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Ann Margaret Lockard Date

Epidemiology of Tuberculosis and Evaluation of Treatment Delay Among Foreign-Born Hispanic Persons in the United States

By

Ann Margaret Lockard

MPH

Global Epidemiology

_____

John McGowan, Jr., MD

Faculty Thesis Advisor

_____

Dolly Katz, PhD

Thesis Field Advisor

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By

Ann Margaret Lockard

B.S., B.A.
Ursinus College
2012

Faculty Thesis Advisor: John McGowan, Jr., MD

Thesis Field Advisor: Dolly Katz, PhD

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ABSTRACT

Epidemiology of Tuberculosis and Evaluation of Treatment Delay
Among Foreign-Born Hispanic Persons in the United States

By Ann Margaret Lockard

Background

In 2012, 63% of cases of tuberculosis (TB) cases in the United States (U.S.) occurred among foreign-born persons, a third of whom were Hispanic. An understanding of the epidemiology of TB among foreign-born Hispanic persons is essential to progress in TB control and prevention. One area of interest is timely diagnosis and treatment of TB; delayed treatment initiation has been associated with worse health outcomes for the patient and increased transmission of the infection. The purpose of this study is first to describe the epidemiology of TB among Hispanic, foreign-born persons in the U.S. and second to identify factors associated with delay in treatment initiation.

Methods

A multi-site study in 2005-2007 recruited foreign-born persons newly diagnosed with TB. This secondary analysis included data only from participants who self-identified as Hispanic. Variables evaluated for association with treatment delay, defined as the interval between symptom onset and treatment initiation, included employment, education, English ability, usual source of medical care, place of diagnosis, self-efficacy (defined by answer to the question "do you think your own actions determine whether you be cured of tuberculosis?"), visa status, and time spent in the U.S. Cox proportional hazards models were used to assess association.

Results

Of the 568 cases included in the analysis, 61.3% were from Mexico, 54.4% were undocumented; 63.0% had a median income of less than $20,000, and 50.0% had less than an 8th grade education. Participants had a median treatment delay of 77.0 days. Those who arrived in the U.S. within two years of symptom onset had longer delay than those who arrived earlier [hazard ratio (HR)=0.69, 95% confidence interval (CI)=0.53,0.91]. Those who answered no to the self-efficacy question also had longer delays (HR=0.60, 95% CI=0.41, 0.87).

Discussion

Foreign-born Hispanic persons who have arrived recently have increased risk of treatment delay. In addition, persons who lack a sense of control over their TB outcomes have greater treatment delays. Approaches to reducing treatment delay could include removal of barriers to healthcare among recent arrivals to the U.S. and tailored public health messages to improve self-efficacy.

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INTRODUCTION

Background

Foreign-born persons are disproportionally affected by tuberculosis (TB) in the United States (U.S.) (1). A third of cases of TB among the foreign-born occurred among Hispanic persons (1). Due to the high number of cases among foreign-born, Hispanic persons, it is essential to study and understand the epidemiology of TB among this population in order to achieve the goal of TB elimination in the U.S. In order to best target prevention programs to this population, risk factors for increased mortality and morbidity and for increased transmission must be understood; one of these risk factors is prolonged duration of symptoms of active TB disease before treatment initiation. Timely diagnosis and treatment are essential to the management and prevention of TB: delayed treatment initiation has been associated with worse health outcomes for the individual patient as well as increased transmission of the infection (2-5).

Research Questions and Hypotheses

The first objective of this analysis is to describe the epidemiology of TB among foreign-born, Hispanic persons in the United States. The second objective is to examine if the following exposures are independently associated with treatment delay, defined at the interval between symptom onset and treatment initiation: visa status at diagnosis, English speaking ability, employment status at diagnosis, education, use of a usual source of medical care, time spent in the United States prior to symptom onset, place of diagnosis, and self-efficacy

(defined by answer to the question "do you think your own actions determine whether you be cured of tuberculosis?"). These variables were selected based on associations described in prior literature among similar populations. Belief in self-efficacy has not previously been evaluated in the literature, but was selected due to its prominence as a construct in many behavioral theories related to care seeking.

Although prior literature has indicated that visa status is positively associated with prolonged symptom duration prior to treatment, it is hypothesized that when the population is restricted to those who are foreign-born and when previously unavailable covariates are considered, the association will not persist. It is hypothesized that English ability, education, having a usual source of medical care, and longer time spent in the U.S. prior to symptom onset will be associated with shorter duration of symptoms prior to treatment due to these variables' associations with ability to navigate the healthcare system in the United States (6-11). It is also hypothesized that self-efficacy will be associated with shorter duration of symptoms prior to treatment. It is hypothesized that place of diagnosis, specifically diagnosis at a private physician's office, will be associated with longer duration of symptoms prior to treatment.

Relevance

Currently, the literature does not specifically address the epidemiology of TB among foreign-born, Hispanic persons throughout the United States. Because these individuals account for a high number of total TB cases in the US, it is

essential to understand the characteristics of this group. Additionally, because of the importance of timely treatment initiation on both individual outcomes and transmission to others, this outcome should specifically be evaluated. Knowing the factors associated with treatment initiation delay among foreign-born Hispanic persons with TB could help to inform policies or programs that work to achieve timely diagnosis and treatment of TB among this population.

BACKGROUND AND LITERATURE REVIEW

Tuberculosis in the United States

TB is a disease caused by the bacterium Mycobacterium tuberculosis (1). TB is spread via airborne droplet nuclei expelled by persons with active disease (1). The majority of persons infected with M. tuberculosis have latent TB infection (LTBI), in which they do not have respiratory or other symptoms and they cannot spread the infection. Without treatment, approximately 5-10% of persons with TB infection develop TB disease, about half of whom develop the disease within two years of infection (12). Persons with LTBI who are immune-compromised (such as those who are HIV positive or have other comorbidities) are more likely to develop active TB (12). Those with TB disease have symptoms that require treatment and are contagious. Symptoms of TB disease include weight loss, night sweats, cough, fever, loss of appetite, fatigue, hemoptysis, and chest pain (12). TB usually affects the respiratory tract, although approximately 20% of cases are extra-pulmonary and affect other areas of the body (1).

In 2012, 9,945 cases of TB disease were reported in the United States (13) (1). All of these cases were reported to the Centers for Disease Control and Prevention (CDC) using the standard Reported Verified Case of Tuberculosis (RVCT) report form (Appendix A). A verified case must meet either laboratory or clinical case criteria (Appendix B). In 2010, there were 569 deaths due to tuberculosis, which translates to a case fatality rate of 5.1 per 100 (1).

Tuberculosis Among Foreign-Born, Hispanic Persons

Several populations in the U.S. are more vulnerable to TB: the homeless, incarcerated populations, racial and ethnic minorities, persons in long-term care facilities, persons who inject drugs, and foreign-born persons (1). Of all cases reported in the U.S. in 2012, 63% were among the foreign-born (1). The rate of TB disease was 11 times higher among foreign-born persons than among US-born persons (15.9 cases per 100,000 and 1.4 cases per 100,000, respectively) (1). Although the overall TB case rate and the number of TB cases have fallen consistently since 1993, the case rate and the number of cases among foreign-born persons have not fallen as dramatically as the rate and number of cases among US-born persons—in 1993 among the foreign-born there was a case rate of 34.0 cases per 100,000, while in 2012 there was a case rate of 15.9 per 100,000 (1). This translates to a 53% decrease in case rate (1). In contrast, the case rate among the U.S.-born dropped from 7.4 to 1.4 cases per 100,000 in the period between 1993 and 2012, which is a 81% decrease (1). As a result, the proportion of TB cases among the foreign-born rose from 29% in 1993 to 63% in 2012 (1).

In 2012, 33% of foreign-born persons with TB disease were Hispanic or Latino (1). In 2012, there were 1,308 cases of TB among persons born in Mexico, representing the highest number of cases among the foreign-born from any single country (1). In 2012, the ten most common countries of origin for foreign-born persons with TB in the U.S. were: Mexico (21% of cases among the foreign-born), Philippines (12%), India (8%), Vietnam (7%), China (6%), Guatemala (3%), Haiti (3%), Ethiopia (3%), Honduras (2%), and the Republic of Korea (2%) (1).

Although TB is not highly endemic in Latin American countries, there is a relatively high burden of TB among persons born in Latin America. This is likely a reflection of the high proportion of immigrants to the United States from Latin American countries compared to other countries. In 2012, the case rate of TB was 23 per 100,000 in Mexico and 60 per 100,000 in Guatemala, which are similar to the rate of TB among foreign-born persons in the U.S (14, 15). In contrast, in 2012 the rate of TB was 265 per 100,000 in the Philippines and 176 per 100,000 in India (16, 17). However, at the time of the 2000 population census there were approximately 16,087,000 people living in the U.S. who emigrated from Latin America, while there were only 8,226,000 who emigrated from Asia (13). This disparity in immigration is likely responsible for the relatively high number of TB cases among foreign-born persons from Latin America.

Importance of Timely Diagnosis and Treatment for Tuberculosis

Timely diagnosis of TB disease and initiation of treatment are essential to preventing transmission of TB. Individuals with TB disease who are not on treatment are highly contagious and risk infecting others (12). Additionally, treatment delay can in many ways be used as proxy for local TB program performance and level of infectious disease present among the population in question (5). A systematic review conducted by Storla et al. revealed the variety of definitions and concepts used to describe the theme of delay: interval between symptom onset and diagnosis, interval between symptom onset and treatment initiation, interval between first clinical visit and treatment, interval between

symptom onset and first clinical visit, and others (18). There are a variety of circumstances in which prolongation of symptom duration before treatment initiation can occur, all of which are important to understand.

Delay in care seeking, diagnosis, or treatment initiation can lead to longer duration of illness, which leads to increased likelihood of transmitting TB to others (3). A study that tested contacts of TB patients with various durations of symptoms prior to treatment initiation found that 40% of contacts of patients who had a symptom duration 90 days or longer prior to treatment initiation tested positive for LTBI, compared to only 24% of contacts of patients who had a symptom duration of less than 90 days (4). In a study of symptomatic TB patients who delayed seeking care for more than 60 days, patients exposed an average of eight contacts during the delay (19). Another study found that individuals who delayed seeking treatment for 60 days or more exposed an average of ten contacts (20).

Despite the importance of timely care seeking, diagnosis, and treatment initiation, delays are common. A study in Los Angeles found a mean care-seeking delay of 74 days, and a study in northern Mexico found a mean delay of 53.5 days (19, 21). Among a cohort of patients in Maryland, the median interval between symptom onset and care seeking was 32 days, the median interval between first clinical visit and treatment initiation was 26 days, and a median total time between symptom onset to treatment initiation was 89 days (22). A striking 49% of individuals in this cohort had an overall time from symptom onset to treatment initiation of longer than 90 days (4). Foreign-born Hispanic TB

patients may be especially at risk of prolonged symptom duration; a study found that over a third of TB patients in this group had a symptom duration before treatment over more than 6 months (23).

Factors Associated with Prolonged Time Between Symptom Diagnosis and Treatment for Tuberculosis

A meta-analysis conducted by Storla et al. in 2008 found 58 studies related to diagnostic delay of tuberculosis; however, very few of these studies were conducted in the United States or Latin America (18). The factors associated with prolonged symptom duration prior to treatment varied greatly depending on the context (18), which may be a reflection of differing healthcare systems or differences in knowledge, attitudes and beliefs about TB. Therefore, only studies on prolonged symptom duration that were conducted in the U.S. will be considered for review here.

In a study that examined clinical outcomes of U.S. born, documented foreign-born, and undocumented foreign-born TB patients, those without documentation had significantly higher odds of having a symptom duration of longer than eight weeks prior to hospitalization [95% confidence interval (CI) odds ratio (OR)=1.7, 10.2] compared to U.S.-born individuals (24). In the same study, unemployment was also independently associated with increased symptom duration before hospitalization (95% CI OR=1.1, 4.5) (24). However, it is important to note that this study did not directly verify documentation status, and the study was restricted to New York City (24).

A study conducted by Asch et al. found that individuals who stated that they had a fear of immigrations authorities as a result of seeking care had an significantly higher odds of delaying treatment for longer than 60 days than those who did not express such fear (95% CI OR=1.34, 11.63) (20). However, it should be noted that this comparison included U.S.-born and documented foreign-born (who presumably had no reason to fear authorities) persons as well as undocumented individuals (20). This study also found that lack of English-speaking ability was associated with delay in care seeking, although the association was not statistically significant (20).

A Los Angeles based study that did not stratify by foreign birth found that delay (defined as a symptom duration greater than 60 days prior to care-seeking) was more common among those who were unemployed, concerned about cost, anticipated prolonged waiting-room time, believed they could treat themselves, anticipated difficulty obtaining an appointment, were uncertain about where to get care, or who feared immigration authorities as a result of care-seeking (19). In logistic regression models, unemployment, uncertainty about where to seek care, and belief in efficacy of self-treatment were independently associated with delay (19). Clinical variables such as sputum smears, symptom severity, and chest radiography did not impact delay (19).

A cohort study in Maryland found that patients who were non-white and less educated had significantly lower hazard ratios (HR) for care-seeking, signifying increased care-seeking delay (95% CI HR=0.39, 0.98; 0.26, 0.72) (22). Patients who did not speak English had significantly lower hazard ratios for

treatment initiation after first clinical visit, signifying increased treatment delay (95% CI HR=0.24, 0.68). Patients who first visited a private physician, who were treated with non-TB antibiotics, or who received a diagnosis other than TB prior to initiating TB treatment also had significantly increased healthcare delays. A study based in northern Mexico also found that those who consulted a private physician first had longer intervals between first clinical visit and diagnosis (21).

While the literature reveals a variety of factors associated with prolonged symptom duration before treatment such as documentation status, English ability, employment, and others, analysis has not been conducted specifically among foreign-born Hispanic persons in the U.S.

METHODS

Data Collection

This is a secondary analysis of deidentified data that was collected from April 2005 to January 2007 by the Tuberculosis Epidemiological Studies Consortium (TBESC) as part of a cross-sectional study with the purpose of identifying missed opportunities for TB prevention in the foreign-born population in the U.S. and Canada. Data were collected from 22 TBESC catchment sites and an additional site in Florida (Appendix C).

Participants were eligible for the TBESC study if they had a reported, verified case of TB, they were born outside of the U.S. and U.S. territories, and they were diagnosed within six months prior to interview. Participants were excluded if they were mentally incapacitated, incarcerated, or no longer living in the research site's jurisdiction. Participants were selected from the sites by random sampling if the site had >250 cases of TB among the foreign-born (6 sites). In all other sites, all eligible cases were petitioned to participate. All participants provided informed consent. Data collection protocol was approved by both local IRBs and the CDC IRB.

Data were collected from a standardized questionnaire administered by a trained interviewer with an interpreter if necessary; health department records; national surveillance data collected by the CDC, and immigration records from the CDC's Division of Global Migration and Quarantine. All information defined as protected health information (PHI) under the Health Insurance Portability

and Accountability Act (HIPAA) were removed from the dataset prior to this analysis, and the study was deemed exempt from IRB approval by the Emory University IRB, eIRB#: IRB00063835 (Appendix D).

Inclusion Criteria

Only foreign-born persons who self-identified as Hispanic and who were interviewed in the U.S. were included in this analysis. Although the TBESC study included two catchment sites in Canada, it was determined that observations from these sites should not be include due to the differences in the healthcare systems of the two countries. After reviewing interview data, one participant who self-identified as Hispanic was determined to likely have been misclassified and was excluded from the analysis. Participants who were born in Latin American countries but who did not self-identify as Hispanic were not included.

Variables Included in Descriptive Statistics

Demographic variables included in descriptive analysis were: age, sex, country of birth, employment status at diagnosis (self-reported), education (self reported; dichotomized to greater than or less than an 8th grade education), English speaking ability (reported by interviewer; answers of "very well" or "well" were defined as English speakers, answers of "not well" or "not at all" were defined not English speakers), income (self-reported; dichotomized into greater than or less than $20,000), homelessness in year before diagnosis (retrieved from CDC RVCT form), visa status at interview (self-reported and confirmed by

interviewer; categorized into permanent, temporary, and undocumented), and time since immigration to the U.S. to symptom onset (defined using self-reported date of immigration and self-reported date of symptom onset; dichotomized into greater than or less than two years).

Healthcare-related variables included in descriptive analysis were: health insurance at symptom onset (self-reported; dichotomized into yes and no), use of a usual source of medical care at symptom onset (self-reported, defined by answer to the question "What is your usual source of medical care?"; answers "none," "emergency room," or "traditional healer" were defined as none), and place of diagnosis (self-reported; categorized into health department, private physician, hospital, and other). Clinical variables included in the descriptive analysis were: cough in year prior to diagnosis (self-reported), pulmonary involvement (retrieved from RVCT form), previous TB diagnosis (self-reported), smoking status (self reported; defined as having smoked >100 cigarettes in lifetime), excess alcohol use in the year before diagnosis (retrieved from RVCT form), and HIV status at interview (retrieved from RVCT form).

Knowledge, attitudes and beliefs (KAB) variables included in descriptive analysis were: self-efficacy (defined by answer to the question "do you think your own actions determine whether you will be cured of tuberculosis?") and fear of deportation due to diagnosis (defined by answer to the question "when you went for tuberculosis treatment, were you afraid you might be sent back to the country you came from?").

Outcome Variables

This analysis examined three outcome variables: overall treatment initiation delay, patient delay, and healthcare delay. It should be noted that the use of the term "delay" does not necessarily signal the intent of delay, but rather is simply a description of the gap in the time. Overall treatment initiation delay was calculated as the difference between the date of therapy start retrieved from the RVCT form and self-reported date of symptom onset. Because only the month and the year were reported for the date of symptom onset, the 15th of the month was used as a placeholder to calculate dates. Therefore, the date reported may have been two weeks before or after the actual date of symptom onset. Values that indicated symptoms began after diagnosis (<-16 days from symptom onset to diagnosis) were set to missing. Although these values are plausible since a patient could have been diagnosed through a screening program, they do not indicate prolonged duration of symptoms prior to treatment initiation, and thus were not included in this analysis.

Patient delay was calculated as the difference between self-reported date of first healthcare visit and self-reported date of symptom onset. Because only the month and year were reported for each variable, derived values have a level of uncertainty of +/- 4 weeks. Values that indicated a patient had a healthcare visit before symptom onset (<0 days from symptom onset to healthcare visit) were set to missing.

Healthcare delay was calculated as the difference between the date of therapy start retrieved from the RVCT form and self-reported date of first

healthcare visit. Because only the month and year were reported for date of first healthcare visit, values have an uncertainty of +/- 2 weeks. Values that indicated that a healthcare visit happened before diagnosis (<-16 days from healthcare visit to diagnosis) were set to missing.

Exposure Variables

Variables evaluated for association with the outcomes were: employment status at diagnosis, education, English speaking ability, visa status at interview, time since immigration to the U.S. to symptom onset, use of a usual source of medical care at symptom onset, place of diagnosis, and self-efficacy.

Statistical Analysis

All analysis was done using SAS 9.3 (Cary, NC). All variables included in the analysis were evaluated for implausible or missing values. Descriptive statistics were calculated for all variables using univariate procedures. Kaplan-Meier curves were created for time from symptom onset to treatment initiation (overall treatment initiation delay), time from symptom onset to first healthcare visit (patient delay), and time from first healthcare visit to diagnosis (healthcare delay).

Median values of the outcome variables were also calculated for the population. Median value of overall treatment initiation delay was calculated for each strata of the exposure variables. Unadjusted Cox proportional hazard models were used to determine the instantaneous “risk” of a treatment initiation.

Cox proportional hazard models were not run for patient delay or for healthcare delay due to the level of uncertainty in these outcome variables. The proportional hazards assumption was checked for each model visually using log-log curves. A significance level of 0.05 was used for all tests.

A multivariate model was built using all exposure variables of interest. It was determined that in addition to the exposure variable of interest, adjusted models would be also include age (dichotomized at the median), sex, cough as symptom, pulmonary involvement, and previous TB diagnosis. These were included to be consistent with previous literature. The proportional hazards assumption was checked visually for each variable in using log-log curves. The multivariate model was assessed for multicollinearity using variance inflation factors (VIFs) and collinear variables were removed.

RESULTS

A total of 1,696 interviews of foreign-born TB patients were completed as a part of the TBESC study (25). A total of 568 cases met the inclusion criteria and were included for this analysis.

Descriptive Statistics

Among all foreign-born, Hispanic persons included in the analysis: 61.3% of participants were from Mexico, 50.0% had an educational level higher than 8th grade, 77.1% reported speaking English "well" or "very well," and 63.0% had an annual household income of less than $20,000. Very few participants were homeless at the time of diagnosis (2.8%) [Table 1]. The majority (54.4%) were undocumented at the time of interview, and 21.3% of participants immigrated to the United States within two years of symptom onset [Table 1].

The majority (73.4%) of participants reported having no medical insurance at the time of symptom onset, including Medicare and Medicaid, and 23.6% of participants reported no usual source of medical care in the United States or no usual source of care of besides the emergency room or traditional healers [Table 1]. The majority (63.8%) of participants were diagnosed at a hospital, while 21.5% of participants were diagnosed at a health department or tuberculosis clinic, and 9.6% were diagnosed at a private physician's office [Table 1].

Most participants reported attitudes of self-efficacy; only 7.8% of participants responded no to the question "do you think your own actions determine whether you be cured of tuberculosis?" [Table 1]. Over a fifth (22.8%)

of participants reported fearing deportation/immigration authorities when they sought TB treatment [Table 1]. This fear differed by documentation status ($p<0.001$): 33.7% of those who were undocumented reported they feared immigration authorities while seeking TB treatment, while 10.0% of those with temporary or permanent visas reported fearing immigration authorities.

The majority (67.8%) of participants reported having a cough as symptom in the twelve months prior to diagnosis, and 85.7% had pulmonary involvement. A total of 4.4% participants had received a diagnosis of tuberculosis in the past, separate from the diagnosis that led to enrollment in the study. Additionally, 35.7% of participants reported being current or ex-smokers, 3.7% had excess alcohol use in the year before diagnosis, and 6.5% reported being HIV positive [Table 1].

Outcome Variables

A total of 88 observations had missing values for overall treatment initiation delay, 80 of which were missing due to unreported date for onset of symptoms, and 8 of which were set to missing due to reported date of symptom onset after diagnosis. A median overall treatment initiation delay (time from symptom onset to treatment initiation) of 77.0 days was observed [inter-quartile range (IQR)=109, n=480] [Table 2]. A total of 25.0% of participants had an overall treatment initiation delay of over 145.5 days, 10% of patients had delays of over 300.0 days, and 12 patients had treatment initiation delays exceeding two years [Figure 1]. A median patient delay (time from symptom onset to first

clinician visit) of 31.0 days was observed (IQR=62, n=347) [Table 2]. Over 30% of participants had no estimated patient delay, but 5% of patients had delay of 250.0 days or more, and 5 patients had delays of more than two years [Figure 2]. A median healthcare delay (time from first clinician visit to treatment initiation) of 27.5 days was estimated (IQR=72.0, n=342) [Table 2]. A total of 25% of patients had healthcare delays of over 80.0 days, and 3 patients had delays of two years or more [Figure 3].

Differences in Overall Treatment Delay

Those who were employed at diagnosis had a longer median overall treatment delay compared to those who were not: 80.0 and 76.0 days, respectively [Table 3]. Similarly, individuals with an 8th grade education or less had a longer median delay than those with more education: 80.0 and 76.0 days, respectively [Table 3]. Those who did not speak English had a longer median delay than those who did (80.0 and 60.0 days, respectively) [Table 3]. Those who spoke English had the shortest delay of any strata used in comparisons. Those with a permanent visa at time of interview had a delay of 70.0 days, those who were undocumented had a median delay of 77.0 days, and those with a temporary visa had a median delay of 96.0 days [Table 3]. Individuals who had been in the U.S. for two years or less prior to symptom onset had a median delay of 84.0 days, compared to a delay of 75.0 days for those who were in the U.S. for longer prior to symptom onset [Table 3]. Those with a usual source of medical care had a longer median delay than those who did not: 80.0 and 71.0 days, respectively) [Table 3]. Those who were diagnosed at a private doctor had a

median delay of 101.5 days, compared to a median delay of 77.5 days for those diagnosed at a health department, 76.0 days for those diagnosed at a hospital, and 57.0 days for those diagnosed elsewhere [Table 3]. Those who did not believe their own actions influenced their TB outcome had the longest median delay of any strata at 125.0 days [Table 3]. In comparison, those who did believe their own actions would determine their TB outcome had a median delay of 76.0 days [Table 3].

In unadjusted Cox proportional hazard models comparing overall treatment initiation delay across strata, those who arrived to the U.S. within two years of symptom onset had a significantly lower instantaneous risk of treatment initiation (longer delay) compared to those who did not (HR=0.78, 95% CI=0.62, 0.98) [Table 4]. Those who answered no to the question "do you think your own actions determine whether you be cured of tuberculosis?" also had a significantly lower risk of treatment initiation (longer delay) compared to those who answered yes (HR=0.66, 95% CI=0.46, 0.94) [Table 4]. No other significant differences were seen in the unadjusted models.

The multivariate model contained all variables included in unadjusted models as well as cough as a symptom in the year prior to diagnosis, previous TB diagnosis, sex, and pulmonary involvement. Visa status at interview was collinear with both age at diagnosis and English ability, and was not included in the final model. Age at diagnosis did not meet the proportional hazard assumption, so was dichotomized at the median (33.7) and fit into the model by stratifying. A total of 408 observations were included in the final model. The association

between overall treatment initiation delay and time from immigration to the U.S. until symptom onset persisted in the adjusted model; those who arrived to the U.S. within two years of symptom onset had a significantly lower instantaneous risk of treatment initiation (longer delay) compared to those who did not (HR=0.69, 95% CI=0.53,0.91) [Table 5]. The association between overall treatment delay and self-efficacy also persisted in the adjusted model; those who answered no to the question "do you think your own actions determine whether you be cured of tuberculosis?" also had a significantly lower risk of treatment initiation compared to those who answered yes (HR=0.60, 95% CI=0.41, 0.87) [Table 5]. No other significant results were observed in the multivariate model. However, the association between diagnosis at a private physician's office and overall treatment initiation delay (HR=0.72, 95% CI=0.49, 1.06) suggests a trend of association.

Differences in Patient Delay

A total of 226 observations had missing values for patient delay. Due to the extent of missing data and the level of uncertainty for this measure (+/- 4 weeks), further analysis of patient delay was not possible.

Differences in Healthcare Delay

A total of 221 observations had missing values for healthcare delay. Due to the extent of missing data for this measure, further analysis of patient delay was not possible.

DISCUSSION

Summary of Results

Foreign-born, Hispanic persons with TB in this analysis were more likely to be male, have a household income of less than $20,000, have been unemployed at diagnosis, speak English, have an undocumented visa status, and have received diagnosis at a hospital.

The magnitude of delay was approximately two months for overall treatment initiation delay, one month for patient delay, one month for healthcare delay. The magnitude of delays observed in this analysis was similar to those observed in other studies (2-5, 18-24). Significant associations were observed between prolonged treatment initiation delay and a time of less than two years spent in the U.S. prior to symptom onset and answering no to the question "do you think your own actions determine whether you will be cured of tuberculosis?"

No significant association was observed between delay and visa status at interview, English ability, employment at diagnosis, education, use of a usual source of medical care, or place of diagnosis. However, those who spoke English had a shorter median overall treatment initiation delay by 20 days than those who did not. Additionally, those who were diagnosed at a private physician's office had a median overall treatment delay 25 days longer than those diagnosed at a health department. Individuals with temporary visas had a median overall treatment delay 26 days longer than those with permanent visas. Although not

significant in proportional hazard models, the differences in medians may have practical significance.

Implications of Findings and Suggestions for Future Research

The epidemiology of TB among forgiven-born Hispanic persons described in this analysis suggests that foreign-born Hispanic persons with TB are likely to be low income, undocumented, and of low education. These findings add to the literature that suggests foreign-born Hispanic persons with TB have lower socio-economic status than other foreign-born persons with TB (26). Programs that target the foreign-born for TB prevention and control should consider this disparity among the foreign-born population with TB.

The lack of a significant association between visa status and treatment delay contradicts previous studies that observed associations between visa status and symptom duration prior to treatment (20, 24). However, the prior studies were not limited to foreign-born Hispanic persons and were conducted in small geographic areas, which could explain the discrepancy in the results. This observation also contradicts some of the current literature on healthcare access, which posits that those without an immigration visa have reduced access to healthcare (6, 9, 10, 27, 28). This contradiction could have occurred for several reasons: the severity of TB symptoms may modify the general association between healthcare access and visa status, visa status may have prompted clinicians to consider TB, or other reasons. Further research, which considers interactions between visa status and other covariates such as English ability,

place of diagnosis, and time spent in the U.S. prior to symptom onset, may give more insight.

Although significant associations between English speaking ability and overall treatment initiation delay were not observed in Cox proportional hazard models, English speakers had a shorter observed median delay. This observation adds to the literature on the importance of English ability for Hispanic persons when interacting with the healthcare system in the U.S. (11) (8). This finding highlights the needs for bilingual resources in order to minimize treatment delays for TB among this population.

The association between amount of time spent in the U.S. prior to symptom onset and treatment delay could have occurred for several reasons: lack of familiarity with the intricate U.S. healthcare system, lack of resources immediately after immigration, lack of social or familial support, lack of stable housing conditions, or others. Prior literature has indicated the importance of acculturation on Mexican American's attitudes and beliefs towards TB (7). Further research on reason for the association between time spent in the U.S. prior to symptom onset and treatment initiation delay, as well as healthcare access in general, is warranted. Additionally, removal of barriers to healthcare access for those who recently arrived to the U.S. is needed in order to reduce delays and prevent and control TB.

The association between self-efficacy, as measured by belief in the ability of one's actions to determine TB outcome, is consistent with many theoretical behavioral models, including the Health Belief Model and the Theory of

Reasoned Action (7). Other research has suggested the importance of these theoretical models for healthcare access among this population (7, 29). Creation of prevention programs and public health messages that are guided by these models may be effective ways to reach this population.

Strengths

The primary strength of this study was the detail available about participants. The TBESC study in which this analysis was nested conducted detailed interviews with a total of 1,696 participants. Detailed data on clinical variables, knowledge attitudes and belief variables, and demographic variables was collected. During the interview, visa status of the participant was asked directly and confirmed with documentation if applicable. In previous studies that analyzed documentation or visa status the information was either obtained indirectly or not verified. In addition, the TBESC sites covered a variety of locations throughout the U.S. (Appendix C), making it reasonable to assume that the population in this analysis was reasonably representative of all foreign-born persons with TB in the U.S. Although the sample size (n=568) was sufficient to detect several statistically significant different in overall treatment delay, a future study with a larger sample size would provide benefit by increasing the precision of the results.

Limitations and Suggestions for Future Research

Several limitations were present in this analysis. After considering several options, it was determined that using self-identification of Hispanic as inclusion criteria was the best method to avoid misclassification of individuals born in Latin American countries who did not identify as Hispanic. However, this resulted in inclusion of a smaller number of observations than other methods for including Hispanic individuals. Additionally, it is possible that some individuals of Hispanic ethnicity were not familiar with the U.S. system of classifying race and ethnicity and thus were incorrectly excluded.

Perhaps the most restrictive factor in this analysis was the level of uncertainty in dates. Because only the month and year were reported for date of symptom onset and day of first care-seeking visit, the 15th of the month was used as an approximation. This resulted in a level of uncertainty of two weeks for healthcare delay and a level of uncertainty of four weeks for patient delay. While the uncertainty would not have affected analysis of aggregate observations as much as it would have affected analysis of a single observation, it is still concerning. Using the 15th of the month as a placeholder resulted in very little variation in these outcomes, particularly patient delay. This could have masked association of the exposures with these outcomes. Additionally, since dates were self-reported several months, or even years, after symptom onset, there could have been recall bias. Because of the data quality issues associated with recalling specific dates, a future study that attempts to amend some of these issues may provide further insight on the issue of delay. Additionally, because analysis of

associations with patient delay and healthcare delay were not possible in this analysis, a future study that examines these outcomes would be valuable.

Another limitation of this analysis was survival bias. Individuals who were not alive at the time of interview were not able to be included. These individuals could have had significantly different characteristics than individuals who were alive, which would bias the results. A study that gathers data at the point of diagnosis could help to minimize this. Another limitation was missing data, particularly for the data for date of symptom onset. If individuals with missing data had characteristics that differed from individuals who did not, the results could be biased. A future study with more complete data on date of symptom onset and first healthcare visit could add to this analysis. Additionally, a future study which considers heterogeneity within the foreign-born, Hispanic population with TB could be valuable since other literature has indicated the extent of diversity within this population in regards to their use of healthcare services and their health outcomes (30).

As the burden of TB continues to shift from U.S.-born to foreign-born persons in the United States, it is increasingly important to address barriers to care in this population. Hispanic persons account for a third of TB cases among all the foreign-born in the United States (1). This and other studies of TB have shown that the foreign-born Hispanic population may be particularly vulnerable to problems with healthcare access associated with low socio-economic status. One aspect of healthcare access is delay in access to treatment. This study has found that recently arrived Hispanic persons have increased risk of treatment

initiation delay for TB. In addition, foreign-born Hispanic persons who lack a sense of control over their TB outcomes also have greater treatment delays. Approaches to reducing treatment delay should include a focus of improving access to care among recent arrivals to the U.S. and public health messages tailored to Hispanic populations to improve self-efficacy.

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TABLES

Table 1. Demographics and other risk factors among foreign-born, Hispanic TB patients (n=568).

Exposure	% (n)	Exposure	% (n)
Age		**Place of diagnosis**	
<18	3.9 (22)	Health depart.	21.45 (121)
18-24	18.0 (102)	Private doctor	9.57 (54)
25-34	32.2 (183)	Hospital	63.83 (360)
35-44	16.9 (96)	Other	5.14 (29)
>45	29.5 (165)		
Female Sex	35.6 (202)	**No usual source of medical care**	23.6 (133)
Country of birth Mexico	61.3 (348)	**Believe own actions determine TB outcome**	92.2 (475)
Employed at diagnosis	54.40 (309)	**Feared deportation when went for treatment**	22.8 (127)
Education ≤ 8th grade	50.0 (281)	**Cough as a symptom**	67.8 (183)
English speaker	77.1 (438)	**Pulmonary involvement**	85.7 (487)
Household income <$20,000	63.0 (358)	**Ever smoked**	35.8 (207)
Homeless at diagnosis	2.8 (16)	**Excess alcohol use**	13.7 (77)
Visa status at interview		**HIV positive**	6.5 (37)
Permanent	36.51 (180)		
Temporary	9.13 (45)		
Undocumented	54.36 (268)		
Time from arrival to US to symptom onset ≤ 2 years	21.0 (102)		
No health insurance at symptom onset	73.4 (378)		

Table 2. Outcomes in treatment delay among foreign-born, Hispanic persons with TB (total n=568). Overall treatment delay was calculated as the difference between the date of therapy start retrieved from the CDC RVCT form and self-reported date of symptom onset. Patient delay was calculated as the difference between self-reported date of first healthcare visit and self-reported date of symptom onset. Healthcare delay was calculated as the difference between the date of therapy start reported on the RVCT form and self-reported date of first healthcare visit.

Outcome	Median	Min	25th percentile	75th percentile	Max	N
Overall delay	77.0	-14.0	36.0	145.5	1729.0	480
Patient delay	31.0	0.0	0.0	62.0	1644.0	347
Healthcare delay	27.5	-15.0	8.0	80.0	1264.0	342

Table 3. Median treatment delays among foreign-born, Hispanic persons with TB (total n=568). Overall treatment delay was calculated as the difference between the date of therapy start retrieved from the CDC RVCT form and self-reported date of symptom onset.

Exposure	Median overall delay in days	n
Employed at diagnosis		465
Yes	80.0	
No	76.0	
Education		461
≤8th grade	80.0	
>8th grade	76.0	
English speaker		465
Yes	60.0	
No	80.0	
Visa status at interview		408
Permanent	70.0	
Temporary	96.0	
Undocumented	77.0	
Time from arrival to US to symptom onset		462
>2 years	75.0	
≤2 years	84.0	
Usual source of medical care		461
Yes	80.0	
No	71.0	
Place of diagnosis		462
Health department	77.5	
Private doctor	101.5	
Hospital	76.0	
Other	57.0	
Believe own actions determine TB outcome		419
Yes	76.0	
No	125.0	

Table 4. Unadjusted Cox Proportional Hazard models for treatment initiation after symptom onset among foreign-born, Hispanic persons with TB (total n=568).

Exposure	Hazard ratio overall delay	95% CI	p-value	n
Employed at diagnosis				465
No	1.00	Ref	Ref	
Yes	0.99	0.83, 1.19	0.92	
Education				461
≤8th grade	1.00	Ref	Ref	
>8th grade	1.08	0.90, 1.30	0.42	
English speaker				465
No	1.00	Ref	Ref	
Yes	1.18	0.95, 1.48	0.14	
Visa status at interview				408
Permanent	1.00	Ref	Ref	
Temporary	0.90	0.62, 1.31	0.58	
Undocumented	1.07	0.87, 1.32	0.53	
Time from arrival to US to symptom onset				462
>2 years	1.00	Ref	Ref	
≤2 years	0.78	0.62, 0.98	0.03	
Use of a usual source of medical care				461
Yes	1.00	Ref	Ref	
No	1.06	0.86, 1.32	0.58	
Place of diagnosis				462
Health department	1.00	Ref	Ref	
Private doctor	0.76	0.54, 1.08	0.12	
Hospital	0.91	0.72, 1.15	0.44	
Other	0.77	0.48, 1.23	0.27	
Believe own actions determine TB outcome				419
Yes	1.00	Ref	Ref	
No	0.66	0.46, 0.94	0.02	

Table 5. Multivariate Cox-Proportional Hazard treatment initiation after symptom onset among foreign-born, Hispanic persons with TB (n=408).

Exposure	Hazard ratio overall delay	95% CI	p-value
Employed at Diagnosis			
Yes	1.00	Ref	Ref
No	0.92	0.75, 1.14	0.44
Education			
<8th grade	1.00	Ref	Ref
>8th grade	1.00	0.80, 1.25	0.99
English Speaker			
Yes	1.00	Ref	Ref
No	1.12	0.86, 1.45	0.71
Time from arrival to US to symptom onset			
>2 years	1.00	Ref	Ref
≤2 years	0.69	0.53, 0.91	0.008
Use of a usual source of medical care			
Yes	1.00	Ref	Ref
No	0.91	0.71, 1.17	0.510
Place of diagnosis			
Health department	1.00	Ref	Ref
Private doctor	0.72	0.49, 1.06	0.09
Hospital	0.87	0.68, 1.12	0.45
Other	0.79	0.48, 1.31	0.37
Believe own actions determine TB outcome			
Yes	1.00	Ref	Ref
No	0.60	0.41, 0.87	0.007

FIGURES

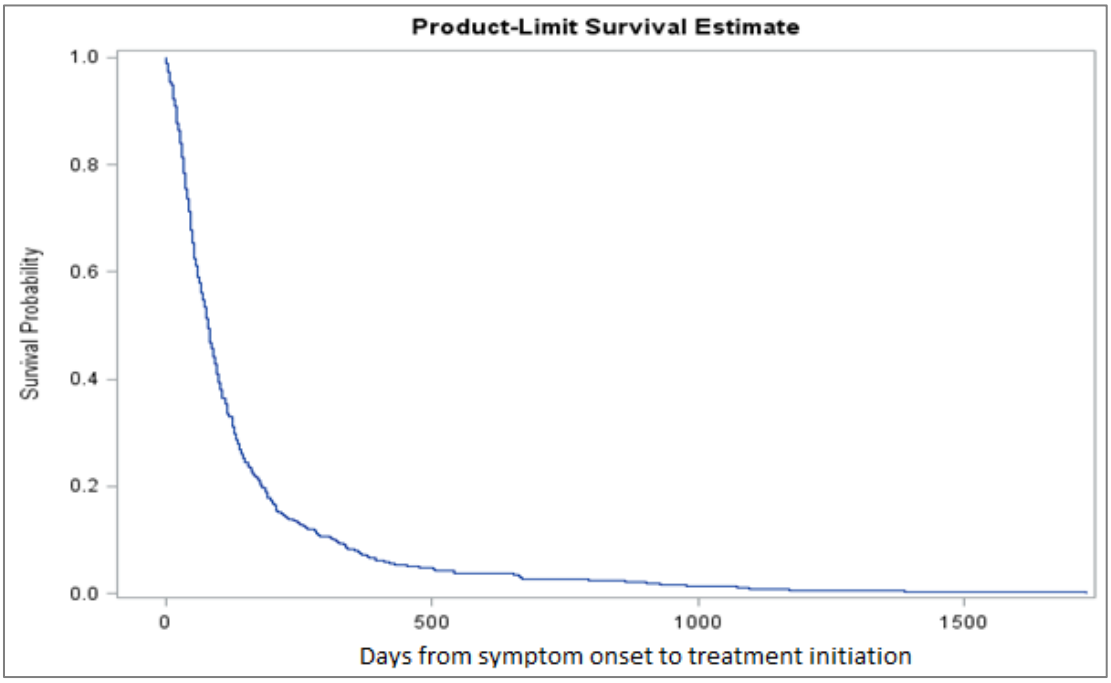


Figure 1. Kaplan-Meyer survival curve for time from symptom onset to treatment initiation among foreign-born, Hispanic persons with (n=480).

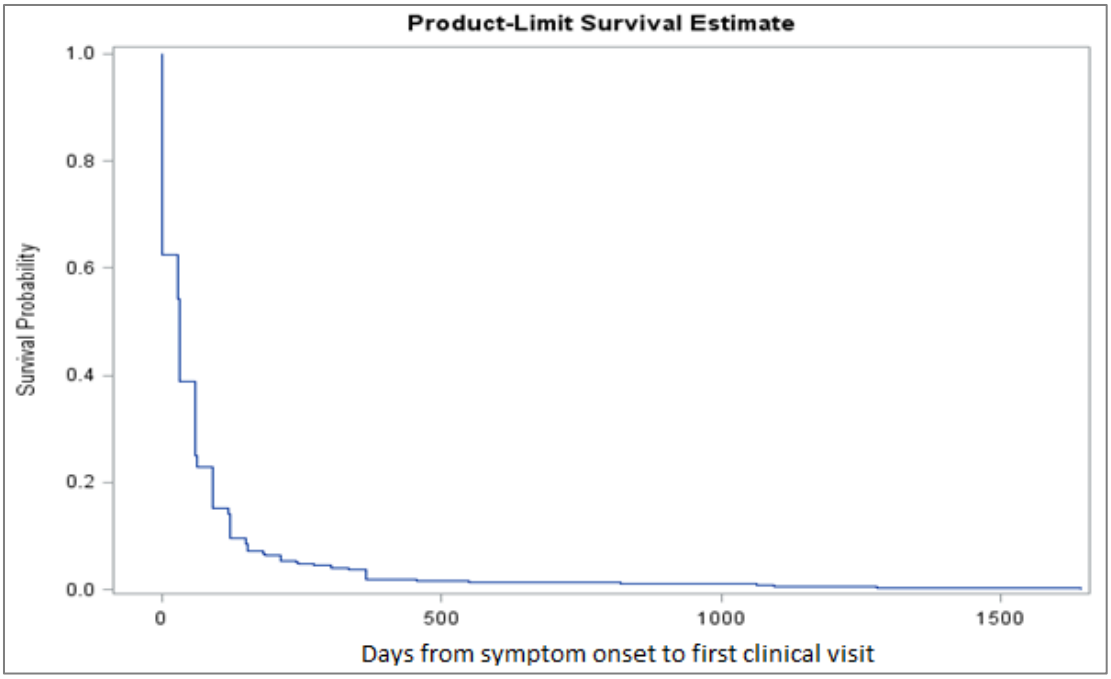


Figure 2. Kaplan-Meyer survival curve for time from symptom onset to first clinical visit among foreign-born, Hispanic persons with TB (n=347).

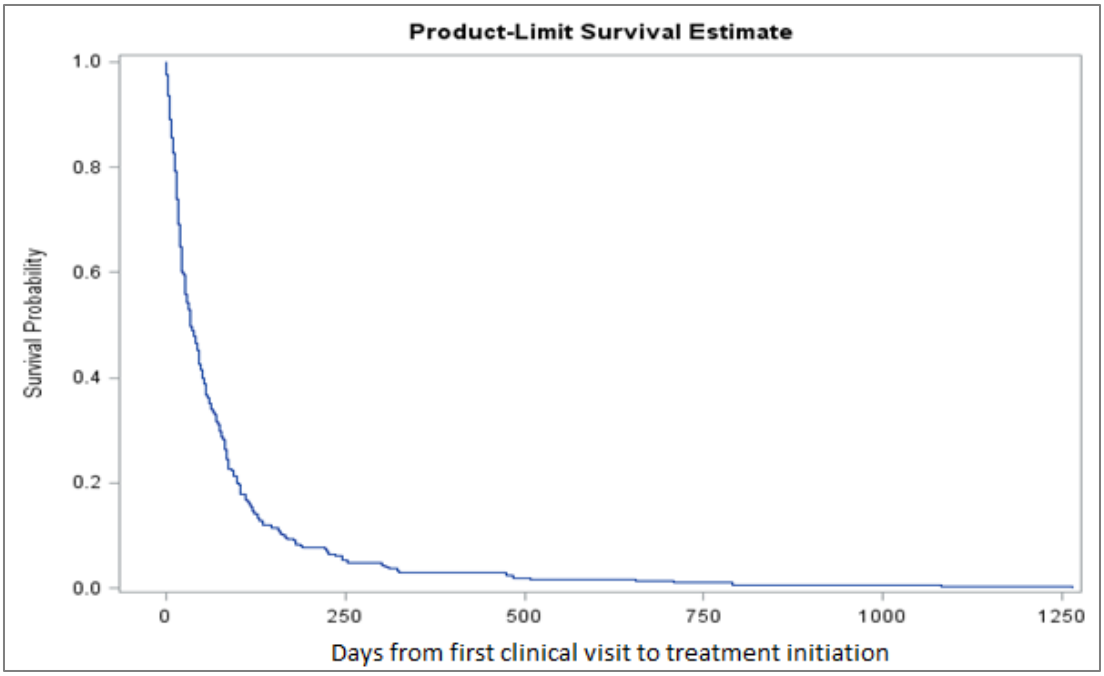
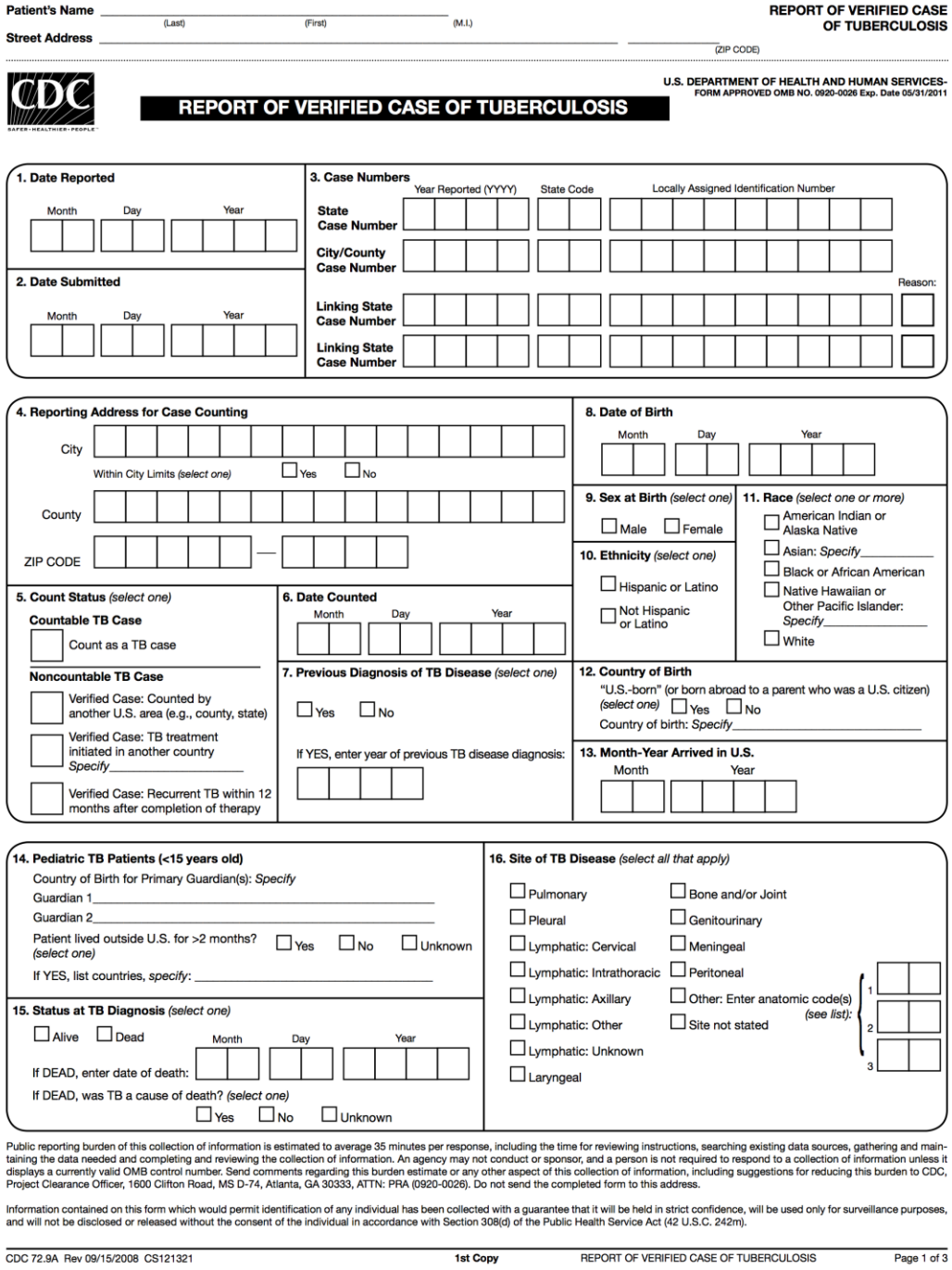


Figure 3. Kaplan-Meyer survival curve for time from first clinical visit to treatment initiation among foreign-born, Hispanic persons with TB (n=342)

APPENDICIES

Appendix A. Reported Verified Case Tuberculosis (RVCT) form



Patient's Name _____ (Last) (First) (M.I.)

Street Address _____ (ZIP CODE)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FORM APPROVED OMB NO. 0920-0026 Exp. Date 05/31/2011

CDC — SAFER·HEALTHIER·PEOPLE™

REPORT OF VERIFIED CASE OF TUBERCULOSIS

1. Date Reported — Month / Day / Year

2. Date Submitted — Month / Day / Year

3. Case Numbers — Year Reported (YYYY) / State Code / Locally Assigned Identification Number

- State Case Number
- City/County Case Number
- Linking State Case Number
- Linking State Case Number

Reason:

4. Reporting Address for Case Counting

City

Within City Limits *(select one)* ☐ Yes ☐ No

County

ZIP CODE

5. Count Status *(select one)*

Countable TB Case

☐ Count as a TB case

Noncountable TB Case

☐ Verified Case: Counted by another U.S. area (e.g., county, state)

☐ Verified Case: TB treatment initiated in another country *Specify*_____

☐ Verified Case: Recurrent TB within 12 months after completion of therapy

6. Date Counted — Month / Day / Year

7. Previous Diagnosis of TB Disease *(select one)*

☐ Yes ☐ No

If YES, enter year of previous TB disease diagnosis:

8. Date of Birth — Month / Day / Year

9. Sex at Birth *(select one)*

☐ Male ☐ Female

10. Ethnicity *(select one)*

☐ Hispanic or Latino

☐ Not Hispanic or Latino

11. Race *(select one or more)*

☐ American Indian or Alaska Native

☐ Asian: *Specify*_____

☐ Black or African American

☐ Native Hawaiian or Other Pacific Islander: *Specify*_____

☐ White

12. Country of Birth

"U.S.-born" (or born abroad to a parent who was a U.S. citizen) *(select one)* ☐ Yes ☐ No

Country of birth: *Specify*_____

13. Month-Year Arrived in U.S. — Month / Year

14. Pediatric TB Patients (<15 years old)

Country of Birth for Primary Guardian(s): *Specify*

Guardian 1_____

Guardian 2_____

Patient lived outside U.S. for >2 months? *(select one)* ☐ Yes ☐ No ☐ Unknown

If YES, list countries, *specify*: _____

15. Status at TB Diagnosis *(select one)*

☐ Alive ☐ Dead

If DEAD, enter date of death: Month / Day / Year

If DEAD, was TB a cause of death? *(select one)* ☐ Yes ☐ No ☐ Unknown

16. Site of TB Disease *(select all that apply)*

☐ Pulmonary
☐ Pleural
☐ Lymphatic: Cervical
☐ Lymphatic: Intrathoracic
☐ Lymphatic: Axillary
☐ Lymphatic: Other
☐ Lymphatic: Unknown
☐ Laryngeal
☐ Bone and/or Joint
☐ Genitourinary
☐ Meningeal
☐ Peritoneal
☐ Other: Enter anatomic code(s) *(see list)*: 1 2 3
☐ Site not stated

Public reporting burden of this collection of information is estimated to average 35 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC, Project Clearance Officer, 1600 Clifton Road, MS D-74, Atlanta, GA 30333, ATTN: PRA (0920-0026). Do not send the completed form to this address.

Information contained on this form which would permit identification of any individual has been collected with a guarantee that it will be held in strict confidence, will be used only for surveillance purposes, and will not be disclosed or released without the consent of the individual in accordance with Section 308(d) of the Public Health Service Act (42 U.S.C. 242m).

CDC 72.9A Rev 09/15/2008 CS121321 **1st Copy** REPORT OF VERIFIED CASE OF TUBERCULOSIS Page 1 of 3

Patient's Name _____ State Case No. _____ REPORT OF VERIFIED CASE OF TUBERCULOSIS
(Last) (First) (M.I.)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

17. Sputum Smear *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
Date Collected: Month Day Year

18. Sputum Culture *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
Date Collected: Month Day Year
Date Result Reported: Month Day Year
Reporting Laboratory Type *(select one)*: ☐ Public Health Laboratory ☐ Commercial Laboratory ☐ Other

19. Smear/Pathology/Cytology of Tissue and Other Body Fluids *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
Date Collected: Month Day Year
Enter anatomic code *(see list)*:
Type of exam *(select all that apply)*: ☐ Smear ☐ Pathology/Cytology

20. Culture of Tissue and Other Body Fluids *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
Date Collected: Month Day Year
Enter anatomic code *(see list)*:
Date Result Reported: Month Day Year
Reporting Laboratory Type *(select one)*: ☐ Public Health Laboratory ☐ Commercial Laboratory ☐ Other

21. Nucleic Acid Amplification Test Result *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
☐ Indeterminate
Date Collected: Month Day Year
Enter specimen type: ☐ Sputum
OR
If not Sputum, enter anatomic code *(see list)*:
Date Result Reported: Month Day Year
Reporting Laboratory Type *(select one)*: ☐ Public Health Laboratory ☐ Commercial Laboratory ☐ Other

Initial Chest Radiograph and Other Chest Imaging Study

22A. Initial Chest Radiograph *(select one)*
☐ Normal ☐ Abnormal* (consistent with TB) ☐ Not Done ☐ Unknown
* For ABNORMAL Initial Chest Radiograph: Evidence of a cavity *(select one)*: ☐ Yes ☐ No ☐ Unknown
Evidence of miliary TB *(select one)*: ☐ Yes ☐ No ☐ Unknown

22B. Initial Chest CT Scan or Other Chest Imaging Study *(select one)*
☐ Normal ☐ Abnormal* (consistent with TB) ☐ Not Done ☐ Unknown
* For ABNORMAL Initial Chest Radiograph: Evidence of a cavity *(select one)*: ☐ Yes ☐ No ☐ Unknown
Evidence of miliary TB *(select one)*: ☐ Yes ☐ No ☐ Unknown

23. Tuberculin (Mantoux) Skin Test at Diagnosis *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
Date Tuberculin Skin Test (TST) Placed: Month Day Year
Millimeters (mm) of induration:

24. Interferon Gamma Release Assay for *Mycobacterium tuberculosis* at Diagnosis *(select one)*
☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
☐ Indeterminate
Date Collected: Month Day Year
Test type:
*Specify*_____

25. Primary Reason Evaluated for TB Disease *(select one)*
☐ TB Symptoms
☐ Abnormal Chest Radiograph (consistent with TB)
☐ Contact Investigation
☐ Targeted Testing
☐ Health Care Worker
☐ Employment/Administrative Testing
☐ Immigration Medical Exam
☐ Incidental Lab Result
☐ Unknown

Patient's Name _____ State Case No. _____ REPORT OF VERIFIED CASE OF TUBERCULOSIS
(Last) (First) (M.I.)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

26. HIV Status at Time of Diagnosis *(select one)*

☐ Negative ☐ Indeterminate ☐ Not Offered ☐ Unknown
☐ Positive ☐ Refused ☐ Test Done, Results Unknown

If POSITIVE, enter:
State HIV/AIDS Patient Number: ☐☐☐☐☐☐☐☐☐☐ City/County HIV/AIDS Patient Number: ☐☐☐☐☐☐☐☐☐☐

27. Homeless Within Past Year *(select one)*

☐ No ☐ Yes ☐ Unknown

28. Resident of Correctional Facility at Time of Diagnosis *(select one)* ☐ No ☐ Yes ☐ Unknown

If YES, *(select one)*:
☐ Federal Prison ☐ Local Jail ☐ Other Correctional Facility
☐ State Prison ☐ Juvenile Correction Facility ☐ Unknown

If YES, under custody of Immigration and Customs Enforcement? *(select one)*
☐ No ☐ Yes

29. Resident of Long-Term Care Facility at Time of Diagnosis *(select one)* ☐ No ☐ Yes ☐ Unknown

If YES, *(select one)*:
☐ Nursing Home ☐ Residential Facility ☐ Alcohol or Drug Treatment Facility ☐ Unknown
☐ Hospital-Based Facility ☐ Mental Health Residential Facility ☐ Other Long-Term Care Facility

30. Primary Occupation Within the Past Year *(select one)*

☐ Health Care Worker ☐ Migrant/Seasonal Worker ☐ Retired ☐ Not Seeking Employment (e.g. student, homemaker, disabled person)
☐ Correctional Facility Employee ☐ Other Occupation ☐ Unemployed ☐ Unknown

31. Injecting Drug Use Within Past Year *(select one)*
☐ No ☐ Yes ☐ Unknown

32. Non-Injecting Drug Use Within Past Year *(select one)*
☐ No ☐ Yes ☐ Unknown

33. Excess Alcohol Use Within Past Year *(select one)*
☐ No ☐ Yes ☐ Unknown

34. Additional TB Risk Factors *(select all that apply)*

☐ Contact of MDR-TB Patient (2 years or less) ☐ Incomplete LTBI Therapy ☐ Diabetes Mellitus ☐ Other *Specify* _____
☐ Contact of Infectious TB Patient (2 years or less) ☐ TNF-α Antagonist Therapy ☐ End-Stage Renal Disease ☐ None
☐ Missed Contact (2 years or less) ☐ Post-organ Transplantation ☐ Immunosuppression (not HIV/AIDS)

35. Immigration Status at First Entry to the U.S. *(select one)*

☐ Not Applicable
- "U.S.-born" (or born abroad to a parent who was a U.S. citizen)
- Born in 1 of the U.S. Territories, U.S. Island Areas, or U.S. Outlying Areas

☐ Immigrant Visa ☐ Tourist Visa ☐ Asylee or Parolee
☐ Student Visa ☐ Family/Fiancé Visa ☐ Other Immigration Status
☐ Employment Visa ☐ Refugee ☐ Unknown

36. Date Therapy Started

Month ☐☐ Day ☐☐ Year ☐☐☐☐

37. Initial Drug Regimen *(select one option for each drug)*

	No	Yes	Unk		No	Yes	Unk		No	Yes	Unk
Isoniazid	☐	☐	☐	Ethionamide	☐	☐	☐	Moxifloxacin	☐	☐	☐
Rifampin	☐	☐	☐	Amikacin	☐	☐	☐	Cycloserine	☐	☐	☐
Pyrazinamide	☐	☐	☐	Kanamycin	☐	☐	☐	Para-Amino Salicylic Acid	☐	☐	☐
Ethambutol	☐	☐	☐	Capreomycin	☐	☐	☐	Other	☐	☐	☐
Streptomycin	☐	☐	☐	Ciprofloxacin	☐	☐	☐	*Specify* _____			
Rifabutin	☐	☐	☐	Levofloxacin	☐	☐	☐	Other	☐	☐	☐
Rifapentine	☐	☐	☐	Ofloxacin	☐	☐	☐	*Specify* _____			

Comments:

_____
_____
_____
_____

Patient's Name _____ (Last) (First) (M.I.)

Street Address _____ (Number, Street, City, State) _____ (ZIP CODE)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
ATLANTA, GEORGIA 30333
FORM APPROVED OMB NO. 0920-0026 Exp. Date 05/31/2011

REPORT OF VERIFIED CASE OF TUBERCULOSIS

Initial Drug Susceptibility Report — (Follow Up Report – 1)

Year Counted ☐☐☐☐

State Case Number ☐☐☐☐ ☐☐ ☐☐☐☐☐☐☐☐☐☐

City/County Case Number ☐☐☐☐ ☐☐ ☐☐☐☐☐☐☐☐☐☐

Submit this report for all culture-positive cases.

38. Genotyping Accession Number

Isolate submitted for genotyping *(select one)*: ☐ No ☐ Yes

If YES, genotyping accession number for episode: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐

39. Initial Drug Susceptibility Testing

Was drug susceptibility testing done? *(select one)* ☐ No ☐ Yes ☐ Unknown

If NO or UNKNOWN, do not complete the rest of Follow Up Report –1

If YES, enter date FIRST isolate collected for which drug susceptibility testing was done:

Month ☐☐ Day ☐☐ Year ☐☐☐☐

Enter specimen type: ☐ Sputum

OR

If not Sputum, enter anatomic code *(see list)*: ☐☐

40. Initial Drug Susceptibility Results *(select one option for each drug)*

	Resistant	Susceptible	Not Done	Unknown
Isoniazid	☐	☐	☐	☐
Rifampin	☐	☐	☐	☐
Pyrazinamide	☐	☐	☐	☐
Ethambutol	☐	☐	☐	☐
Streptomycin	☐	☐	☐	☐
Rifabutin	☐	☐	☐	☐
Rifapentine	☐	☐	☐	☐
Ethionamide	☐	☐	☐	☐
Amikacin	☐	☐	☐	☐
Kanamycin	☐	☐	☐	☐

	Resistant	Susceptible	Not Done	Unknown
Capreomycin	☐	☐	☐	☐
Ciprofloxacin	☐	☐	☐	☐
Levofloxacin	☐	☐	☐	☐
Ofloxacin	☐	☐	☐	☐
Moxifloxacin	☐	☐	☐	☐
Other Quinolones	☐	☐	☐	☐
Cycloserine	☐	☐	☐	☐
Para-Amino Salicylic Acid	☐	☐	☐	☐
Other	☐	☐	☐	☐
Specify _____				
Other	☐	☐	☐	☐
Specify _____				

Comments:

_____

_____

_____

_____

_____

_____

Patient's Name _____ (Last) (First) (M.I.)

Street Address _____ (Number, Street, City, State) _____ (ZIP CODE)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
ATLANTA, GEORGIA 30333
FORM APPROVED OMB NO. 0920-0026 Exp. Date 05/31/2011

REPORT OF VERIFIED CASE OF TUBERCULOSIS

Case Completion Report

(Follow Up Report – 2)

Year Counted ☐☐☐☐

State Case Number ☐☐☐☐ ☐☐ ☐☐☐☐☐☐☐☐☐☐

City/County Case Number ☐☐☐☐ ☐☐ ☐☐☐☐☐☐☐☐☐☐

Submit this report for all cases in which the patient was alive at diagnosis.

41. Sputum Culture Conversion Documented *(select one)* ☐ No ☐ Yes ☐ Unknown

If YES, enter date specimen collected for FIRST consistently negative sputum culture:

Month ☐☐ Day ☐☐ Year ☐☐☐☐

If NO, enter reason for not documenting sputum culture conversion *(select one)*:

☐ No Follow-up Sputum Despite Induction ☐ Patient Refused ☐ Patient Lost to Follow-Up
☐ No Follow-up Sputum and No Induction ☐ Other *Specify* _____
☐ Died ☐ Unknown

42. Moved

Did the patient move during TB therapy? *(select one)* ☐ No ☐ Yes

If YES, moved to where *(select all that apply)*:

☐ In state, out of jurisdiction *(enter city/county)* *Specify* _____ *Specify* _____
☐ Out of state *(enter state)* *Specify* _____ *Specify* _____
☐ Out of the U.S. *(enter country)* *Specify* _____ *Specify* _____

If moved out of the U.S., transnational referral? *(select one)* ☐ No ☐ Yes

43. Date Therapy Stopped

Month ☐☐ Day ☐☐ Year ☐☐☐☐

44. Reason Therapy Stopped or Never Started *(select one)*

☐ Completed Therapy ☐ Not TB
☐ Lost ☐ Died
☐ Uncooperative or Refused ☐ Other
☐ Adverse Treatment Event ☐ Unknown

If DIED, indicate cause of death *(select one)*:

☐ Related to TB disease ☐ Unrelated to TB disease
☐ Related to TB therapy ☐ Unknown

45. Reason Therapy Extended >12 months *(select all that apply)*

☐ Rifampin Resistance ☐ Non-adherence ☐ Clinically Indicated – other reasons
☐ Adverse Drug Reaction ☐ Failure ☐ Other *Specify* _____

46. Type of Outpatient Health Care Provider *(select all that apply)*

☐ Local/State Health Department (HD) ☐ IHS, Tribal HD, or Tribal Corporation ☐ Inpatient Care Only ☐ Unknown
☐ Private Outpatient ☐ Institutional/Correctional ☐ Other

Comments:

_____
_____
_____
_____
_____

Patient's Name _____ State Case No. _____

(Last) (First) (M.I.)

REPORT OF VERIFIED CASE OF TUBERCULOSIS

CDC

SAFER·HEALTHIER·PEOPLE

REPORT OF VERIFIED CASE OF TUBERCULOSIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
ATLANTA, GEORGIA 30333
FORM APPROVED OMB NO. 0920-0026 Exp. Date 05/31/2011

Case Completion Report - *Continued*

(Follow Up Report – 2)

47. Directly Observed Therapy (DOT) *(select one)*

- ☐ No, Totally Self-Administered
- ☐ Yes, Totally Directly Observed
- ☐ Yes, Both Directly Observed and Self-Administered
- ☐ Unknown

Number of weeks of directly observed therapy (DOT) ☐☐☐

48. Final Drug Susceptibility Testing

Was follow-up drug susceptibility testing done? *(select one)* ☐ No ☐ Yes ☐ Unknown

If NO or UNKNOWN, do not complete the rest of Follow Up Report –2

If YES, enter date FINAL isolate collected for which drug susceptibility testing was done:

Month ☐☐ Day ☐☐ Year ☐☐☐☐

Enter specimen type: ☐ Sputum

OR

If not Sputum, enter anatomic code *(see list)*: ☐☐

49. Final Drug Susceptibility Results *(select one option for each drug)*

	Resistant	Susceptible	Not Done	Unknown
Isoniazid	☐	☐	☐	☐
Rifampin	☐	☐	☐	☐
Pyrazinamide	☐	☐	☐	☐
Ethambutol	☐	☐	☐	☐
Streptomycin	☐	☐	☐	☐
Rifabutin	☐	☐	☐	☐
Rifapentine	☐	☐	☐	☐
Ethionamide	☐	☐	☐	☐
Amikacin	☐	☐	☐	☐
Kanamycin	☐	☐	☐	☐

	Resistant	Susceptible	Not Done	Unknown
Capreomycin	☐	☐	☐	☐
Ciprofloxacin	☐	☐	☐	☐
Levofloxacin	☐	☐	☐	☐
Ofloxacin	☐	☐	☐	☐
Moxifloxacin	☐	☐	☐	☐
Other Quinolones	☐	☐	☐	☐
Cycloserine	☐	☐	☐	☐
Para-Amino Salicylic Acid	☐	☐	☐	☐
Other	☐	☐	☐	☐
Specify _____				
Other	☐	☐	☐	☐
Specify _____				

Comments:

Appendix B. Tuberculosis Case Definition for Public Health Surveillance

Revised May 13, 2009

Clinical description

A chronic bacterial infection caused by Mycobacterium tuberculosis, usually characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved.

Clinical case definition

A case that meets all of the following criteria:

- A positive tuberculin skin test result or positive interferon gamma release assay for M. tuberculosis
- Other signs and symptoms compatible with tuberculosis (TB) (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease)
- Treatment with two or more anti-TB medications
- A completed diagnostic evaluation

Laboratory criteria for diagnosis

- Isolation of M. tuberculosis complex from a clinical specimen,

or

- Demonstration of M. tuberculosis complex from a clinical specimen by nucleic acid amplification test,

or

- Demonstration of acid-fast bacilli in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated.

Case classification

Confirmed: a case that meets the clinical case definition or is laboratory confirmed

Comment

A case should not be counted twice within any consecutive 12-month period. However, a case occurring in a patient who had previously had verified TB disease should be reported and counted again if more than 12 months have elapsed since the patient completed therapy. A case should also be reported and counted again if the patient was lost to supervision for greater than 12 months and TB disease can be verified again. Mycobacterial diseases other than those caused by M. tuberculosis complex should not be counted in tuberculosis morbidity statistics unless there is concurrent tuberculosis.

Appendix C. Tuberculosis Epidemiological Studies Consortium Task Order 9 Data Collection Sites

Appendix D. Emory IRB Exemption

EMORY UNIVERSITY | Institutional Review Board

February 15, 2013

Ann Lockard,
Principal Investigator
Public Health

RE: Determination: No IRB Review Required
eIRB#: IRB00063835
Title: *Determinants of Late Tuberculosis Diagnosis among Mexican-Born Persons in the United States*
PI: Ann Lockard

Dear Ms. Lockard:

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the materials you provided, we have determined that it does not require IRB review because it does not meet the definition(s) of "research" or "clinical investigation" involving "human subjects" as set forth in Emory policies and procedures and federal rules, if applicable. Specifically, in this project, you will investigate the time from symptom onset to tuberculosis diagnosis among Mexican-born persons living in the United States. You will be using a de-identified data set to conduct this investigation that will not permit the identification of individuals from the data used or in combination with other data.

Please note that this determination does not mean that you cannot publish the results. If you have questions about this issue, please contact the IRB office.

This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Thank you for consulting the IRB.

Sincerely,

Regina Drake, M.Div, CIP
Senior Research Protocol Analyst
This letter has been digitally signed.

Emory University
1599 Clifton Road, 5th Floor - Atlanta, Georgia 30322
Tel: 404.712.0720 - Fax: 404.727.1358 - Email: irb@emory.edu - Web: http://www.irb.emory.edu