# INITIATION OF TREATMENT FOR LATENT TUBERCULOSIS INFECTION IN THE SHELTERED HOMELESS IN MULTNOMAH COUNTY, OREGON

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CERTIFICATE OF APPROVAL

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This is to certify that the Master's thesis of

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ATS | American Thoracic Society |
| BCG | Bacille Calmette-Guérin |
| CDC | Centers for Disease Control and Prevention |
| CHN | Community Health Nurse |
| CHS | Community Health Specialist |
| CI | Confidence Interval |
| INH | Isoniazid |
| LTBI | Latent Tuberculosis Infection |
| OR | Odds ratio |
| TB | Tuberculosis |
| TST | Tuberculin Skin Test |
| US | United States |

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**ABSTRACT**

The goal of the project was to evaluate Multnomah County Health Department's Tuberculosis (TB) Control and Prevention Program's homeless screening outreach activities, focusing on a comparison of foreign-born and United States (US)-born clients in initiation of treatment for latent tuberculosis infection (LTBI). Although TB incidence in Oregon was 2.2 cases per 100,000 in 2007, foreign-born and homeless persons are at higher risk than the general population. While research about foreign-born persons as well as homeless persons with LTBI are common, studies of the overlapping at-risk population of the foreign-born homeless are rare. The study employed a retrospective cohort design using data collected from 2002 through 2008 during screening for TB and a follow up evaluation at Multnomah County Health Department's TB Clinic. We hypothesized that the foreign-born homeless clients would start treatment for LTBI at a higher proportion than US-born homeless clients. Descriptive statistics included characteristics of the 916 clients for whom treatment was recommended, a comparison of characteristics between foreign-born and US-born clients and separately between clients who began treatment and clients who did not begin. We stratified the foreign-born and treatment initiation association by potential confounders and effect modifiers which included age, sex, race/ethnicity, shelter, and substance abuse. Chi-square tests were performed to compare the primary association of interest between foreign-born versus US-born and treatment initiation, as well as the association between potential confounders and the exposure and the outcome. Interaction by age was statistically assessed using an interaction term in logistic regression. Finally, multiple logistic

regression was employed to build a model that would account for confounders. After adjusting for race/ethnicity, we found that foreign-born clients had significantly higher odds of initiating treatment than US-born clients in the sheltered homeless population for the 30-49 [OR 2.13, 95% CI 1.29, 3.52] and 50 and above [OR 6.03, 95% CI: 2.69, 13.52] age groups, but we did not find evidence of a difference in the 18-29 age group [OR 1.29, 95% CI 0.60, 2.79]. There are multiple approaches that can be taken to improve treatment initiation, including but not limited to increased focus on encouraging treatment initiation in all clients given that the percentage starting treatment was low overall. Older foreign-born clients could be encouraged to begin treatment more strongly since they tend to start at higher percentages than US-born clients and may need less encouragement to begin treatment, which would increase the percentage of clients starting treatment even more. Another strategy could be to focus on the US-born clients in all age groups since the percentage starting treatment is low across all age groups.

## INTRODUCTION

Local health departments hold an essential role in maintaining tuberculosis (TB) control and preventing new cases of disease in the United States by treating infected individuals, conducting contact investigations, screening at-risk populations, and assessing programs and disease frequency. Efforts at the local, state, federal, and international levels have reduced the incidence of TB in the United States from 30.7 per 100,000 in 1960 to 10.4 per 100,000 in 1991, reaching only 4.4 cases per 100,000 population (for an absolute number of 13,299 cases) in 2007. [1] In Oregon, only 2.2 cases per 100,000 population were reported in 2007 (94 cases).[1] In contrast to the general population, foreign born from high incidence countries (such as Mexico, the Philippines, Vietnam, India, and China), immunocompromised, homeless, and incarcerated individuals have a higher risk of infection.[2,3]

To reduce current levels of disease, we need to improve our focus on control and prevention efforts.[2,3] According to the Institute of Medicine's 2000 report entitled *Ending Neglect: The Elimination of Tuberculosis in the United States*, a minimum basic level of resources is necessary to prevent increased incidence and to further reduce TB incidence.[3] Given the limited resources at health departments, finding more efficient ways to treat identified latent tuberculosis infection (LTBI) in at-risk populations will assist in lowering the basic minimum resource level necessary to carry out their duties. For this project, we explored the influence of foreign-born versus United States (US)-born status and initiation of treatment for LTBI in the homeless population.

Clinical aspects of TB and LTBI

TB is characterized by two distinct stages – latent TB infection and active TB disease.[1-4] LTBI is infection with *Mycobacterium tuberculosis* in which the immune system successfully inhibits growth of the organism.[3,4] If the immune system weakens, an individual progresses to active TB disease, at which point symptoms develop and individuals can become infectious.[3,4] Symptoms of active TB include cough, fever, weight loss, hemoptysis (coughing up blood), night sweats, fatigue, and loss of appetite.[4] [3] Additionally there will be changes to lung tissue as viewed by a chest x-ray in cases of pulmonary tuberculosis.[3,4]

Active TB is important because an individual who is sick needs treatment and could transmit the *M tuberculosis* to others.[3] LTBI is important to identify because infected individuals are the only people who can get active TB disease. Prophylactic treatment of individuals with LTBI prevents progression to active TB.[2-4]

Testing for LTBI is typically carried out with a tuberculin skin test (TST), although other methods are starting to be used but are limited by higher cost and the need for blood collection.[3,4] Bennett et. al. describe skin testing as an imperfect tool in which positive predictive value of the TST decreases as prevalence increases and false negative interpretation of the test can result from presence of non-tuberculosis mycobacterium or reader inexperience.[5] Recent vaccination with Bacille Calmette-Guérin (BCG), which is commonly administered to children in many parts of the world, can result in a false positive TST. The American Thoracic Society and Centers for Disease Control and Prevention do not discourage skin testing for persons who were vaccinated with BCG.[6] Of practical importance in a homeless screening program, positive TST results are likely

to be due to infection (ie. true positive) rather than a false positive result from BCG in high-risk populations.[7]

In the natural history between exposure to *M. tuberculosis* and death from active TB disease, there are multiple points at which intervention can occur (Figure 1). Actions can be taken to prevent exposure, to inhibit infection, to prevent LTBI from progressing to active disease, and to prevent death from active TB.

Treatment of latent TB infection is important - even though the infected individuals are not infectious - because about 10% of people who have LTBI progress to active TB if not treated[6] and between 9.5 and 14.7 million people in the US have LTBI. [2] HIV infected and otherwise immunocompromised individuals are more likely to progress to active disease.[4]

At-risk groups

Congregate living situations are known to increase the risk of infection [2], and recent outbreaks in homeless shelters in New York and Seattle show that shelters remain an ideal environment for TB spread.[8,9] Using data reported to the CDC from all 50 states and the District of Columbia, Haddad et al. found that 6.4% (range 6.1% to 6.7%) of active TB cases between 1994 and 2003 were classified as homeless (both sheltered and not sheltered persons).[10] In Los Angeles, LTBI was present in 32% of the homeless population surveyed as part of the UCLA Homeless Health Survey.[11]

In Multnomah County, Oregon there were an estimated 5,103 homeless people in 2005 and 4,456 in 2007 according to the National Alliance to End Homelessness.[12] Of these, about 2,748 were estimated to reside in shelters in 2005 and 3,018 in 2007. To

improve monitoring of TB status and to prevent large outbreaks, clearance cards indicating a complete TB evaluation are required for shelter residence in the West Burnside area and must be renewed annually.[13] The Multnomah County Health Department TB Control and Prevention program plays an essential role in TB control within the homeless population in the county. One service provided by the TB Control and Prevention program is homeless shelter outreach, which is the sole issuer of clearance cards; other services of the program are identifying and treating latent infection and active disease, and conducting contact investigations.[13]

The American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America cite controlling TB among the foreign-born as one of the major challenges of TB control in the United States.[2] TB has been reported in the US in immigrants from over 150 countries and about 75% of immigrants come from high incidence countries. [2] In 2003, 53 percent of reported cases of TB in the United States were in foreign-born persons.[2] Foreign-born TB incidence is striking compared to US-born; the incidence of TB among the foreign-born was 20.7 per 100,000 in 2007 while the incidence in US-born persons was 2.1 per 100,000.[1] In Oregon, 72.3% of the 94 reported cases were foreign-born.[1]

While TB and LTBI in both foreign-born and homeless populations have been studied, little is known about the dually at-risk population of homeless foreign-born persons. In an analysis of reported cases of TB in the homeless population nationally, Haddad et. al. found that 23 percent of homeless TB cases in 2007 were foreign-born, which was an increase from 14 percent in 1994.[10] Nationally, nearly 50% of the homeless foreign-born TB cases were from Mexico.

Treatment for LTBI

Current treatment standards for LTBI based on CDC recommendations is nine months of isoniazid (INH), although six months of treatment is sufficient.[6] Treatment for six months (as compared to nine months) tends to provide a more cost-effective approach while maintaining successful outcomes.

Treating individuals with LTBI can be challenging. As Hirsch-Moverman et al. point out, "treatment for latent TB infection involves the psychological challenge of convincing patients of the need to treat a non-contagious infection that may never develop into active disease with a prolonged treatment that may cause potential adverse effects" .[14] For homeless persons with LTBI, there are additional barriers to treatment; Haddad et al. found that homeless persons with active TB were significantly more likely to consume excessive alcohol, use injected or non-injected drugs, and have HIV co-infection than housed persons with active TB.[10] Gelberg et al. state that a "disproportionate number of individuals with serious mental health problems… have been found among the homeless".[11] Mental health and substance abuse problems can hinder taking anti-LTBI pills regularly.

We were unable to find studies that examined treatment initiation comparing foreign-born and US-born populations, however there were data on adherence to LTBI treatment regimens. Foreign-born participants were found to have greater odds of adhering to treatment for LTBI than US-born participants in both an inner-city population that included some homeless individuals (OR 4.06, 95% CI 1.78, 9.29)[15] and in a public health clinic (OR 1.4, 95% CI 1.1-1.7).[16]

Methods to improve treatment adherence include direct methods like directly observed therapy, drug-level measurement, and clinic attendance as well as indirect methods like patient self-report, provider assessment, electronic monitoring devices, pill count, and prescription refill rate.[14] Adherence to treatment in the foreign-born has been between 22% and 90% and similar percentages (between 27% and 92%) were found in high-risk groups including the homeless, health care workers, and HIV clinic patients, although some of these studies involved interventions specifically to improve adherence.

Significance, goal, hypothesis, and aims of the project

Only 1-2% of shelter screening encounters lead to starting treatment for LTBI [A. Sullivan, personal communication], which is particularly worrisome given the high infection rate and risk factors for progression to active disease in the homeless population. In order to improve the percentage of encounters with this at-risk population that result in treatment initiation, we must understand what affects treatment acceptance. The results can be used by the Multnomah County Tuberculosis Control and Prevention Program to make adjustments to their current program to increase the percentage of the population that begins treatment for LTBI, and may be applicable to other homeless screening programs throughout the nation. On a larger scale, more treatment coverage for LTBI will reduce the number of active TB cases in the homeless population, which is necessary to reach the TB elimination goals supported by the Institute of Medicine[3] and Congress.[17]

The goal of the project was to evaluate Multnomah County Health Department's Tuberculosis Control and Prevention Program's homeless screening outreach activities,

focusing on initiation of treatment for latent tuberculosis infection. Specifically, this analysis centers around understanding the role of foreign-born versus US-born status on treatment initiation among homeless clients for whom treatment for LTBI is recommended while considering potential confounders and effect modifiers.

We hypothesized that the foreign-born sheltered population would initiate treatment at a higher percentage than the US-born population. We assessed whether initiation of treatment among the homeless population followed the same pattern as adherence observed in similar populations.

Using 2002-2007 Multnomah County Health Department tuberculosis screening data for the sheltered population, the project aimed to:

1. Describe characteristics of the homeless population that has LTBI and for whom treatment is recommended by running and reviewing descriptive statistics and chi-square tests

2. Determine whether the foreign-born population began treatment at a higher proportion than the US-born population

## METHODS

Overview of study design and TB program

The study employed a retrospective cohort design using data collected from 2002 through 2008 during screening for tuberculosis for Multnomah County sheltered homeless persons.

The Multnomah County Health Department's TB Control and Prevention Program ran the targeted screening program for the sheltered homeless population in the West Burnside Street area of Portland and collected the data for the purpose of public health practice. As part of the screening program, the County issued clearance cards – also known as "blue cards" - to each individual after screening; the card was required to stay in Multnomah County shelters in the West Burnside Street area for longer than a short grace period and renewal was required annually.[13] Any person with active TB disease could not stay in the shelter, but persons with untreated latent tuberculosis infection could stay.

Screenings during the period examined in this analysis were held three days per week at the Salvation Army Harbor Light, decreasing to two days in the summer months.[18] A community health nurse (CHN) and community health specialist (CHS) conducted the screening. The CHS set up the screening, assisted clients with form completion as needed, and entered client demographics into a roster. The CHN assessed the clients' symptoms; placed and read the TST as indicated; recorded tuberculin lot number, expiration date, and test results in the roster as indicated; and referred clients to the Multnomah County TB Clinic as necessary. The process that the CHN follows for

each client is described below. Data from the roster and from clinic evaluations were entered into the TB Program database by an office assistant.

Screening for each individual was dependent on each client's prior testing or disease status.[13,19] For homeless clients who had no prior tuberculin skin test (TST), prior negative results, unknown prior results, or undocumented prior positive results, the screening began with the placement of a TST. Upon reading of the test 48-72 hours after placement, clients with a negative (< 10 millimeters) test received a clearance card. If the test result was positive (≥ 10 mm), the client was referred to the Multnomah County TB Clinic for further evaluation. If a test result was negative but symptoms for active TB were present, the client was referred to the clinic for further evaluation. For homeless clients who had a documented prior positive test or prior active TB at the time they presented for screening, a TST was not placed and instead the clients were referred to the clinic for evaluation. The evaluation at the clinic consisted of collecting a medical and social history. A chest x-ray was completed for clients who lacked up-to-date imaging or who presented with symptoms consistent with progression to active TB. If the chest x-ray was normal or abnormal but inconsistent with TB, a clearance card was issued. If the chest x-ray was abnormal consistent with TB, sputum was collected and analyzed. If sputum was collected, a temporary clearance card was issued until initial smear results were received. There were no difference in the screening process between US-born and foreign-born homeless clients.

A client was positive for LTBI if the TST reaction was 10 mm or greater of induration and the chest x-ray was negative. The chest x-ray was necessary to rule out

active TB.[6] A TB Clinic nurse recommended treatment if a client has LTBI and did not meet any of the following conditions:

- multiple treatment initiation attempts with default
- multiple medications for other diseases or conditions
- deemed unreliable
- planning to leave town within a few months
- already completed treatment

For sheltered clients, there was no upper age limit for recommending treatment.[20] In the foreign-born population, the standing orders for starting treatment indicated an upper age limit of 50 years old, but for the homeless foreign-born population there was no upper age limit consistent with the sheltered client procedure. The sheltered homeless procedure superseded the foreign-born procedure for clients who fell into both categories per the TB Program nursing supervisor and two TB Clinic nurses.

When recommending treatment, the nurse educated the client about both LTBI and active TB. Additionally, the nurse told the client that homelessness and medical problems put them at greater risk for progressing to active TB.[19] For clients who agreed to begin treatment, a follow up appointment was scheduled for about two weeks after the evaluation.

A simplified diagram of the screening process is presented in Figure 2.

Study Population

The study population included the sheltered homeless age 18 and older who began the screening process by Multnomah County Health Department's TB Control and

Prevention program between January 1, 2002 and December 31, 2007 and received a recommendation for treatment for LTBI. All clients included in the analysis were seen in the TB Clinic because treatment recommendations only occur after referral for an evaluation as described on the previous page. Clients excluded from the analysis included any contacts identified in prior TB contact investigations, any client who previously had active TB disease, or clients suspected of having active TB disease. Additionally, any clients who did not begin treatment because they moved out of the county, sought services of a private provider, had debilitating mental illness, or were told that they were no longer recommended for treatment due to a newly identified medical problem were excluded.

All clients who met these criteria were included in the study, so no sampling method was required.

Participants were not reimbursed for their participation in the screening. They received a clearance card required by local shelters.

Data collection, measurement, and preparation

Data were collected at the time of screening at Salvation Army Harbor Light in Portland, Oregon as well as during evaluation and treatment initiation visit at the Multnomah County Health Department TB Clinic. A single 'screening event' included the TST (unless a prior positive TST is documented) and any resulting evaluation in the MCHD TB Clinic. The screening event could have occurred over multiple days and multiple interactions with TB Clinic staff. A description of how the data were collected is noted in the 'Overview of study design and TB Program' section above.

*Clients in the analysis*

All encounters coded as 'is sheltered' from 2002 through 2007 were extracted from the TB database with one record representing a single screening event. Additionally, a Health Information System (HIS) dataset for TB Program encounters prior to 2002 was pulled. All screening events for any client with a TB Clinic encounter prior to 2002 according to the HIS dataset were excluded from the TB database dataset. The resulting dataset represented screening events for clients who were first screened by the Multnomah County TB Program between 2002 and 2007. Only the first screening event at which treatment for LTBI was recommended was retained for each client.

All screening events that ended in an unread TST or a negative TST were excluded from the dataset because those results indicated unknown or negative LTBI status, respectively. The exclusion of unread and negative TSTs reflected our initial broad case definition, which retained a less specific group of clients who may or may not eventually receive a treatment recommendation. Our narrow case definition included clients who were offered treatment. All clients with LTBI for whom treatment was not recommended were excluded because this analysis was concerned with who begins treatment for LTBI, which could only occur in the subset of clients for whom treatment was recommended. All screening events involving a new or prior positive TST but lacking a complete evaluation at the TB Clinic were excluded because treatment was only offered to clients who completed the evaluation. Additionally, clients who were initially recommended for treatment but later had a reason for not starting treatment with the Multnomah County Health Department (moved to another county, sought care with a private provider, identified new medical conditions that changed the treatment

recommendation) were excluded. Any client who previously had active TB disease, was a contact to an active TB case, or was a suspect TB case was excluded from the analysis because treatment for LTBI either wasn't recommended or was thought to start at higher proportions compared to the general homeless population.

For clients younger than 18 years old at the first visit when treatment was recommended, all visits were excluded regardless of whether a later screening event when the client was over 18 years old occurred. Since the dataset only included the first visit when treatment was recommended, any later visit when treatment was recommended – assuming treatment did not begin after the first screening event - would not meet the 'first visit' definition.

The resulting dataset included the first screening event at which treatment for LTBI was recommended for clients screened between 2002 and 2007, for a total of 916 clients (Figure 3).

New variables were coded for the analysis as described below.

*Exposure variable*

The exposure variable of interest was foreign-born status. This dichotomous variable took the value of either 'foreign-born' or 'US-born'. The foreign-born variable was created by categorizing any client with a listed country of origin as 'foreign-born' and all other clients as 'US-born'. Only clients born outside the United States had a country recorded.

*Covariates*

Potential confounders and effect modifiers were identified by considering which of the available variables in the database might be related to treatment initiation; we considered age, sex, substance abuse, race/ethnicity, and shelter. Measurement information and rationale for including the covariate are provided (Table 1). Variable coding is described below.

*Age*

Age was determined by subtracting the date of birth from the first day of the screening event, thus it was recorded as a continuous variable. Although modeling age as a continuous variable seemed appropriate based on plotting the log-odds by the mid-point for age groups, the difference in age between foreign-born and US-born clients led us to examine age as a categorical variable in this analysis.

Initially, we chose 10-year age increments (with 18 and 19 year olds added to the 20 -29 age group) since this is a standard way to categorize age, however we combined categories based on small numbers in some categories. After these modifications, our age categories were: 18 – 29; 30 – 49; and 50+.

*Sex*

The original sex variable from the TB Database was sufficient to use without modifications, thus we kept the ‘male’ and ‘female’ categories as recorded.

*Substance abuse*

The substance abuse variable was a combination of two substance abuse-related variables – in drug treatment and intravenous drug use. These variables were collected during the history conducted by the nurse at the clinic evaluation visit. If a client answered yes to either or both of the original variables, the new substance abuse variable was coded as 'Yes'. All other clients were coded as 'No'.

*Race/Ethnicity*

The race/ethnicity variable had three strata and combined the race and ethnicity variables - which were self-reported by the clients early in the screening process - from the TB database. The 'Hispanic' stratum included any client who reported ethnicity as Hispanic regardless of race. The 'non-Hispanic white' stratum combined the non-Hispanic ethnicity category with the white race category. All other non-Hispanic race groups including Black, Asian, other uncommon race categories in this population, and unknown race made up the 'Other/Unknown' category.

*Shelter*

There were four large shelters in the Burnside area – Portland Rescue Mission, Salvation Army Harbor Light, Transition Projects Inc., and City Team Ministries - as well as numerous smaller shelters, each varying on characteristics such as size, acceptability of intoxication, sobriety requirements, waiting list, and support services. Portland Rescue Mission had the most minimal rules and support services and thus this shelter might have attracted a different population than the other shelters. Given the

variation between shelters and the small number of clients from some shelters, we categorized shelter as ‘Portland Rescue Mission’ versus ‘Other’.

*Outcome variable*

The outcome variable was treatment initiation within 60 days of recommendation for treatment of LTBI. The dichotomous variable was coded as ‘yes’ or ‘no’.

Given that a screening event could extend over multiple days and the exact day when treatment was recommended was not recorded in the database, we chose the first day of the first screening event when treatment was recommended as a proxy for the treatment recommendation date. The difference in number of days between the treatment start date and the proxy treatment recommendation date was obtained. If the number of days was 60 or fewer, the client was categorized as ‘yes’ for the outcome variable. All other clients, whether they started treatment after 60 days or never started treatment, were categorized as ‘no’. The cutoff point of 60 days was chosen to allow for sufficient time for treatment to begin. According to the TB Program Nursing Supervisor, treatment usually began about two weeks after the evaluation in the TB Clinic. Allowing 60 days permits for rescheduling or other delays in the evaluation or the treatment initiation appointment. Additionally, we considered cutoff points of 30, 90, and 120 days to check if the results differed based on the number of days between treatment recommendation and initiation.

## Analysis

### *Overview of analysis*

Descriptive statistics were run for specific aim 1. For specific aim 2, the hypothesis that foreign-born homeless clients would initiate treatment at a higher proportion than US-born homeless clients was tested using a multiple logistic regression modeling. All data management and analyses were conducted with SAS 9.1 (SAS Institute, Inc., Cary, NC).

### *Descriptive statistics (Specific Aim 1)*

The data were examined using cross-classification tables for exposure and outcome, exposure and potential confounders, and outcome and potential confounders. Odds ratios, 95 percent confidence intervals, and chi-square tests were used to further identify differences within the tables.

To assess any differences in the exposure-outcome association by characteristics of the population, we stratified by the potential confounders/effect modifiers. We ran chi-square tests except when the expected value for any cell was less then 5, in which case we ran Fisher Exact tests.

### *Statistical Models (Specific Aim 2)*

For specific aim 2, logistic regression was employed to test the hypothesis that foreign born sheltered homeless clients begin treatment at a higher proportion than US-born sheltered homeless clients.

The initial model consisted of foreign-born status as the independent variable and treatment initiation within 60 days from recommendation as the dependent variable, producing a crude odds ratio for the association of interest.

Each potential confounder was entered individually into the univariate model. This allowed us to assess any changes between the crude and adjusted odds ratio for the foreign born and treatment initiation association.

We statistically examined potential effect modification by age in the primary association of interest by creating a model with foreign-born, age, and foreign-born x age because the stratified analysis indicated that age appeared to modify the association between foreign-born and treatment initiation.

Next, we performed backwards elimination to create a preliminary model[21]. Foreign born, age (categorical), and the age x foreign-born interaction term were forced into the model. After the preliminary model was determined, each potential confounder was individually added into the preliminary model to assess whether confounding was present. A change of 10 percent or more between the foreign-born versus US-born odds ratios stratified by age in the preliminary model and the same odds ratios from the models in which potential confounders were added individually defined a confounder. Variables that met the 10 percent requirement remained in the model whether or not the p-value for the term is less than 0.05.

To assess how the cutoff point of 60 days for the period between treatment recommendation and treatment initiation may have impacted the results, we conducted a sensitivity analysis. Leaving the predictors the same, we changed the outcome to treatment initiation within 30 days, 90 days, and 120 days from recommendation.

The Multnomah County Health Department and Oregon Health & Science University Institutional Review Boards determined that this project was not human subjects research given that we evaluated a public health practice program.

## RESULTS

*Descriptive Statistics (Specific Aim 1)*

Of the 916 sheltered homeless clients for whom treatment was recommended, 236 (25.8%) started treatment. The foreign-born population represented one-fifth of the included clients. The majority of the clients were in the 30-49 age group (n=508), while almost 30 percent of the clients were age 50 or over. Mean age was 43.3 (+- 11.46) years and median age was 43.5 years. Males far outnumbered females, making up nearly 90% of the clients. Only 47 clients (5%) reported substance use. Hispanic, non-Hispanic White, and Other/Unknown race/ethnicity represented 30%, 44%, and 27% percent, respectively. About 35% of the clients were sheltered at the Portland Rescue Mission. Client characteristics are presented in Table 2. Medical conditions and HIV variables were excluded from further analysis given the insufficient numbers with the conditions recorded in the database.

With the exception of shelter, all covariates were significantly associated with foreign-born status (Table 3). Foreign-born clients tended to be young, male, Hispanic, and not substance abusers. Of the 210 foreign-born clients, 87 % were from Mexico. Mean age for foreign-born was 38.6 (±10.3) and for US born was 44.7 (±11.4)

The percentage of clients starting treatment did not differ by population characteristics except foreign-born versus US-born status (Table 4) About one-third of the clients who started treatment were foreign-born. Of all foreign-born clients, 37.1% started treatment while only 22.4% of all US-born clients started treatment. Foreign-born homeless clients had twice the odds of initiating treatment for LTBI as US-born homeless clients (OR: 2.05; 95% CI: 1.47, 2.85).

Most of the stratum-specific odds ratios for the association between foreign-born versus US-born and treatment initiation remained close to the crude odds ratio of 2.05 suggesting no confounding or effect modification, however age was a notable exception (Table 5). Foreign-born clients in the 18-29 age group had nearly the same odds of initiating treatment as the US-born clients in the same age group (OR: 1.16; 95% CI: 0.55, 2.46). For the 30-49 age group, foreign-born clients greater odds of initiating treatment as compared to the US-born clients with borderline significance (OR: 1.85; 95% CI: 0.98, 3.53). Initiation of treatment for LTBI in the 50 and above age group was much higher for the foreign-born clients than the US-born clients (OR: 5.13; 95% CI: 2.40, 10.96). While our analysis produced a large difference between the male and female odds ratios for nationality and treatment initiation, we did not examine this further given the small cell counts and resulting imprecision as shown by the wide confidence interval.

Examining the descriptive statistics for treatment initiation as well as covariates stratified by foreign-born versus US-born status and age provides useful information about the difference in treatment initiation and covariates by age for foreign-born versus US-born clients (Table 6). While both the foreign-born and US-born clients start

treatment at similar proportions (29% v 26%) in the 18-29 age group, the foreign-born clients become more likely to initiate treatment in the older age groups (to 36% and 55% for the 30-49 and 50+ age groups) while the US-born clients stay about the same or slightly decrease treatment initiation (to 24% and 19% for the 30-49 and 50+ age groups). Figure 4 shows the percentage starting treatment for LTBI by age group and nationality.

*Statistical Models (Specific Aim 2)*

Only the race/ethnicity variable changed the odds of starting treatment between the foreign-born and US-born more than 10% from the crude odds ratio (Table 7). Consistent with the variation in stratum-specific odds ratios for age, the foreign-born by age interaction term was significant (p=0.018).

Treatment initiation in the foreign-born compared to the US-born in the 18-29 age group was not statistically different (OR 1.16, 95% CI .55-2.46), but foreign-born clients had about 1.8 times (95% CI 1.18, 2.83) the odds of starting treatment than the US-born clients in the 30-49 age groups, and 5 times (95% CI 2.40, 10.96) the odds of starting in the 50 and above age group (Table 8). Further, after adjusting for race/ethnicity the odds ratios increased by over 10 percent, indicating that negative confounding was occurring. Adding race/ethnicity followed a similar pattern with no evidence for nationality having a role in treatment initiation for the 18-29 age group, while the odds of foreign-born clients in the 30-49 age group starting treatment were twice (95% CI 1.29, 3.52) that of the US-born clients and six times (95% CI: 2.69, 13.52) in the 50 and above age group (Table 9). The race/ethnicity variable was not statistically significantly associated with treatment initiation (p=0.426).

Our sensitivity analysis showed that the odds ratios for the association between foreign-born and treatment initiation for each age group were qualitatively the same and thus the results did not depend of the selection of the cut off point (Table 10).

## DISCUSSION

### Overview of results

Our analysis found that foreign-born status interacts with age in relation to who initiates treatment for LTBI in the sheltered homeless for whom treatment is recommended. While the crude odds ratio for the association between foreign-born status and treatment initiation indicated that foreign-born clients had about twice the odds of initiating treatment as US-born clients, examining this association for different age groups showed that the relationship was more complex. Our hypothesis that foreign-born homeless clients are more likely to start treatment than US-born homeless clients was correct for the 30-49 and 50 and above age groups when holding race/ethnicity constant, however we do not have evidence that treatment initiation occurs at different proportions for the 18-29 age group.

The finding that foreign-born clients have greater odds of initiating treatment for LTBI than US-born clients was consistent with two studies that examined adherence to treatment for LTBI in similar populations – an inner city population [15] and a public health clinic. [16] Neither study examined effect modification by age, so we are not able to determine if the same pattern - a strong association between foreign-born status and

treatment initiation for the oldest age group and the lack of an observed association for the youngest age group - was present in their study.

Marks, DeLuca, and Walton's analysis of knowledge, attitudes, and risk perception from the US National Health Interview Survey provides some useful insight into our results[22]. According to their analysis, foreign-born persons were 90% more likely to know that TB is curable than US-born persons. Foreign-born persons who had lived in the United States for 15 or more years were 8% more likely to know that TB is curable than foreign-born persons who had been in the US for less than 1 year. Marks et. al. noted regional variations, indicating that recent Hispanic immigrants were among the least likely to know that TB is curable. The 18-24 and 25-44 age groups were both about 60% less likely than the 45 and above age group to know that TB is curable. While the Marks et. al. study reflects knowledge, attitudes, and risk perception about active TB rather than LTBI, their results may still be applicable to our findings. If a group tends to feel at higher risk for active TB and they are told that treatment for LTBI can greatly decrease the risk of developing active TB, this could explain in part why people in that group tend to start treatment for LTBI more frequently. It is also possible that we observed a cohort effect in which the older foreign-born population is different from the younger foreign-born population based on the period during which they were born rather than the age difference. The older foreign-born population may have witnessed more TB deaths and have more knowledge about TB than the younger population, which may increase their likelihood of wanting to initiate treatment.

For confounding by race/ethnicity, the strong association between foreign-born status and race/ethnicity drove the change in the odds ratio. While the distribution of

treatment initiation in the three race/ethnicity groups varied slightly, the difference did not reach statistical significance. We cannot rule out that we had insufficient power to detect an association between race/ethnicity and treatment status.

## Alternative explanations

### *Chance*

While chance can never be ruled out entirely, it is unlikely that it explains the results based on a small p-value and evaluation of the confidence intervals. The p-value for the interaction term is small (p=0.015). The odds ratio for the 18-29 age group was not significantly different than the null value of one thus there is not an observed association that needs to be assessed for alternative explanations. It is possible that the lack of an observed association for this age group could be due to insufficient power. For the 30-49 age group, the confidence interval is narrow due to the large number of clients in the stratum and does not cross the null value of one. Given the large odds ratio for the 50 and above age group and the lower limit of the confidence interval being far from the null value of one, chance seems very unlikely to play a role even with the wide confidence interval. Random error does not seem to be a likely explanation of the observed results for the 30-49 and 50+ age groups.

*Bias*

*Selection bias*

Selection bias would result if the clients who were excluded from the study were different in some way that was related to both foreign-born status and treatment initiation. Sampling was not used in this study since it was an evaluation of a specific program and all clients who met the inclusion and exclusion criteria were included. All clients in the data set needed to receive a recommendation for treatment to be included for analysis, so recommendation for treatment would need to differ for both foreign-born status and treatment initiation for selection bias to have occurred. Not recommending a client for treatment could happen because the client was unlikely to complete treatment, but the judgment that a client should not be recommended for treatment would have to be related to foreign-born status to result in selection bias. Although some judgment was involved in determining who was recommended for treatment, there were written standing orders for the nursing staff to follow.

If potential clients died from TB prior to the screening period, they would not have been included in the data set. US-born clients would be expected to have died from TB prior to entering the study less often than foreign-born clients. Foreign-born clients who are still living may have witnessed more TB-associated deaths throughout their lives, and thus may be more likely to initiate treatment. These patterns would be expected more in the older age groups than the youngest age group given the more years lived equates to a higher likelihood of infection with *M. tuberculosis* and progression to active disease. Even if this pattern occurred, it would represent the true state of

tuberculosis in these populations, and not an error in how the clients were selected into the evaluation because sampling was not necessary for this study.

Given that the study used a historical cohort design, loss to follow up could lead to selection bias if the clients who were recommended for treatment but did not attend the treatment initiation visit were systematically different in foreign-born or US-born status. Clients who were deemed unlikely to complete treatment by the nursing staff would not have been recommended for treatment, so they would not have been in the data set for the evaluation and would not be susceptible to be lost to follow-up. For clients who received a recommendation for treatment, there is only one point at which they could be lost to follow-up – between the recommendation for treatment during the evaluation visit and the treatment initiation visit. The end of the same period is when a client either begins or does not begin treatment. If loss to follow-up between the evaluation and treatment initiation visit occurred in the US-born population but less so in the foreign-born population, loss to follow-up could explain the lower percentage of US-born clients who initiated treatment in the older age groups. The reason for a client declining treatment was not recorded, so we are unable to determine if the client was lost to follow-up or declined treatment for some other reason. If a client indicated the intent to begin treatment with a primary care physician or in another county, the client was excluded from the analysis. Thus a client would only be lost to follow up if treatment was initiated at another location but the client did not inform the health department. If US-born clients were more likely to have a source of care outside the health department than foreign-born clients, part of our findings – at least for the older age groups – could be explained by starting treatment in another place.

*Information bias*

The exposure and outcome are unlikely to be subject to recall bias. Participants are likely to recall whether they were born in the United States or in another country. Treatment initiation was not based on client recall, rather it is a measure obtained from the clinic.

For investigator bias, it is unlikely that nurses would record treatment initiation information differently for foreign-born versus US-born clients because treatment initiation is a concrete event tied to a date. It there were entry errors, there is no apparent reason why the entry would happen differently for foreign-born as compared to US-born clients.

Errors in measurement are likely to have occurred in the data collection process, however these errors are unlikely to be related to both foreign-born status and treatment initiation. If these errors occurred, the bias would be toward the null and the true association would be strong than observed.

Foreign-born clients may have been misclassified as US-born if no information was obtained or recorded about their country of origin because the coding of the variable categorized every client without information about their country of origin as US-born. Misclassification of the exposure variable given the coding method would only happen in the direction of foreign-born being misclassified since a US-born client would not have a country of origin and date of entry. This misclassification may have occurred less often for clients who initiated treatment because they had more contact with the program staff. If the foreign-born who were classified as US-born started treatment more often than the correctly classified US-born, the true association would be stronger than the observed

association. If the foreign-born who were classified as US-born started less often than the correctly classified US-born – the more likely situation - then the observed association between foreign-born and treatment initiation would be an overestimate.

Any clients who started treatment at another location but did not tell the TB clinic of that plan would have been counted as not starting treatment. If the client told the client of the plan to move, they would not have been recommended for treatment or they would have been excluded from the data set if they had received a recommendation. The number of clients in this situation is estimated to be very low.

Any data entry errors would not seem to be systematic in that foreign-born or US-born clients would not be more or less likely to have treatment initiation status entered incorrectly and treatment initiation status would not be likely to have been entered incorrectly more for one nationality or the other; the data entry errors would be random. Thus any data entry errors would be non-differential and would bias the observed association toward the null.

Misclassification of potential confounders is addressed in the confounding section below.

*Confounding*

Race/ethnicity was found to confound the association between nationality and treatment initiation, however given that race/ethnicity functioned as a negative confounder the observed association was strengthened after adjustment rather the approaching the null value of one. Since adding race/ethnicity did not decrease the odds

ratio toward the null value of one, race/ethnicity is not in the causal pathway between foreign-born status and treatment initiation.

Although race/ethnicity was the only variable deemed a confounder in this analysis, the possibility remains that confounding could play a role. Most of the potential confounders considered in this analysis were likely not measured accurately, so residual confounding could be present. Misclassification of substance abuse is very likely to have occurred based on the variables used to code the substance abuse variable. During the evaluation at the TB Clinic, a question about substance abuse separate from drug treatment and intravenous drug use was asked, however the response was not entered into the database. We believe that the percentage of clients who abuse substances is significantly higher than the observed five percent. As a comparison, the Bock et. al. study of the inner city population in Atlanta found that 44 percent of participants reported substance abuse. [15] If the US-born clients in the older age groups were more likely to abuse substances than the foreign-born clients in the older age groups, the observed association between foreign-born status and treatment initiation might be explained substantially by confounding. The substance abuse variable as measured in this project shows that about 2.5 percent of foreign-born clients reported substance abuse while about six percent of US-born clients reported substance abuse, which equates to 2.5 times the substance abuse in US-born than foreign-born clients. While it is not clear that having more complete data about substance abuse would follow the same pattern, the likelihood that substance abuse could explain – at least in part - the observed association is substantial. Additionally, small cell sizes are more susceptible to the effect of misclassification. While sex is unlikely to have been misclassified, the number of

foreign-born or treatment initiators who are male or female could have been misclassified in the stratified analysis. Small cell sizes destabilize the observed stratified associations, therefore small sample size may have inhibited the ability to detect confounding or effect modifier. Larger sample size could have helped with this problem by improving the stability of the measure of association.

Unmeasured potential confounders should be considered. Given the purpose of data collection is screening, collecting data for all possible confounders was not a goal. HIV infection status and existing medical conditions are important risk factors for progressing to active TB disease – and thus starting treatment - thus having useful measurements in the database would have been helpful in determining if these factors confound the association between nationality and treatment initiation for the three age groups. These data were collected in the database, however the very small numbers identified prevented us from including them in our analysis. Additionally, being able to differentiate newly positive tests, prior positive tests that converted to positive in the last two years, and prior positive tests from over 2 years might indicate who is more likely to begin treatment. It would be useful to collect data about the "complex social context" such as education and psychiatric disorders[10]. Additionally, perceptions of risk for progression to active disease, beliefs about tuberculosis, and understanding of treatment for LTBI should be examined given that they could be in the pathway between foreign-born status and treatment initiation[23]. All of these potential confounders would need to have different distributions among the foreign-born and US-born clients to confound the association. For these potential confounders to explain the association between foreign-born status and treatment initiation, the foreign-born clients in the upper two age groups

would need to have more medical conditions, higher levels of HIV infection, or more newly positive test results than US-born clients.

Unknown confounders may exist. According to Winkelstein el. al.'s analysis of the necessary strength of association between a confounder and the outcome to explain the observed association, the unknown or unmeasured confounder would need to have an odds ratio of 3.76 for treatment initiation versus not for the 30-49 age group and 11.6 for the 50 and above age group [24]. Only a positive confounder would be able to explain the observed association for the 30-49 and 50 and above age groups. While an unmeasured or unknown confounder may exist, it seems unlikely that we would find such a variable with an odds ratio of 11.6 for clients age 50 and above. Even substance abuse – if measured well – would most likely not reach an odds ratio of 11.6 and thus would only explain part of the observed association for the 50 and above age group.

## Limitations

### *Population*

The data were collected for public health practice. While this project evaluated a program within the realm of public health practice, the accuracy of the dataset was still important. Additionally, given the many steps of a screening event for a client for whom treatment is recommended, the dataset was complex. Because information is also in the medical chart, it is possible that certain data did not make it into the database. One data element that would have been useful is why a client who did not begin treatment declined.

Only homeless persons who stayed in shelters were targeted for testing and included in the dataset. The congregate setting of a homeless shelter would be expected to hold higher risk than outdoors. Homeless individuals currently staying outdoors may have consistently stayed in a shelter in the past and could have been exposed to *M. tuberculosis* and have latent infection that needs treatment. It is unclear how adding foreign-born status into the picture would impact the estimate because the distribution of foreign-born and US-born homeless persons who stay in shelters versus stay outdoors is unknown.

The homeless population can pose challenges to follow up in part due to mobility[25], so the required screening for the clearance card builds in motivation for screening on the part of the population. Homeless persons who chose not to initiate treatment for LTBI can still obtain a clearance card, thus the clearance card requirement does not impact our outcome.

The purpose of the evaluation was not generalizability, rather we wanted to assess the specific screening program. At the same time, our results may be similar for the sheltered homeless in other low TB incidence counties in which the foreign-born population is predominately Mexican.

*Database issues*

The database was created for reporting on public health practice TB activities, so the data were not structured in a way that was consistent with evaluating program outcomes.

Some variables involved a check box, which may have been easy to overlook when entering data. According to the nursing supervisor, there were no checks in place to ensure accuracy of data entry.

Multiple people have entered data into the database over time. This could result in some inconsistencies during the time period examined. Additionally, much of the data entry is done by office assistants who are not familiar with TB.

*Sample size*

While the total sample size was not a limitation for most elements of the analysis, the number of clients in some cells of the stratified analysis was very low for reasons described in the bias section below. For this reason, more total clients could have improved the stratified analysis and improved the precision of the stratum-specific estimates.

Implications

The results raise two primary questions - what about the foreign-born clients make them more likely to initiate treatment at older ages and why do US-born clients have somewhat similar treatment initiation proportions across the age groups? We do not have the data to answer the questions, however the program may choose to examine these questions given the results of this evaluation.

The results will be presented to the medical director, program manager, and nursing supervisor of the TB Program. Given that resources are limited – and even more so this year than in recent years – the results may be one of many factors that impact

practices surrounding screening and treatment when indicated. There are multiple approaches that can be taken, including but not limited to increased focus on encouraging treatment initiation in all clients given that the percentage starting treatment was low overall. Older foreign-born clients could be encouraged to begin treatment more strongly since they tend to start at higher percentages than US-born clients and may need less encouragement to begin treatment, which would increase the percentage of clients starting treatment even more. Another strategy could be to focus on the US-born clients in all age groups since the absolute number of clients who initiate treatment is lower than the foreign-born clients and the percentage starting treatment is low across all age groups.

The ATS and CDC recommend targeted tuberculin testing for high-risk groups. [6] While local epidemiology of TB and budget concerns can impact decision making about screening practices, the Institute of Medicine stresses that screening groups that are likely to have large numbers of individuals with LTBI is preferable over waiting until individuals develop active TB or die from TB. [3] Targeted testing seems particularly important in the sheltered homeless population given that an active case can spread *M. tuberculosis* in a crowded environment and access to healthcare can be limited if the population is not aware of clinics that serve the homeless or are impacted by other barriers to healthcare.

Strengths of the evaluation

A major strength of the analysis was that we examined a population comprised of overlapping high-interest groups – foreign-born and homeless risk groups. Although

these two high-risk groups individually tend to be the focus of studies, carrying out analyses to understand the overlap between the high-risk groups happens infrequently.

Conducting the sensitivity analysis was important and strengthened the evaluation. The choice of a cutoff point can impact how many clients are coded as starting treatment, while a client who did not start treatment would be in the 'no' group no matter what cutoff point was chosen. Our sensitivity analysis showed that the odds ratios were qualitatively similar for all cutoff points and thus the results did not depend of the selection of the cut off point.

The availability of longitudinal data allowed us to use a period of time rather than only assessing whether treatment began or not.

Future studies

Other ways to examine the question in the future could include another historical cohort study using a supplemental data source and a prospective cohort study.

Using a historical cohort study design, the TB database could be supplemented by chart review. While this would require more resources to complete, the benefit would be improved data about the clients given that additional history that affects clinical care was recorded in the medical record beyond the history included in the TB database. In particular, the chart review could assess HIV status, medical risk factors, and substance abuse more completely than was possible from examining the TB database extract. All clients for whom treatment is recommended received an evaluation at the TB Clinic, thus all clients in the data set would have a chart for review. Another source of additional data that could be of use is medical records from local clinics that serve the homeless. The

local clinic data would be useful in determining existing risk factors such as substance abuse and mental health.

Another method to assess the hypothesis would be a prospective cohort study. All clients who attend their first Multnomah County Health Department screening could be interviewed to ascertain additional information about their risk factors, perceived risk, and knowledge and attitudes about TB and the role of LTBI in active TB disease. The interview could be conducted at the time the TST is placed, so the data would be collected prior to the client obtaining TST results in order to decrease information bias. A benefit of this design over the retrospective cohort design is that the study staff would be able to collect and enter the data following predefined procedures to improve the accuracy. Additionally, the way that questions are asked would be specific to the study to ensure that the way the question are asked reflected the intended meaning in contrast to using existing variables that were asked for reporting and clinical purposes rather than epidemiologic ones.

A related but different question of interest pertains to who completes treatment rather than who initiates treatment. The question is important because finishing treatment ultimately is what prevents progression from LTBI to active TB disease. Understanding how treatment completion differs between foreign-born and US-born clients, and improving understanding of what characteristics predict who will completed treatment of all clients who initiated treatment would be useful in knowing how to intervene to improve adherence to treatment.

## SUMMARY AND CONCLUSIONS

Foreign-born sheltered homeless clients had about twice the odds of initiating treatment within 60 days from treatment recommendation as the US-born sheltered homeless clients in the 30- 49 age group after adjusting for race/ethnicity. In the 50 and above age group, foreign-born clients had about six times the odds of initiating treatment as US-born clients after adjusting for race/ethnicity. We did not find evidence for a difference in treatment initiation between nationality groups for the 18-29 age group. Even though other potential confounders of interest – especially substance abuse - were not able to be assessed in this evaluation, the results still provide useful information about where to intervene.

The Multnomah County Health Department TB Program will be presented the results of this evaluation. Limited resources may drive programmatic cuts, thus the results from this evaluation could be one piece of information that contributes to decisions about where best to use program resources.

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Figure 1. Schematic time course of stages of progression through the infectious process from exposure to death. (Adapted from Rothman, Greenland, and Lash[26(p.550)])

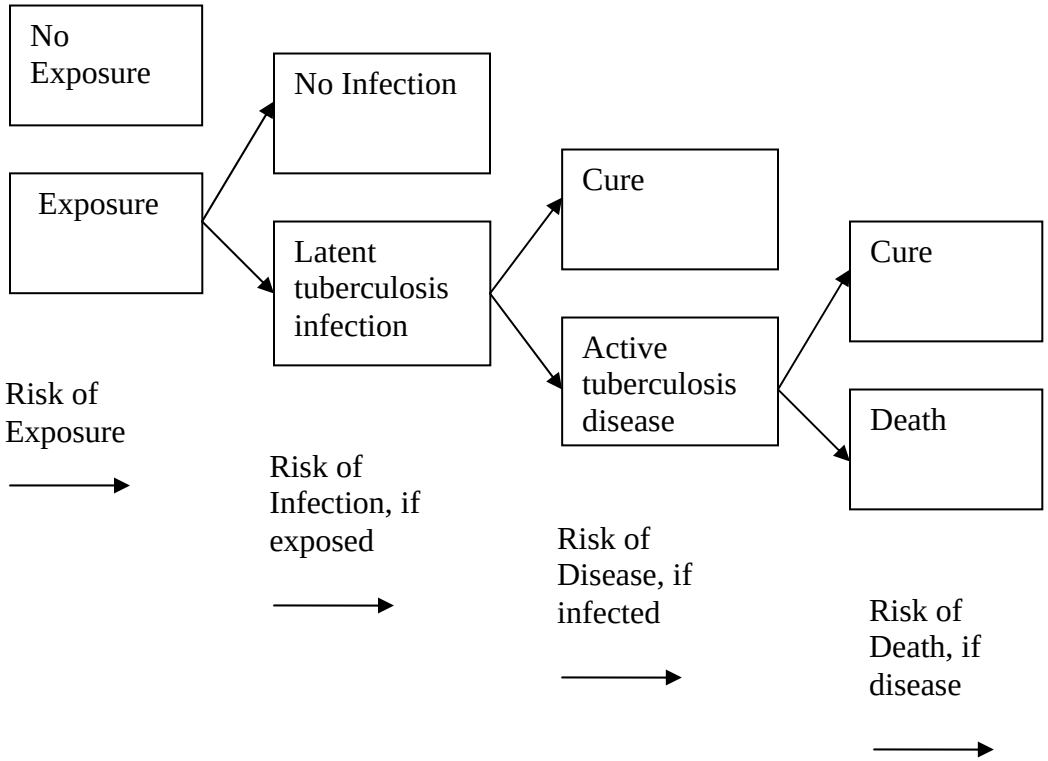

Figure 2. Screening process (simplified) for Multnomah County Health Department Homeless Outreach Program

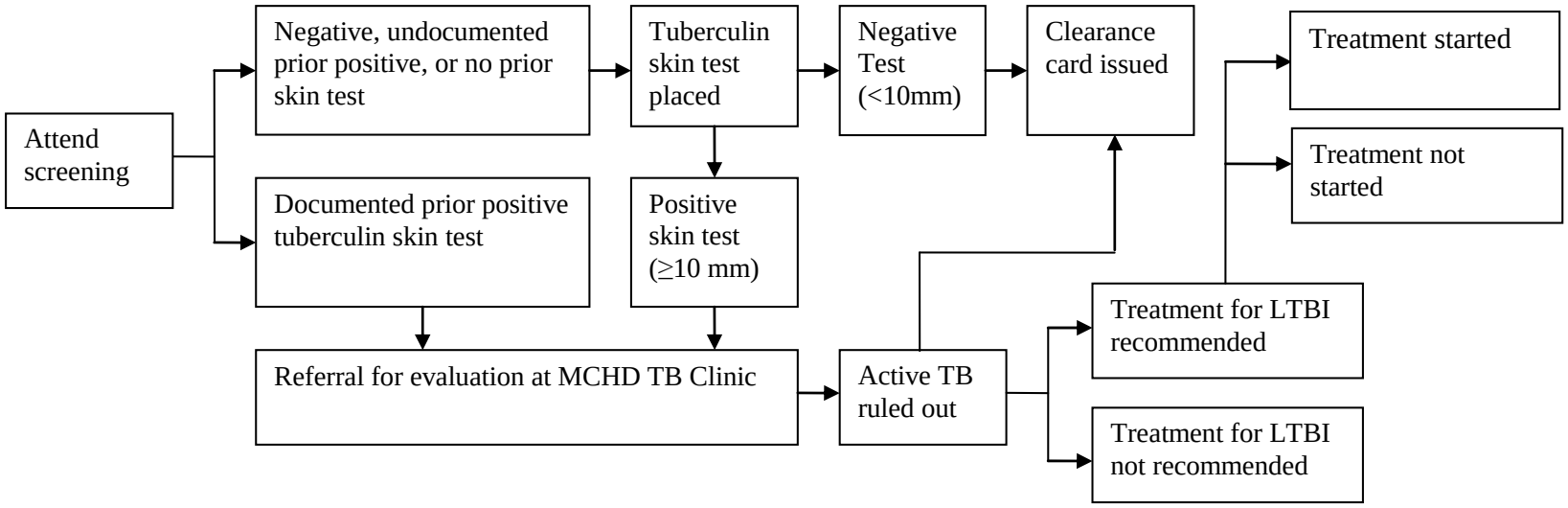

Figure 3. Process to identify clients included in the analysis

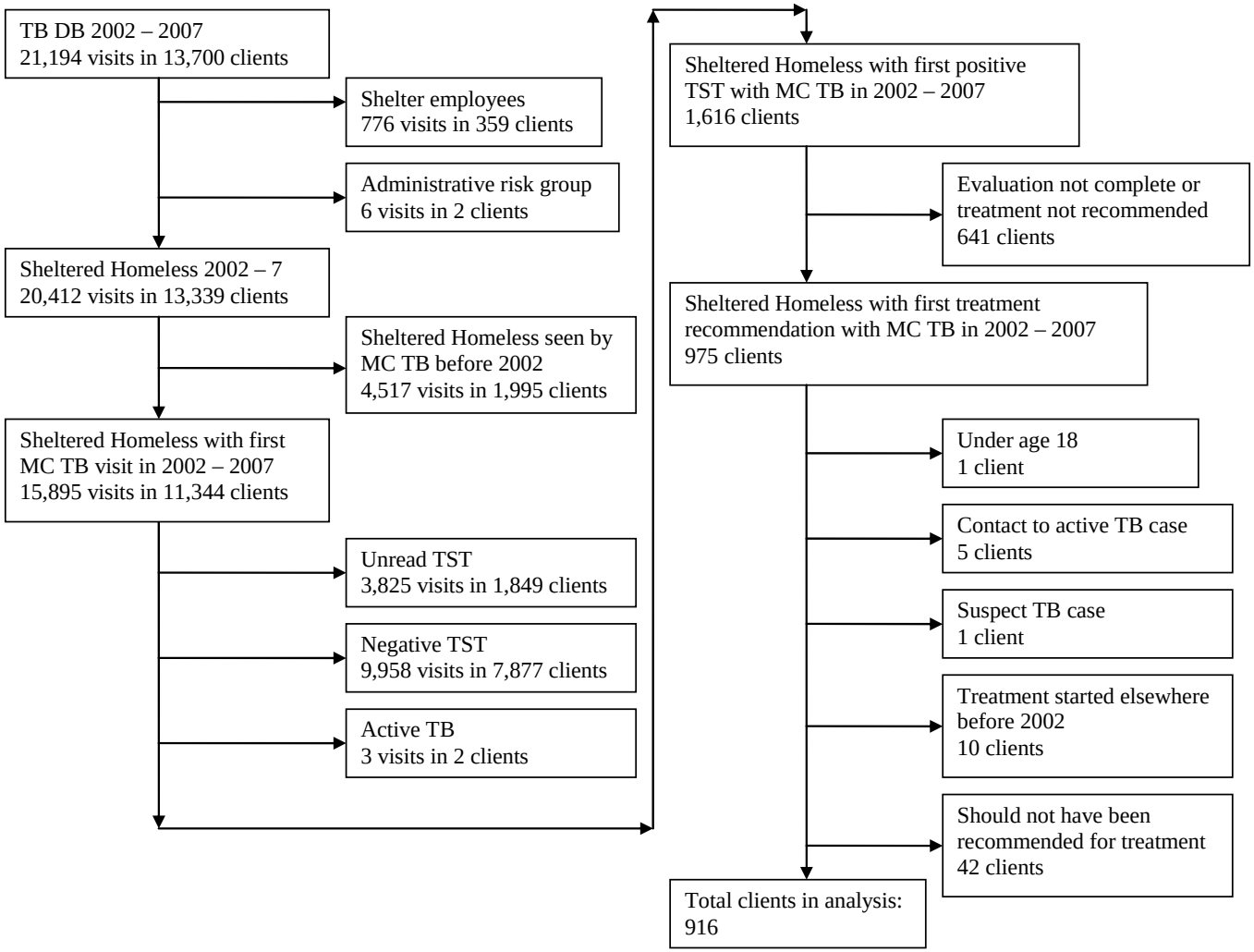

Figure 4. Percent of sheltered homeless who initiate treatment by age group and foreign-born status

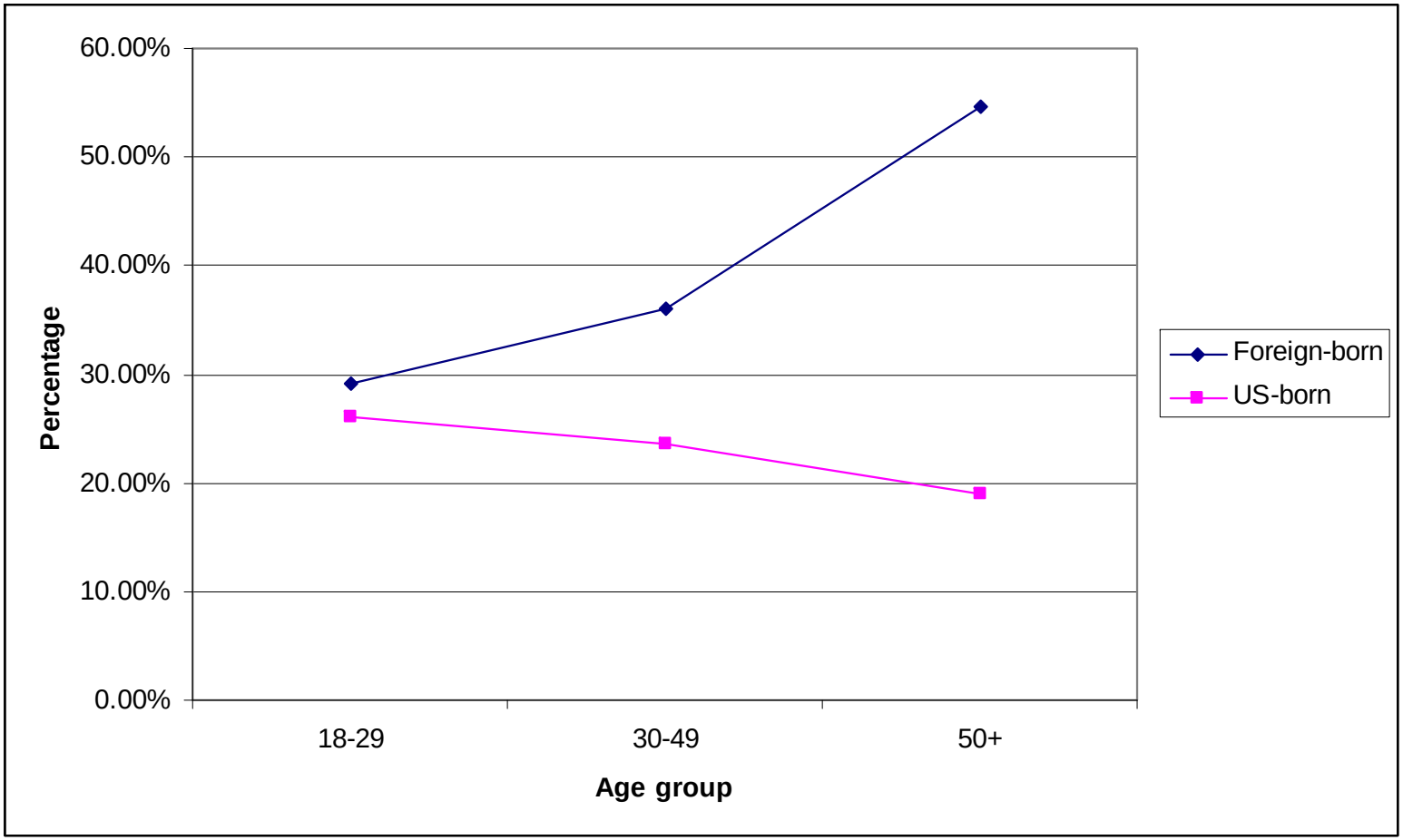

Table 1. Potential Confounders

| **Potential Confounder** | **Measurement** | **Rationale** |
|---|---|---|
| Age | Categorical; 18 – 29, 30 – 49, 50+ | Beliefs about preventive medication may vary by age |
| Gender | Categorical; Female, Male | Males and females may view the usefulness of preventive medications differently. |
| Race/Ethnicity | Categorical; Non-Hispanic White, Hispanic, Other/Unknown | People of varying races may tend to view the medical establishment differently, and may therefore be more or less willing to initiate treatment. |
| Shelter | Categorical; Portland Rescue Mission vs. Other shelters | Different shelters may attract different people who vary of factor such as temporary or chronic homelessness, drug use, mental illness, etc. |
| Medical Condition (Other than HIV) | Categorical; Yes/No | Certain medical conditions (ie. diabetes) increase the risk of converting from latent infection to active disease, thus people with one of these conditions may be more likely to begin treatment. |
| HIV Status | Categorical; Yes/No | Due to increase risk of progression to active TB in people infected with HIV, people with HIV may be more likely to take preventive treatment than others in the sheltered homeless population. |
| Substance abuse | Categorical; Yes/No | Substance abuse could hinder the ability to regularly take a medication. |

Table 2. Characteristics of clients with latent tuberculosis infection for whom treatment was recommended.

| | n [%] |
|---|---|
| n | 916 [100.00] |
| Foreign-born vs US-born | |
| Foreign-born | 210 [22.93] |
| US-born | 706 [77.07] |
| Start treatment within 60 days | |
| Yes | 236 [25.76] |
| No | 680 [74.24] |
| Age | |
| 18-29 | 143 [15.61] |
| 30-49 | 508 [55.46] |
| 50+ | 265 [28.93] |
| Sex | |
| Female | 117 [12.77] |
| Male | 799 [87.23] |
| Substance Abuse | |
| Yes | 47 [5.13] |
| No | 869 [94.87] |
| Race/Ethnicity | |
| Hispanic | 273 [29.80] |
| Non-hispanic white | 399 [43.56] |
| Other/Unknown | 244 [26.64] |
| Shelter | |
| Portland Rescue Mission | 327 [35.70] |
| Other | 589 [64.30] |

Table 3. Characteristics of clients with latent tuberculosis infection for whom treatment was recommended who were born in the United States vs born in another country.

| | Foreign-born n [%] | US-born n [%] | OR (95% CI) | $\chi^2$ | p (a) |
|---|---|---|---|---|---|
| n | 210 [22.93] | 706 [77.07] | … | … | … |
| Age | | | | 36.324 | <0.0001 |
| 18-29 (Ref) | 55 [38.46] | 88 [61.54] | 1.00 | | |
| 30-49 | 122 [24.02] | 386 [75.98] | 0.51 (0.34, 0.75) | | |
| 50+ | 33 [12.45] | 232 [87.55] | 0.23 (0.14, 0.37) | | |
| Sex | | | | 13.884 | 0.0002 |
| Female (Ref) | 11 [9.40] | 106 [90.60] | 1.00 | | |
| Male | 199 [24.91] | 600 [75.09] | 3.20 (1.68, 6.07) | | |
| Substance Abuse | | | | 4.233 | 0.040 |
| Yes (Ref) | 5 [10.64] | 42 [89.36] | 1.00 | | |
| No | 205 [23.59] | 664 [76.41] | 2.59 (1.01, 6.64) | | |
| Race/Ethnicity | | | | 269.150 | <0.0001 |
| Hispanic | 156 [57.14] | 117 [42.86] | 31.90 (18.32, 55.55) | | |
| Non-hispanic white (Ref) | 16 [4.01] | 383 [95.99] | 1.00 | | |
| Other/Unknown | 38 [15.57] | 206 [84.43] | 4.41 (2.40, 8.11) | | |
| Shelter | | | | 0.682 | 0.409 |
| Portland Rescue Mission | 80 [24.46] | 247 [75.54] | 0.87 (0.64, 1.20) | | |
| Other (Ref) | 130 [22.07] | 459 [77.93] | 1.00 | | |

(a): p-value is chi-square test for overall variable, not for each level of each variable

OR: odds ratio; CI: confidence interval; Ref: referent group

Table 4. Characteristics of clients with latent tuberculosis infection starting vs not starting treatment within 60 days from recommendation for treatment.

| | Start treatment within 60 | | | | |
|---|---|---|---|---|---|
| | Yes | No | | | |
| | n [%] | n [%] | OR (95% CI) | $\chi^2$ | p (a) |
| n | 236 [25.76] | 680 [74.24] | … | … | … |
| Foreign-born vs. US-born | | | | 18.444 | <0.0001 |
| Foreign-born | 78 [37.14] | 132 [62.86] | 2.05 (1.47, 2.85) | | |
| US-born (Ref) | 158 [22.38] | 548 [77.62] | 1.00 | | |
| Age | | | | 1.122 | 0.571 |
| 18-29 (Ref) | 39 [27.27] | 104 [72.73] | 1.00 | | |
| 30-49 | 135 [26.57] | 373 [73.43] | 0.97 (0.64, 1.47) | | |
| 50+ | 62 [23.40] | 203 [76.60] | 0.81 (0.51, 1.30) | | |
| Sex | | | | 0.506 | 0.477 |
| Female (Ref) | 27 [23.08] | 90 [76.92] | 1.00 | | |
| Male | 209 [26.16] | 590 [73.84] | 1.18 (0.75, 1.87) | | |
| Substance Abuse | | | | 0.001 | 0.970 |
| Yes (Ref) | 12 [25.53] | 35 [74.47] | 1.00 | | |
| No | 224 [25.78] | 645 [74.22] | 1.01 (0.52, 1.99) | | |
| Race/Ethnicity | | | | 2.597 | 0.273 |
| Hispanic | 80 [29.30] | 193 [70.70] | 1.27 (0.90, 1.80) | | |
| Non-hispanic white (Ref) | 98 [24.56] | 301 [75.44] | 1.00 | | |
| Other/Unknown | 58 [23.77] | 186 [76.23] | 0.96 (0.66, 1.39) | | |
| Shelter | | | | 0.685 | 0.408 |
| Portland Rescue Mission | 79 [24.16] | 248 [75.84] | 1.14 (0.84, 1.56) | | |
| Other | 157 [26.66] | 432 [73.34] | 1.00 | | |

(a): p-value is chi-square test for overall variable, not for each level of each variable

OR: odds ratio; CI: confidence interval; Ref: referent group

Table 5. Foreign born status and treatment inititation within 60 days, stratified by potential confounders/effect

| | Treatment Start within 60 days | | | | | |
|---|---|---|---|---|---|---|
| | Yes | | No | | | |
| | FB (n) | USB (n) | FB (n) | USB (n) | OR (a) | 95% CI |
| n | 78 | 158 | 132 | 548 | … | … |
| Age | | | | | | |
| 18-29 | 16 | 23 | 39 | 65 | 1.16 | 0.55, 2.46 |
| 30-49 | 44 | 91 | 78 | 295 | 1.83 | 0.98, 3.53 |
| 50+ | 18 | 44 | 15 | 188 | 5.13 | 2.40, 10.96 |
| Sex | | | | | | |
| Female | 8 | 19 | 3 | 87 | 12.21 | 2.96, 50.35 |
| Male | 70 | 139 | 129 | 461 | 1.80 | 1.27, 2.55 |
| Substance Abuse | | | | | | |
| Yes | 2 | 10 | 3 | 32 | 2.13 | 0.31, 14.62 |
| No | 76 | 148 | 129 | 516 | 2.05 | 1.47, 2.88 |
| Race/Ethnicity | | | | | | |
| Hispanic | 56 | 24 | 100 | 93 | 2.17 | 1.25, 3.78 |
| Non-hispanic white | 6 | 92 | 10 | 291 | 1.90 | 0.67, 5.36 |
| Other/Unknown | 16 | 42 | 22 | 164 | 2.84 | 1.37, 5.88 |
| Shelter | | | | | | |
| Portland Rescue Mission | 29 | 50 | 51 | 197 | 2.24 | 1.29, 3.89 |
| Other | 49 | 108 | 81 | 351 | 1.97 | 1.30, 2.98 |

(a): Odds ratio compares treatment initiation within 60 days between foreign-born and US-born

OR: odds ratio; CI: confidence interval; FB: foreign-born; USB: United States-born

Table 6. Characteristics of each foreign born status and age pairing, stratified by potential confounders/effect modifiers

| | Foreign Born | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yes | | | | | | No | | | | | |
| | Age | | | | | | Age | | | | | |
| | 18-29 | | 30-49 | | 50+ | | 18-29 | | 30-49 | | 50+ | |
| | n | % (a) | n | % (a) | n | % (a) | n | % (a) | n | % (a) | n | % (a) |
| n | 55 | 100.00% | 122 | 100.00% | 33 | 100.00% | 88 | 100.00% | 386 | 100.00% | 232 | 100.00% |
| Start treatment | | | | | | | | | | | | |
| Yes | 16 | 29.09% | 44 | 36.07% | 18 | 54.55% | 23 | 26.14% | 91 | 23.58% | 44 | 18.97% |
| No | 39 | 70.91% | 78 | 63.93% | 15 | 45.45% | 65 | 73.86% | 295 | 76.42% | 188 | 81.03% |
| Sex | | | | | | | | | | | | |
| Female | 1 | 1.82% | 6 | 4.92% | 4 | 12.12% | 13 | 14.77% | 58 | 15.03% | 35 | 15.09% |
| Male | 54 | 98.18% | 116 | 95.08% | 29 | 87.88% | 75 | 85.23% | 328 | 84.97% | 197 | 84.91% |
| Substance Abuse | | | | | | | | | | | | |
| Yes | 3 | 5.45% | 1 | 0.82% | 1 | 3.03% | 6 | 6.82% | 25 | 6.48% | 11 | 4.74% |
| No | 52 | 94.55% | 121 | 99.18% | 32 | 96.97% | 82 | 93.18% | 361 | 93.52% | 221 | 95.26% |
| Race/Ethnicity | | | | | | | | | | | | |
| Hispanic | 40 | 72.73% | 91 | 74.59% | 25 | 75.76% | 29 | 32.95% | 63 | 16.32% | 25 | 10.78% |
| Non-hispanic white | 6 | 10.91% | 8 | 6.56% | 2 | 6.06% | 41 | 46.59% | 213 | 55.18% | 129 | 55.60% |
| Other/Unknown | 9 | 16.36% | 23 | 18.85% | 6 | 18.18% | 18 | 20.45% | 110 | 28.50% | 78 | 33.62% |
| Shelter | | | | | | | | | | | | |
| Portland Rescue Mission | 24 | 43.64% | 44 | 36.07% | 12 | 36.36% | 34 | 38.64% | 143 | 37.05% | 70 | 30.17% |
| Other | 31 | 56.36% | 78 | 63.93% | 21 | 63.64% | 54 | 61.36% | 243 | 62.95% | 162 | 69.83% |

(a): percentage for each foreign-born status and age group that falls into each level of each variable
ex. 29.09% of 18-29 year old foreign-born clients started treatment.
ex. 72.73% of 18-29 year old foreign-born clients were Hispanic.

Table 7. Crude and adjusted odds ratios for foreign-born and treatment with latent tuberculosis infection when individually controlled for each potential confounder

| | Treatment Initiation within 60 days |
|---|---|
| | OR, Foreign-born (95% CI) (a) |
| Foreign-born | 2.05 (1.47, 2.85) |
| Age | 2.05 (1.46, 2.88) |
| Sex | 2.04 (1.46, 2.85) |
| Substance Abuse | 2.06 (1.48, 2.87) |
| Race/Ethnicity | 2.31 (1.54, 3.47) |
| Shelter | 2.06 (1.48, 2.87) |

(a): The odds ratios compare treatment initiation in the foreign-born and US-born groups. The first odds ratio listed next to Foreign-born is a crude odds ratio. All other odds ratios are adjusted for the variable listed to the left when added to the foreign-born and treatment initiaiton model individually.

OR: odds ratio; CI: confidence interval

Table 8. Multiple Logistic Regression - Backwards Elimination

Treatment Initiation within 60 days

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | p (a) | OR (95% CI) | p (a) | OR (95% CI) | p (a) | OR (95% CI) | p (a) | OR (95% CI) | p (a) |
| Foreign-born x age interaction term (b) | | 0.013 | | 0.013 | | 0.014 | | 0.017 | | 0.018 |
| Foreign-born vs US-born (Ref.) | | | | | | | | | | |
| Age | | | | | | | | | | |
| 18 - 29 | 1.275 (0.588, 2.762) | | 1.275 (0.589, 2.762) | | 1.294 (0.598, 2.800) | | 1.169 (0.551, 2.480) | | 1.159 (0.547, 2.458) | |
| 30-49 | 2.096 (1.267, 3.469) | | 2.096 (1.267, 3.467) | | 2.111 (1.277, 3.490) | | 1.827 (1.179, 2.832) | | 1.829 (1.180, 2.834) | |
| 50+ | 6.100 (2.716, 13.700) | | 6.103 (2.718, 13.703) | | 6.050 (2.697, 13.572) | | 5.190 (2.425, 11.106) | | 5.127 (2.398, 10.961) | |
| Sex | | 0.500 | | 0.499 | | | | | | |
| Male | 1.182 (0.727, 1.923) | | 1.183 (0.727, 1.923) | | … | | … | | … | |
| Female (Ref) | 1.00 | | 1.00 | | … | | … | | … | |
| Substance Abuse | | 0.962 | | | | | | | | |
| No | 0.984 (0.494, 1.960) | | … | | … | | … | | … | |
| Yes (Ref) | 1.00 | | … | | … | | … | | … | |
| Race/Ethnicity | | 0.439 | | 0.431 | | 0.461 | | | | |
| Hispanic | 0.754 (0.485, 1.171) | | 0.753 (0.486, 1.166) | | 0.765 (0.495, 1.181) | | … | | … | |
| Other/Unknown | 0.865 (0.589, 1.270) | | 0.864 (0.589, 1.268) | | 0.860 (0.587, 1.262) | | … | | … | |
| Non-Hispanic White (Ref) | 1.00 | | 1.00 | | 1.00 | | … | | … | |
| Shelter | | 0.292 | | 0.292 | | 0.357 | | 0.315 | | |
| Other | 1.192 (0.860, 1.654) | | 1.192 (0.860, 1.654) | | 1.162 (0.845, 1.598) | | 1.177 (0.856, 1.618) | | … | |
| Portland Rescue Mission (Ref) | 1.00 | | 1.00 | | 1.00 | | 1.00 | | … | |

Age, foreign-born, and age x foreign born forced into the model

Model 1: Foreign-born, age, age x foreign-born, sex, substance abuse, race/ethnicity, shelter
Model 2: Foreign-born, age, age x foreign-born, sex, race/ethnicity, shelter
Model 3: Foreign-born, age, age x foreign-born, race/ethnicity, shelter
Model 4: Foreign-born, age, age x foreign-born, shelter
Model 5: Foreign-born, age, age x foreign-born

(a): p-value in foreign-born row is the foreign born x age interaction term; all other p-values refer to the overall variable significance of the variable listed to the left
(b): odds ratios in the foreign-born x age interaction term section compare treatment initiation between foreign born vs US-born groups separately for each age group

Ref: Referent group; OR: Odds Ratio; CI: Confidence Interval

Table 9. Preliminary model containing foreign-born, age, and age x foreign born interaction term, and final model obtained by adding potential confounders individually

| | **Preliminary Model** | | **Final Model (c)** | |
|---|---|---|---|---|
| | OR (95% CI) | p (a) | OR (95% CI) | p (a) |
| Foreign-born x age interaction term (b) | | 0.018 | | 0.015 |
| Foreign Born vs. US-born (Ref.) | | | | |
| Age | | | | |
| 18 - 29 | 1.159 (0.547, 2.458) | | 1.291 (0.597, 2.793) | |
| 30-49 | 1.829 (1.180, 2.834) | | 2.128 (1.288, 3.515) | |
| 50+ | 5.127 (2.398, 10.961) | | 6.031 (2.690, 13.522) | |
| Race/Ethnicity | | … | | 0.426 |
| Hispanic | … | | 0.755 (0.489, 1.164) | |
| Other/Unknown | … | | 0.856 (0.584, 1.256) | |
| Non-Hispanic White (Ref) | … | | 1.00 | |

Preliminary Model: Foreign-born, age, age x foreign-born
Final Model: Foreign-born, age, age x foreign-born, race/ethnicity

(a): p-value in foreign-born row is the foreign born x age interaction term; p-value in the race/ethnicity row refers to the overall variable significance of the race/ethnicity variable
(b): odds ratios in the foreign-born x age interaction term section compare treatment initiation between foreign born vs US-born groups separately for each age group
(c): The only potential confounder that changed the foreign-born by age ORs by over 10% when added into the preliminary model was race/ethnicity

Ref: Referent group; OR: Odds Ratio; CI: Confidence Interval

Table 10. Sensitivity analysis comparing treatment start date cutoff points used in the analysis (60 days) versus alternate cutoff points (30, 90, and 120 days)

| | Analyzed cut off point | | Alternate cut off points | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Treatment start - 60 days | | Treatment start - 30 days | | Treatment start - 90 days | | Treatment start - 120 days | |
| | OR (95% CI) | p (a) | OR (95% CI) | p (a) | OR (95% CI) | p (a) | OR (95% CI) | p (a) |
| Foreign-born x age interaction term (b) | | 0.015 | | 0.006 | | 0.022 | | 0.022 |
| Foreign-born | | | | | | | | |
| Age | | | | | | | | |
| 18 - 29 | 1.291 (0.597, 2.793) | | 1.136 (0.503, 2.563) | | 1.334 (0.616, 2.889) | | 1.443 (0.673, 3.094) | |
| 30-49 | 2.128 (1.288, 3.515) | | 2.259 (1.337, 3.815) | | 2.226 (1.353, 3.664) | | 2.261 (1.380, 3.704) | |
| 50+ | 6.031 (2.690, 13.522) | | 6.701 (2.953, 15.208) | | 5.834 (2.609, 13.045) | | 6.100 (2.728, 13.640) | |
| Not foreign-born (Ref) | | | | | | | | |
| Race/Ethnicity | | 0.426 | | 0.277 | | 0.227 | | 0.050 |
| Hispanic | 0.755 (0.489, 1.164) | | 0.695 (0.440, 1.098) | | 0.694 (0.451, 1.067) | | 0.610 (0.398, 0.934) | |
| Other/Unknown | 0.856 (0.584, 1.256) | | 0.818 (0.547, 1.224) | | 0.813 (0.557, 1.185) | | 0.720 (0.496, 1.045) | |
| Non-Hispanic White (Ref) | 1.00 | | 1.00 | | 1.00 | | 1.00 | |

All models include Foreign-born, age, age x foreign-born, and race/ethnicity

(a): p-value in foreign-born row is the foreign born x age interaction term; all other p-values refer to the overall variable significance of the variable listed to the left
(b): odds ratios in the foreign-born x age interaction term section compare treatment initiation between foreign born vs US-born groups separately for each age group

Ref: Referent group; OR: Odds Ratio; CI: Confidence Interval