This is important in identifying active TB and also allows for initiation of LTBI therapy if needed. Because refugees have medical coverage and are required to be screened to adjust their status, there are fewer barriers to initiating a domestic screening within 30 days. Class B immigrants most often to not have medical coverage upon arrival in the US and they have already obtained citizenship so compelling domestic screening is more difficult. In order to decrease the barrier of cost, Washington State Health Care Authority should have a program in place to rapidly link newly arrived immigrants with subsidized health insurance and TB programs should provide low cost or free domestic screening for class B immigrants.

Because nonimmigrant visa holders and those with an other immigration status do not have an overseas medical exam or a domestic TB screening finding opportunities for TB screening is more difficult. It takes partnership between various entities public and private, medical and nonmedical to reach this portion of the population. Colleges and universities may need to create or strengthen TB screening policy for foreign-born students, work places that employ large numbers of foreign-born workers may benefit from a TB screening program, and ethnic faith-based organizations may help in disseminating information to foreign-born congregations. Based on the information gathered in this study Washington State DOH should collaborate with these stakeholders to create standardized TB screening policy and procedure templates that are effective.

Opportunities and the feasibility of identifying LTBI in adults overseas should be explored. Currently adult immigrants and refugees are only required to be screened for active disease; however, children under 15 years of age are screened for LTBI via a TB skin or blood test.[xi] Considering that in industrialized countries reactivation of imported LTBI among foreign-born is a driver of TB cases[xliii], if the current guidelines were expanded upon to include screening for LTBI it would provide important information for domestic follow-up care. If screening for LTBI overseas is not feasible then consideration of making domestic TB screening a mandatory requirement for all immigrants (regardless of their class B status) and refugees would allow opportunity to identify persons with LTBI who would otherwise go undiagnosed.

In addition, further research on the national burden of TB disease among nonimmigrants should be pursued to determine if overseas TB screening of LTBI and active disease would be effective. While nonimmigrant visas are temporary and time bound, this study found that persons who entered with a nonimmigrant visa were still being diagnosed many years after arrival. This means either they extended their visa, left the US and reentered with an immigrant visa (receiving an overseas medical exam), or overstayed their visa and were in the US illegally, which is not uncommon.[xlv] Requiring overseas TB screenings for certain nonimmigrant visa holders from high-burden countries may be a way to prevent potential cases of TB in a population that may otherwise be difficult to target, especially if they end up residing in the US with an undocumented status. For example, because this study showed that student visa holders were diagnosed about 13 years after arrival, if colleges and universities required TB screening for international students it would be beneficial not only in preventing transmission while the student is on campus but also prevent cases of TB years down the road.

For those who arrive with an undocumented status interventions are much more difficult because this population is more elusive to the healthcare system. Again, collaboration with entities such as the work place and faith-based organizations may be necessary as well as decreasing barriers and increasing access to medical care for this population. Washington State DOH and local TB programs should work closely with migrant workers associations to implement TB screening and education programs to

reach the undocumented population. Further research on how best to engage this population would be beneficial.

Diabetes as a TB risk characteristic

Diabetes mellitus (DM) has been gaining more frequent attention by TB providers in the last several years. Compared to persons without diabetes, those with DM had a 3-fold increased risk of developing TB disease.[xlvi] Worldwide about 10% of TB cases are linked to DM.[xlvii] This study suggested the link between DM and TB to be even higher in the cases analyzed and showed the risk of DM to be significantly higher than other risk factors analyzed. Nearly 30 million persons in the US have diabetes[xlviii] and racial and ethnic minority groups are disproportionately affected by diabetes, with Hispanics having the highest burden of disease.[xlix] With a large proportion of the cohort that did not receive overseas TB screening being Hispanic, it is concerning that the risk of DM and TB is high in this population.

In addition to DM being a risk factor for TB, it can also make TB treatment more difficult. Persons with DM and TB have higher rates of treatment failure and are at nearly 5 times greater risk of death.[l] Approximately 7 million adults in the US are living with undiagnosed diabetes.[li] One of the strategies that the World Health Organization (WHO) suggests implementing is detecting and managing diabetes in patients with TB which includes screening TB patients for diabetes and ensuring high-quality diabetes management among TB patients.[xlvii] With so many persons unaware of their diabetes status and considering the negative impact on TB treatment outcomes, further research

should be done to determine if adopting this strategy would be necessary and/or effective in Washington State.

While detecting diabetes in persons with TB may be beneficial for decreasing poor treatment outcomes, detecting TB in high-risk diabetics is a strategy that may promote TB disease prevention. Education regarding the risk of DM and TB should be disseminated to medical providers and others who are involved in the care of persons with DM. In a review of current Washington State diabetes publications, there was no mention of DM being a risk factor for TB disease.[lii] Furthermore, Washington State diabetes publications are only available in Spanish and English. Publications and guidelines should be updated to reflect the important co-morbidity of TB and diabetes and be available in a variety of languages.

Characteristics of TB disease

Based on CDC guidelines for degree of infectiousness,[liii] contacts at highest risk for infectiousness have pulmonary TB, positive sputum smear results, and cavitary chest radiograph findings. Cases that are sputum smear positive and/or have a cavitary chest radiograph have the highest priority for conducting a transmission investigation.[xxix] In this study, 47% of the cases would be considered to have a high risk of infectiousness warranting a transmission investigation. With an average of 10 contacts per case identified during a contact investigation, with 20-30% having LTBI and 1% having TB disease[liii], each investigation conducted uses valuable resources.

While cases that are high risk for infectiousness are most likely to transmit TB to others it is not guaranteed that they will do so. Genotyping information, however, can suggest linkage and transmission between culture positive active cases. Furthermore, cases can be divided into clusters based on the genotyping information. Clustering information guides TB programs to look further for epidemiologic links between cases that may represent transmission. This study found half of the cases to be part of a Washington cluster, with 23% of these clustered cases being the being the first incident case identified in the Washington cluster. Only one other research article was found which specifically analyzed genotyping data for foreign-born TB patients. Interestingly that study found 22% of the cohort to be part of a cluster[liv], which is a much lower clustered proportion then what was found in this study. This study was unique compared to other studies in that it analyzed the first incident case identified in the cluster. This data is beneficial in helping order the train of transmission.

Limitations

There were several limitations to this study. The study cohort was relatively small. Initial findings of this study suggest analyzing a larger data set, such as on a national scale, would be worth exploring. Also, for a majority of cases within this study's cohort, key study variables such as visa type, race/ethnicity and country of birth were self-reported and could not be verified by EDN data. This leaves the potential for recall bias and misclassification. In addition, analyses for association and differences was not

adjusted for potential confounders so that finding (i.e. p-values) on these associations may be overly biased.

Another limitation is that female gender and Asian race may not fully be represented because extra-pulmonary TB cases were excluded from this study. It is known that women and Asians are more likely to have extra-pulmonary TB compared to men and other racial and ethnic groups.[lv] As a result analyses on gender and race/ethnicity have the potential to be biased.

In regard to medical risk factors for TB, while protocol stipulates that report of medical risk factors should be based on the documented medical record, these data may not capture the true underlying prevalence of such risk. Medical risk factors that are undiagnosed or undisclosed through medical records remain unknown.

Finally, limitations surrounding genotyping data make it difficult to determine the true impact of these cases in furthering disease transmission. Due to factors such as variable specimen collection dates and undiagnosed infectious cases there may be late identification or unknown sources of transmission. Further investigation is needed to determine the existence of a direct epidemiologic link between clustered cases.

Conclusion

In conclusion, this study was able to describe the burden and characteristics of pulmonary TB disease among foreign-born persons in Washington State who did not receive overseas TB screening as well as among the entire cohort of foreign-born

pulmonary TB cases. This was achieved by determining overseas TB screening status and by describing characteristics of the foreign-born pulmonary TB cases overall and more specifically in those who did not receive an overseas TB screening. By analyzing the cohort in this way, this study contributed to knowledge of the burden and characteristics of foreign-born pulmonary TB cases in Washington State, especially those without an overseas TB screening. This information helped identify opportunities for targeted interventions and policy changes (see table 6) to address TB in the Washington State foreign-born population.

It is evident from this study that while overseas refugee and immigrant TB screening for active TB is an effective strategy, the scope of its effectiveness is very limited. Not only are nonimmigrant visa holders not included in this strategy, but LTBI detection and treatment is ignored. Unless a strategy is implemented so that all high-risk foreign-born persons are screened for active and latent TB, and LTBI treatment is made a priority, Washington State will continue to see a disproportionate number of TB cases in this population. If TB elimination in Washington State and in the US is to be achieved, gaps in preventing, diagnosing and treating TB in the foreign-born population must continue to be identified and addressed at the global, national, state and local levels.

Tables:

Table 1: Overseas TB Classifications[iii]		
Classification	**Definition**	**Comment**
Class A	Abnormal chest radiograph suggestive of active TB disease, and one or more sputum smears positive for acid-fast bacteria or one or more cultures positive for TB	Persons with class A TB may not immigrate unless a waiver is granted
Class B1-Pulmonary, No treatment	Abnormal chest radiograph suggestive of active TB, and three negative sputum smears and cultures, not diagnosed with TB or can wait to have treatment in the US	Treatment is not required prior to immigration
Class B1-Pulmonary, Completed treatment	Diagnosed with pulmonary TB and completed DOT prior to immigration	Completion of treatment for active pulmonary TB is required before immigration, unless a Class A waiver is granted
Class B1- Extra-pulmonary	Evidence of extrapulmonary TB, and no evidence of pulmonary TB	Treatment for extrapulmonary TB may or may not be initiated Overseas No waiver is needed for extrapulmonary TB
Class B2- LTBI	Positive TB test and no evidence of active TB	Only persons under 15 years of age are screened for LTBI
Class B3- Contact	Recent contact to a known case of active pulmonary TB	LTBI therapy for infected contacts typically not be initiated overseas

Table 2: TB Screening by Immigration Status			
Immigration Status	**Overseas Screening**	**Domestic Screening***	**Comments**
Immigrant Visa	X	X**	**Domestic screening only required for those with a class B TB status
Refugee Visa	X	X	
Nonimmigrant Visa • Tourist • Work • Student			No TB screening
Visa Waiver***			No TB screening
Undocumented			No TB screening

*Domestic TB screening is conducted on Class B immigrants and all refugees. Domestic screening includes a physical exam and health history, TB test (if not completed overseas), chest radiograph for those with a TB classification or positive TB test, and sputum testing if indicated.[xiii]

***The following 38 countries are Visa Waiver Program participants: Andorra, Australia, Austria, Belgium, Brunei, Chile, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovakia, Slovenia, South Korea, Spain, Sweden, Switzerland, Taiwan, and United Kingdom.[lvi]

Table 3: Tuberculosis Case Definitions[xxxv]	
Laboratory Case	Isolation of *M. tuberculosis* complex from a clinical specimen. The use of rapid identification techniques for *M. tuberculosis* performed on a culture from a clinical specimen, such as DNA probes and high-pressure liquid chromatography (HPLC), is acceptable under this criterion. **OR** Demonstration of *M. tuberculosis* from a clinical specimen by nucleic acid amplification (NAA) test. NAA tests must be accompanied by cultures of mycobacterial species. However, for surveillance purposes, CDC will accept results obtained from NAA tests approved by the Food and Drug Administration (FDA) and used according to the approved product labeling on the package insert, or a test produced and validated in accordance with applicable FDA and Clinical Laboratory Improvement Amendments (CLIA) regulations. **OR** Demonstration of acid-fast bacilli (AFB) in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated; historically this criterion has been most commonly used to diagnose TB in the postmortem setting.
Clinical Case	In the absence of laboratory confirmation of *M. tuberculosis* complex after a diagnostic process has been completed, persons must have **all** of the following criteria for clinical TB: Evidence of TB infection based on a positive tuberculin skin test result or positive interferon gamma release assay for *M. tuberculosis* **AND** One of the following: (1) Signs and symptoms compatible with current TB disease, such as an abnormal chest radiograph or abnormal chest computerized tomography scan or other chest imaging study, **OR** (2) Clinical evidence of current disease (e.g., fever, night sweats, cough, weight loss, hemoptysis) **AND** Current treatment with two or more anti-TB medications
Provider Diagnosed	A case of TB that does not meet the case definition of a laboratory or clinical case of TB, but the provider believes the person has active TB disease.

Table 4. Demographic characteristics of Washington State foreign-born active pulmonary TB cases stratified by overseas TB screening based on visa status in TB-PHIMS, Washington State 2009-2013 (N=562)

	Total	No overseas TB screening[1]	Received overseas TB screening[2]	Overseas screening unknown[3]	P-value
		126 (22.4)	297 (52.9)	139 (24.7)	
Age at arrival, in years					
Mean	34.8	30.1	37.3	33.6	0.0004
Median	30	26	34	29	
Standard deviation	17.7	15.8	18.1	17.8	
<5	17 (3.1)	4 (3.2)	7 (2.4)	6 (4.3)	
5-14	26 (4.7)	5 (4.0)	17 (5.7)	4 (2.9)	
15-24	139 (25.1)	47 (37.3)	54 (18.2)	38 (27.3)	
25-44	218 (39.3)	48 (38.1)	114 (38.4)	56 (40.3)	
45-64	115 (20.7)	13 (10.3)	83 (28.0)	19 (13.7)	
65+	40 (7.2)	7 (5.6)	21 (7.1)	12 (8.6)	
Unknown	7 (1.3)	2 (1.6)	1 (0.3)	4 (2.9)	
Age at diagnosis, in years					
Mean	47.8	41.3	50.4	48.0	0.0003
Median	44	36	49	45	
Standard deviation	21.2	18.9	21.7	21.1	
<5	6 (1.1)	1 (0.8)	3 (1.0)	2 (1.4)	
5-14	8 (1.4)	1 (0.8)	7 (2.4)	-	
15-24	53 (9.4)	18 (14.3)	23 (7.7)	12 (8.6)	
25-44	216 (38.4)	64 (50.8)	98 (33.0)	54 (38.9)	
45-64	126 (22.4)	19 (15.1)	71 (23.9)	36 (25.9)	
65+	153 (27.2)	23 (18.3)	95 (32.0)	35 (25.2)	
Time from arrival to diagnosis, in years					
Mean	12.6	10.5	12.9	13.9	0.0871
Median	9	7	8	11	
Standard deviation	12.7	12.0	13.0	12.6	
<1	94 (16.7)	26 (20.6)	58 (19.5)	10 (7.2)	
1-4	107 (19.0)	28 (22.2)	54 (18.2)	25 (18.0)	
5-9	84 (15.0)	19 (15.1)	42 (14.1)	23 (16.6)	
10-14	67 (11.9)	18 (14.3)	26 (8.8)	23 (16.6)	
15-19	46 (8.2)	8 (6.4)	24 (8.1)	14 (10.1)	
20+	155 (27.6)	25 (19.8)	91 (30.6)	39 (28.1)	
Unknown	9 (1.6)	2 (1.6)	2 (0.7)	5 (3.6)	
Gender					
Female	241 (42.9)	44 (34.9)	131 (44.1)	66 (47.5)	0.0981
Male	321 (57.1)	82 (65.1)	166 (55.9)	73 (52.5)	
Race/Ethnicity					
Asian	336 (59.8)	48 (38.1)	207 (69.7)	81 (58.3)	<0.0001
Black	85 (15.1)	10 (7.9)	53 (17.9)	22 (15.8)	
NHOPI	1 (0.2)	-	1 (0.3)	-	
White	37 (6.8)	4 (3.2)	23 (7.7)	10 (7.2)	
Multi-race	4 (0.7)	-	3 (1.0)	1 (0.7)	
Hispanic, any race	98 (17.4)	64 (50.8)	10 (3.4)	24 (17.3)	
Unknown	1 (0.2)	-	-	1 (0.7)	
Country of birth					
Philippines	105 (18.7)	3 (2.4)	69 (23.2)	33 (23.7)	<0.0001
Mexico	80 (14.2)	52 (41.3)	8 (2.7)	20 (14.4)	
Vietnam	73 (13.0)	9 (7.1)	51 (17.2)	13 (9.4)	
Ethiopia	41 (7.3)	7 (5.6)	23 (7.7)	11 (7.9)	

Table 4. Demographic characteristics of Washington State foreign-born active pulmonary TB cases stratified by overseas TB screening based on visa status in TB-PHIMS, Washington State 2009-2013 (N=562)

	Total	No overseas TB screening[1]	Received overseas TB screening[2]	Overseas screening unknown[3]	P-value
		126 (22.4)	297 (52.9)	139 (24.7)	
India	29 (5.2)	9 (7.1)	11 (3.7)	9 (6.5)	
South Korea	27 (4.8)	9 (7.1)	15 (5.1)	3 (2.2)	
Cambodia	20 (3.6)	2 (1.6)	12 (4.0)	6 (4.3)	
China	20 (3.6)	4 (3.2)	10 (3.4)	6 (4.3)	
Burma	17 (3.0)	-	16 (5.4)	1 (0.7)	
Somalia	14 (2.5)	-	7 (2.4)	7 (5.0)	
Ukraine	13 (2.3)	1 (0.8)	10 (3.4)	2 (1.4)	
Other	123 (21.9)	30 (23.8)	65 (21.9)	28 (20.1)	
Drug Susceptibility					
First-line susceptible	424 (75.4)	94 (74.6)	221 (74.4)	109 (78.4)	0.8137
INH mono-resistant	49 (8.7)	10 (7.9)	27 (9.1)	12 (8.6)	
RIF mono-resistant	1 (0.2)	1 (0.8)	-	-	
PZA mono-resistant	7 (1.3)	2 (1.6)	4 (1.4)	1 (0.7)	
MDR (INH and RIF resistant)	8 (1.4)	3 (2.4)	4 (1.4)	1 (0.7)	
Unable to classify	64 (11.4)	15 (11.9)	36 (12.1)	13 (9.4)	
Medical Risk Factors					
Diabetes at diagnosis	88 (15.7)	15 (11.9)	53 (17.9)	20 (14.4)	0.3387
HIV+ at diagnosis	14 (2.5)	4 (3.2)	6 (2.0)	4 (2.9)	
Other immunosuppression[4]	21 (3.7)	2 (1.6)	11 (3.7)	8 (5.8)	
History of TB	32 (5.7)	9 (7.1)	15 (5.1)	8 (5.8)	
Multiple medical risks	28 (5.0)	2 (1.6)	16 (5.4)	10 (7.2)	
Culture Confirmed	505 (89.9)	111 (88.1)	265 (89.2)	129 (92.8)	
Likelihood to Transmit					
Sputum smear (+) / Cavitary	137 (24.4)	40 (31.8)	66 (22.2)	31 (22.3)	0.1859
Sputum smear (+)	129 (23.0)	28 (22.2)	72 (24.2)	29 (20.9)	
Sputum smear (-)	270 (48.0)	51 (40.5)	147 (49.5)	72 (51.8)	
Other[5]	26 (4.6)	7 (5.6)	12 (4.0)	7 (5.0)	
Confirmation of Tx Completion	456 (81.0)	92 (73)	247 (83.2)	117 (84.2)	
Linked to WA Cluster	278 (49.5)	61 (48.4)	137 (46.1)	80 (57.6)	
Index in WA Cluster[6]	65 (23.4)	12 (19.7)	23 (16.8)	30 (37.5)	

[1] Employment, student, tourist visa; Other immigration status

[2] Immigrant, Refugee visas

[3] Asylee or parolee, family/fiancé visa; Unknown immigration status; or otherwise unreported

[4] Immunosuppressing conditions include: TNF alpha-antagonist therapy, post-organ transplantation, end-stage renal disease, and immunosuppression (not HIV/AIDS, DM).

[5] Sputum smear not performed or results unknown.

[6] Defined as the first incident case among WA cases linked by genotype to a given WA case cluster, based on chronologically-ordered specimen collection dates when data were available, or case report date otherwise.

Table 5. Characteristics of Washington State foreign-born active pulmonary TB cases not receiving overseas TB screening stratified by specific visa status at first entry to U.S., Washington State 2009-2013 (N=126)

	Work Visa[1]	Student Visa[2]	Tourist Visa[3]	Other[4]	P-value
	14 (11.1)	23 (18.3)	20 (15.9)	69 (54.8)	
Age at arrival, in years					
Mean	32.2	23.9	45.3	27.2	0.0008
Median	27	24	36	22	
Standard deviation	12.6	8.4	20.5	14.0	
<5	-	1 (4.4)	-	3 (4.4)	
5-14	-	-	1 (5.0)	4 (5.8)	
15-24	5 (35.7)	12 (52.2)	-	30 (43.5)	
25-44	7 (50.0)	10 (43.5)	11 (55.0)	20 (29.0)	
45-64	2 (14.3)	-	2 (10.0)	9 (13.0)	
65+	-	-	6 (30.0)	1 (1.5)	
Unknown	-	-	-	2 (2.9)	
Age at diagnosis, in years					
Mean	41.2	37.4	50.9	39.9	0.0859
Median	35.5	29	47	36	
Standard deviation	17.8	18.8	18.8	18.7	
<5	-	-	-	1 (1.5)	
5-14	-	-	-	1 (1.5)	
15-24	2 (14.3)	5 (21.7)	-	11 (15.9)	
25-44	8 (57.1)	11 (47.8)	9 (45.0)	36 (52.2)	
45-64	1 (7.1)	4 (17.4)	3 (15.0)	11 (15.9)	
65+	3 (21.4)	3 (13.0)	8 (40.0)	9 (13.0)	
Time from arrival to diagnosis, in years					
Mean	8.6	13.1	5.3	11.6	0.0208
Median	1.5	5	1.5	10	
Standard deviation	13.7	16.1	6.9	10.9	
<1	4 (28.6)	4 (17.4)	9 (45.0)	9 (13.0)	
1-4	5 (35.7)	7 (30.4)	3 (15.0)	13 (18.8)	
5-9	1 (7.1)	4 (17.4)	3 (15.0)	11 (15.9)	
10-14	1 (7.1)	1 (4.4)	4 (20.0)	12 (17.4)	
15-19	-	-	-	8 (11.6)	
20+	3 (21.4)	7 (30.4)	1 (5.0)	14 (20.3)	
Unknown	-	-	-	2 (2.9)	
Gender					
Female	5 (35.7)	9 (39.1)	11 (55.0)	19 (27.5)	0.1456
Male	9 (64.3)	14 (60.9)	9 (45.0)	50 (72.5)	
Race/Ethnicity					
Asian	11 (78.6)	20 (87.0)	13 (65.0)	4 (5.8)	<0.0001
Black	1 (7.1)	1 (4.4)	3 (15.0)	5 (7.3)	
NHOPI	-	-	-	-	
White	-	2 (8.7)	1 (5.0)	1 (1.5)	
Multi-race	-	-	-	-	
Hispanic, any race	2 (14.3)	-	3 (15.0)	59 (85.5)	
Country of birth					
Philippines	-	-	2 (10.0)	1 (1.5)	<0.0001
Mexico	1 (7.1)	-	2 (10.0)	49 (71.0)	
Vietnam	-	6 (26.1)	2 (10.0)	1 (1.5)	
Ethiopia	-	-	3 (15.0)	4 (5.8)	
India	5 (35.7)	2 (8.7)	2 (10.0)	-	

Table 5. Characteristics of Washington State foreign-born active pulmonary TB cases not receiving overseas TB screening stratified by specific visa status at first entry to U.S., Washington State 2009-2013 (N=126)

	Work Visa[1]	Student Visa[2]	Tourist Visa[3]	Other[4]	P-value
	14 (11.1)	23 (18.3)	20 (15.9)	69 (54.8)	
South Korea	1 (7.1)	5 (21.7)	1 (5.0)	2 (2.9)	
Cambodia	-	-	2 (10.0)	-	
China	3 (21.4)	-	1 (5.0)	-	
Burma	-	-	-	-	
Somalia	-	-	-	-	
Ukraine	-	-	-	1 (1.5)	
Other	4 (28.6)	10 (43.5)	5 (25.0)	11 (15.9)	
Drug Susceptibility					
First-line susceptible	12 (85.7)	14 (60.9)	16 (80.0)	52 (75.4)	0.1229
INH mono-resistant	-	2 (8.7)	3 (15.0)	5 (7.3)	
RIF mono-resistant	-	-	-	1 (1.5)	
PZA mono-resistant	-	1 (4.4)	-	1 (1.5)	
MDR (INH and RIF resistant)	-	3 (13.0)	-	-	
Unable to classify	2 (14.3)	2 (8.7)	1 (5.0)	10 (14.5)	
Medical Risk Factors					
Diabetes at diagnosis	2 (14.3)	-	5 (25.0)	8 (11.6)	0.6109
HIV+ at diagnosis	-	-	2 (10.0)	2 (2.9)	
Other immunosuppression[4]	-	-	-	2 (2.9)	
History of TB	1 (7.1)	2 (8.7)	1 (5.0)	5 (7.3)	
Multiple medical risks	-	-	-	2 (2.9)	
Culture Confirmed	12 (85.7)	21 (91.3)	19 (95.0)	59 (85.5)	
Likelihood to Transmit					
Sputum smear (+) / Cavitary	6 (42.9)	7 (30.4)	6 (30.0)	21 (30.4)	0.8328
Sputum smear (+)	1 (7.1)	7 (30.4)	5 (25.0)	15 (21.7)	
Sputum smear (-)	6 (42.9)	9 (39.1)	7 (35.0)	29 (42.0)	
Other[6]	1 (7.1)	-	2 (10.0)	4 (5.8)	
Confirmation of Tx Completion	12 (85.7)	17 (73.9)	17(85)	46(66.7)	
Linked to WA Cluster	6 (42.9)	11 (47.8)	10 (50.0)	34 (49.3)	
Index in WA Cluster[7]	1 (16.7)	2 (18.2)	1 (10.0)	8 (23.5)	

[1] Visa obtained to work for a specific period. Includes migrant work visa.
[2] Visa obtained for a specific period to pursue a full course of study in an approved institution.
[3] Visa obtained for a specific period for business or pleasure.
[4] Those who entered with no official immigration status (e.g. undocumented), and those entering the US for <90days from a country that is part of the US visa waiver program (e.g. Canada).
[5] Immunosuppressing conditions include: TNF alpha-antagonist therapy, post-organ transplantation, end-stage renal disease, and immunosuppression (not HIV/AIDS, DM).
[6] Sputum smear not performed or results unknown.
[7] Defined as the first incident case among WA cases linked by genotype to a given WA case cluster, based on chronologically-ordered specimen collection dates when data were available, or case report date otherwise.

Table 6: Summary of Recommendations and Potential Policy Changes	
State Level	• ensure that TB programs and medical providers are made aware of key demographic statistics associated with active TB disease • make providing resources for targeted testing and LTBI treatment a priority • implement a program to rapidly link newly arrived immigrants with subsidized health insurance • collaborate with these stakeholder's (colleges, workplaces, faith-based organizations) to create standardized TB screening policy and procedure templates that are effective • work closely with migrant workers associations to implement TB screening and education programs to reach the undocumented population • update diabetes publications and guidelines to reflect the important co-morbidity of TB and diabetes and be available in a variety of languages
National Level	• expand overseas TB screening requirements to include LTBI screening • make domestic TB screening a mandatory requirement for all immigrants (regardless of their class B status) and refugees • pursue further research on the national burden of TB disease among nonimmigrants to determine if overseas TB screening of LTBI and active disease would be effective
Local Level	• TB programs should make priority and implement targeted testing outreach to high-risk foreign-born persons. • every reasonable effort should be made to assure follow-up with a domestic TB screening initiated within 30 days of arrival in the US • TB programs should provide low cost or free domestic screening for class B immigrants. • test for diabetes in TB patients
Other	• all medical provider's should seek out opportunities to identify and screen foreign-born persons for LTBI regardless of how many years they have lived in the US • primary care providers should routinely screen new patients who are high-risk for TB • obstetricians should screen foreign-born women especially if infertility issues are present • colleges and universities should create or strengthen TB screening policy for foreign-born students • work places that employ large numbers of foreign-born workers may benefit from a TB screening program • ethnic faith-based organizations should be utilized in disseminating information to foreign-born congregations • medical providers having diabetic patients should screen them for TB

Figures:

Figure 1:

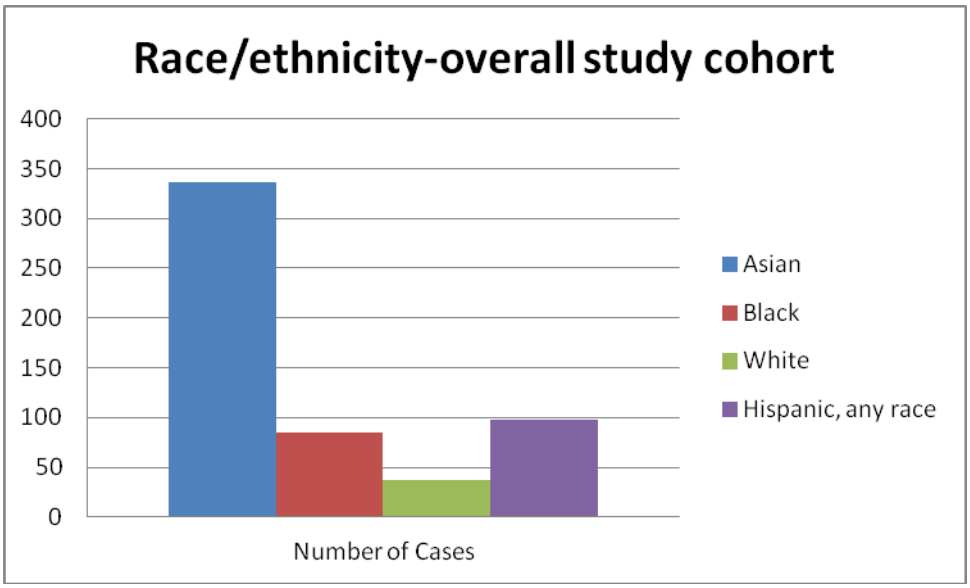


Figure 2:

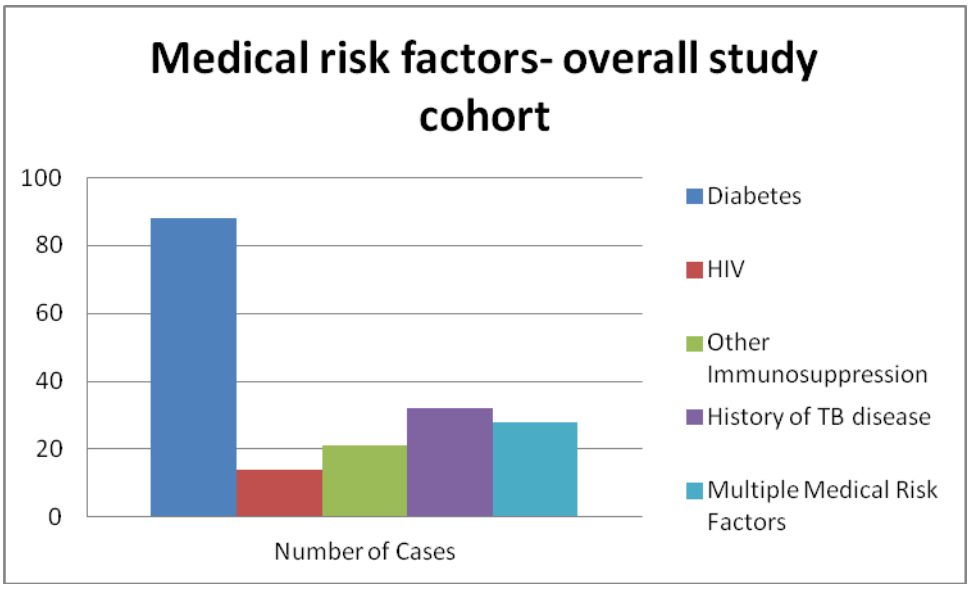


Figure 3:

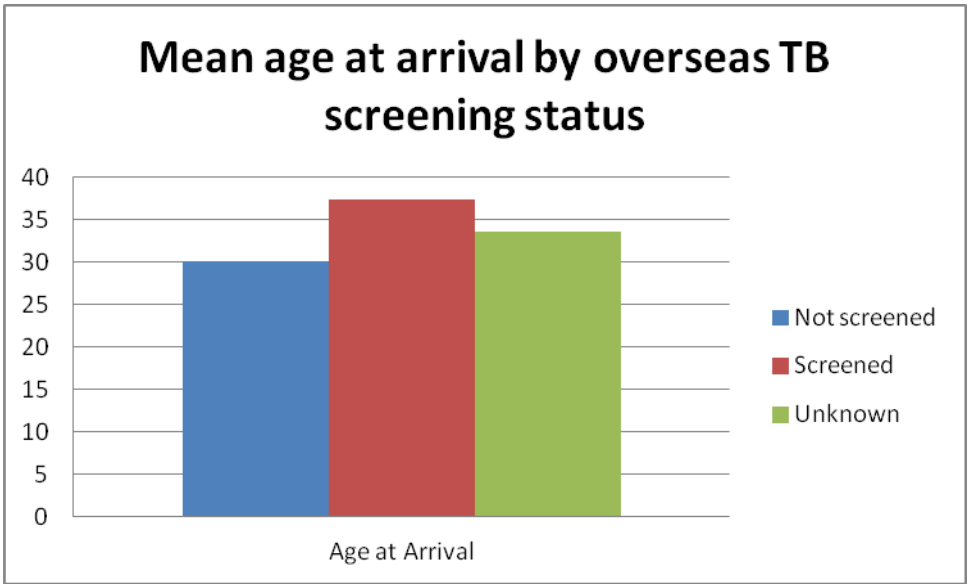


Figure 4:

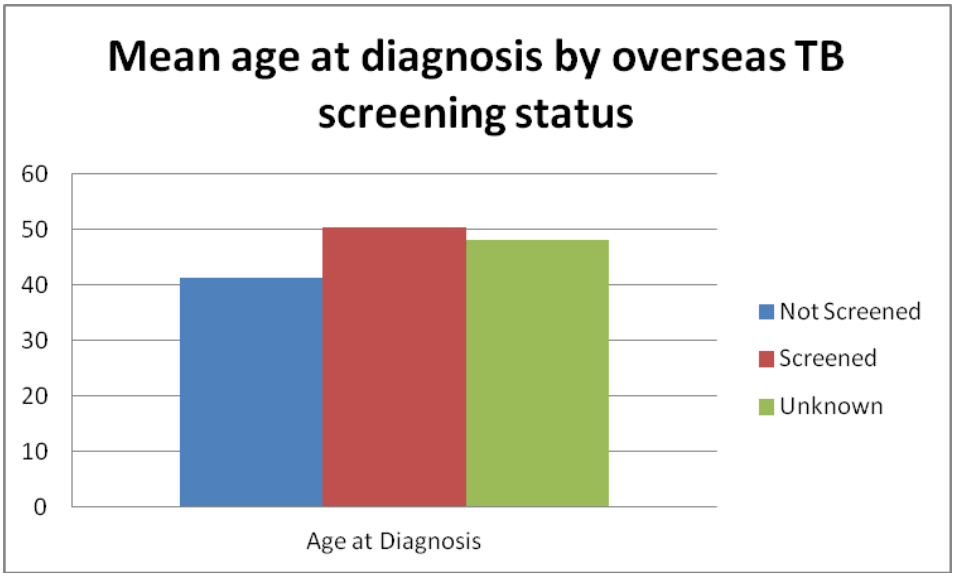


Figure 5:

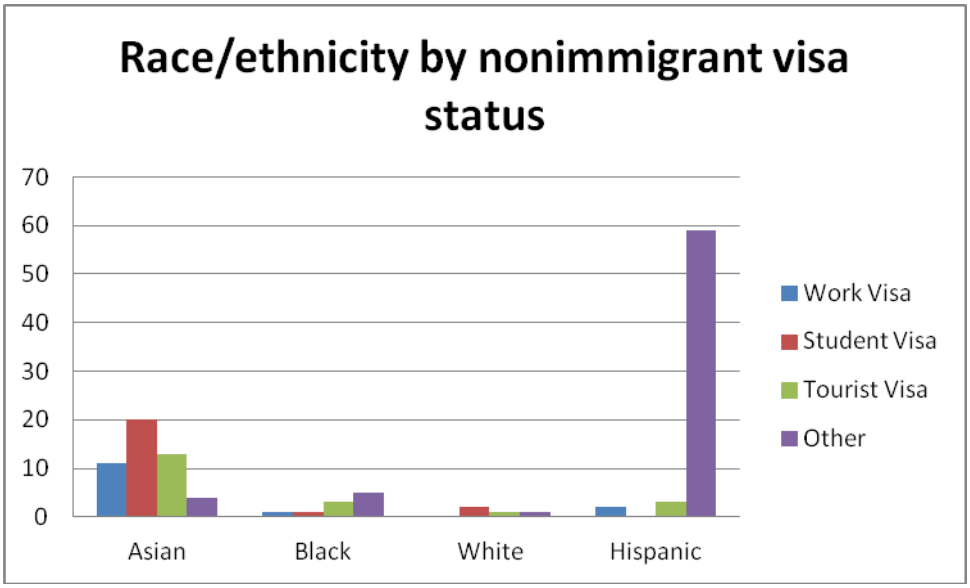


Figure 6:

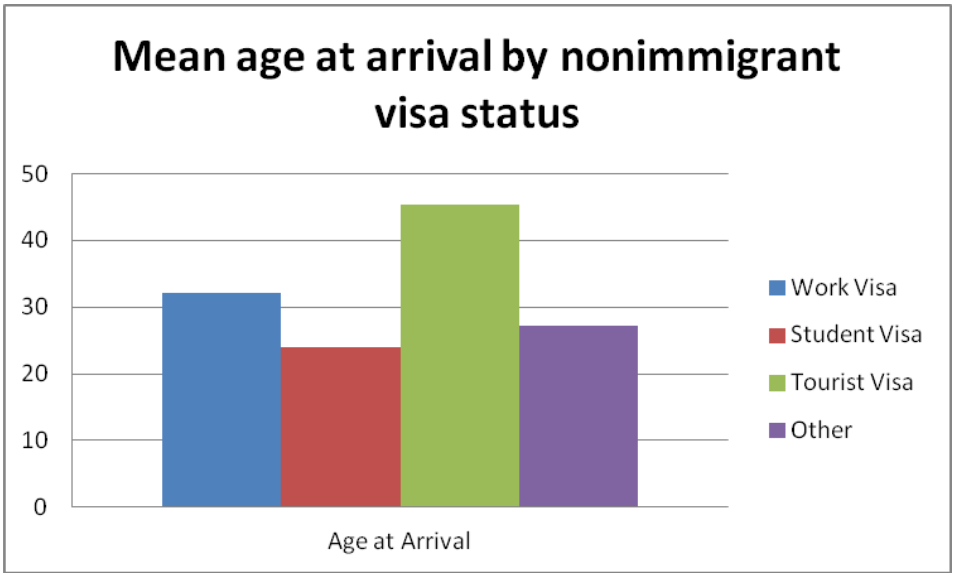
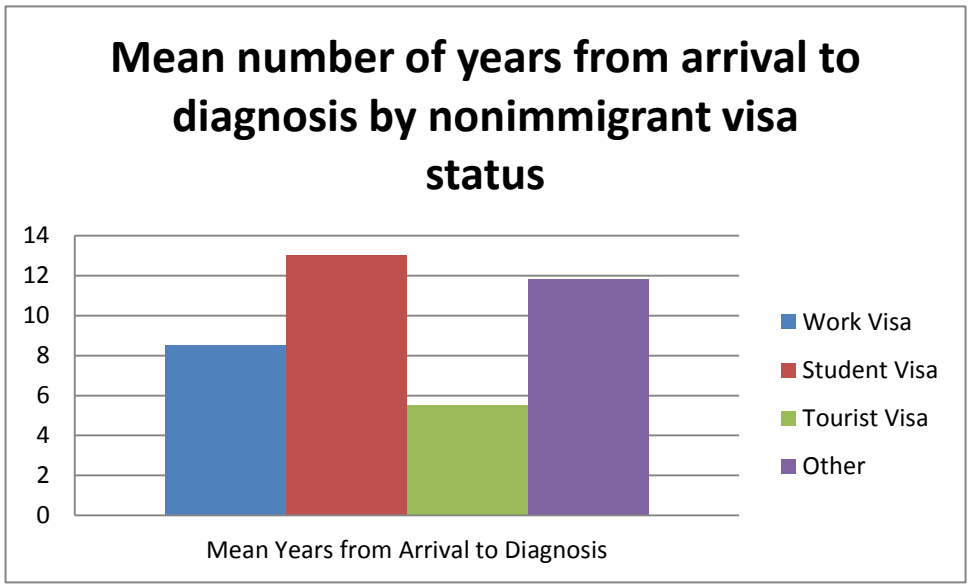


Figure 7:


Mean number of years from arrival to diagnosis by nonimmigrant visa status
14
12
10
8
6
4
2
0
Work Visa
Student Visa
Tourist Visa
Other
Mean Years from Arrival to Diagnosis

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