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Investigating Missed Opportunities for Prevention of Mycobacterium Tuberculosis Transmission Within Contacts of Tuberculosis Cases in Shelby County, Tennessee

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INVESTIGATING MISSED OPPORTUNITIES FOR PREVENTION OF MYCOBACTERIUM TUBERCULOSIS TRANSMISSION WITHIN CONTACTS OF TUBERCULOSIS CASES IN SHELBY COUNTY, TENNESSEE

by

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DEDICATION

I would like to dedicate this thesis to my husband, Trevor Reish, and my family. Without their support and love, I would not be able to motivate myself to achieve such a great accomplishment in my profession. They give me encouragement and drive me during my academic career. Additionally, I would like to express gratitude to God for putting me in the setting that allows me to collaborate with public health professionals who assist me with the knowledge I need to complete my thesis and graduate studies.

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ABSTRACT

Since 2010, Tuberculosis (TB) incidence in Shelby County, Tennessee has been steady with little fluctuation. During these years, however, TB incidence has been decreasing in Tennessee and the United States; except for 2015. The discrepancy between these trends may be due to sub-optimal TB prevention and/or treatment measures in Shelby County as compared to Tennessee and the United States. Therefore, it is pertinent to examine factors potentially associated with TB prevention among close contacts of TB cases to assess missed opportunities for prevention and eventually decrease the incidence of TB. Data from Shelby County TB cases during 2013-2015, and their contacts, are analyzed to describe the TB contacts magnitude and calculate number of contacts needed to receive preventive treatment to prevent one new case of TB. The study suggests that for every 100 people who go through preventive therapy, 1.5 individuals may be prevented from developing TB.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CHAPTER 1

INTRODUCTION

One-third of the population in the world is infected with Tuberculosis (TB) bacteria. This infectious disease has been around for thousands of years and still causes turmoil in countless parts of the globe.[1] TB ranked 9th cause of death worldwide in 2015 and is one of the world's top infectious disease killers alongside human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), diarrheal diseases, lower respiratory tract infections, and malaria.[2,3] These five killers alone contribute to over one-eighth of the world's death toll.[3] TB, HIV/AIDS, and malaria collectively are responsible for almost 5 million deaths each year.[4] In 2014, TB deaths surpassed the amount of HIV-related deaths worldwide with 1.5 million deaths compared to the 1.2 million deaths caused by HIV/AIDS.[5] These numbers testify to the enormity of the burden of TB on public health globally.

TB has been known as a poverty-related disease and the death toll is more prominent within low-income and low-middle-income compared to higher-income communities.[4,6] However, even though TB is not a top ten killer within the upper-middle-income and high-income economies, it can still be a disease problem in these societies. In 2015, 10.4 million people were ill with TB and most were from low-income to middle-income countries. However, on average, since 2000 the world TB incidence has decreased at 1.5% per year according to the World Health Organization (WHO).[7] The elimination of TB is far in the future, but preventive measures and new treatment options have already allowed public health professionals to battle this disease on the forefront.[6]

Developed nations differ in regards to TB incidence and prevalence. The United States has a low TB incidence, but still experiences the affliction of the disease every year.[6] Per the Centers for Disease Control and Prevention (CDC), the number of TB deaths reported throughout the United States has decreased since 1992 by 67% resulting in the longest consecutive decrease in TB for the nation (Figure 1).[8,9]

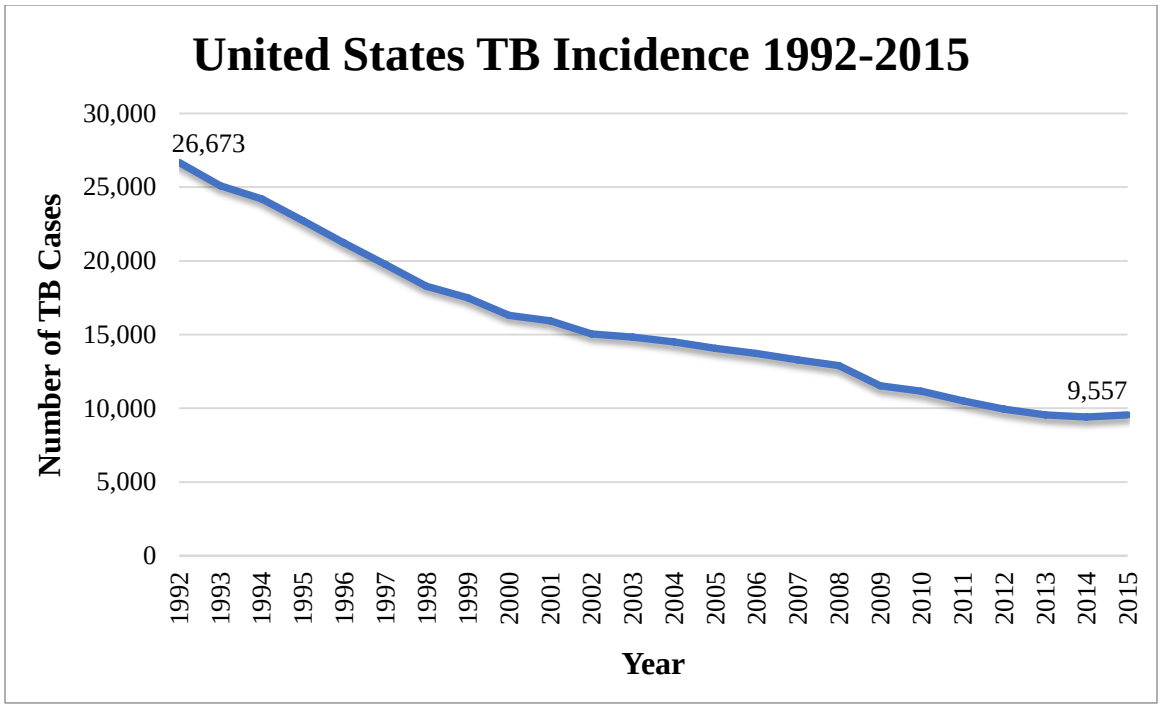


Figure 1. Decreasing trend of TB incidence in the United States between 1992 to 2015. Incidence data from the United States was obtained through the CDC.[8] In 1992, the United States experienced the start of a 23-year decrease in incidence. This decrease was not apparent during the year 2015 when there was an increase of 151 cases from 2014.

There are 4 states throughout the nation that account for 50.6% of the TB incidence in the United States: California, Florida, New York, and Texas. Within the rest of the 46 states, a majority have a case rate that is lower than the 3.0 per 100,000 population case rate of the whole United States.[10] However, there are counties throughout these states that represent a large portion of the TB cases reported in that state. One of these counties is Shelby County, Tennessee. The area of Shelby County is made up of 7

cities including Memphis, Germantown, Arlington, Bartlett, Collierville, Lakeland, and Millington.[11]

The effect of TB in the community of Shelby County, Tennessee continues to be significant from year to year (Figure 2). With a higher case rate in this region compared to the whole state of Tennessee and the United States, this endemic public health topic needs to be evaluated to comprehend what factors are making Shelby County more susceptible to TB.[8,11-21] During the years 2006 to 2015, Shelby County had an average case rate of 6.9 cases per 100,000 population which was double the average case rate of Tennessee and the United States: 3.0 cases per 100,000 and 3.6 cases per 100,000 respectively (Figure 3).[8,11-21] Within the years 2006, 2008, 2012, 2014, and 2015 the TB rate of Shelby County was greater than the rates of Tennessee and the United States combined.

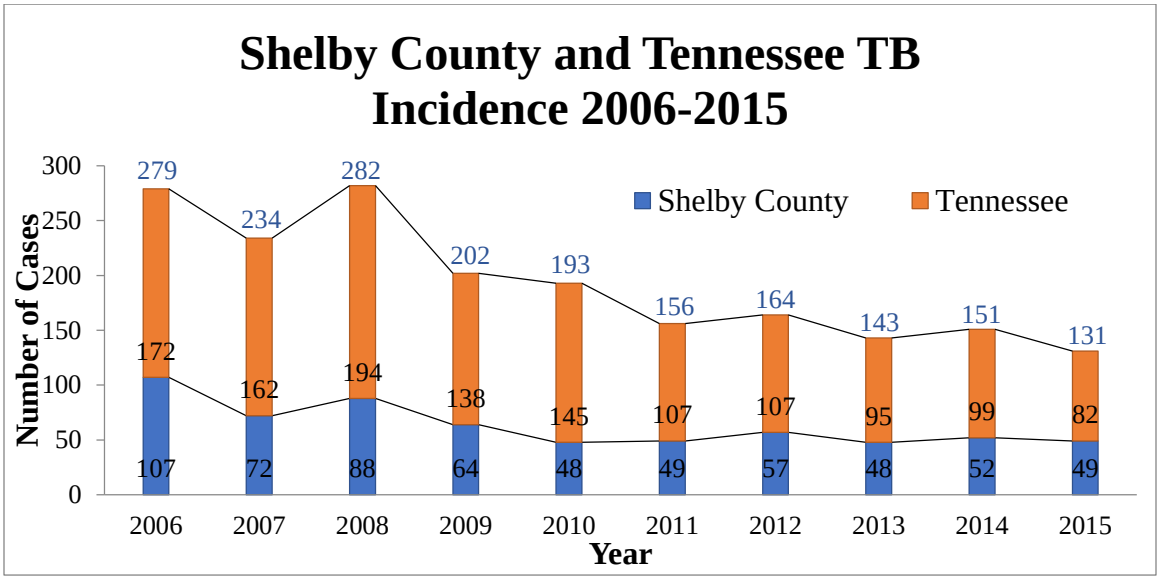
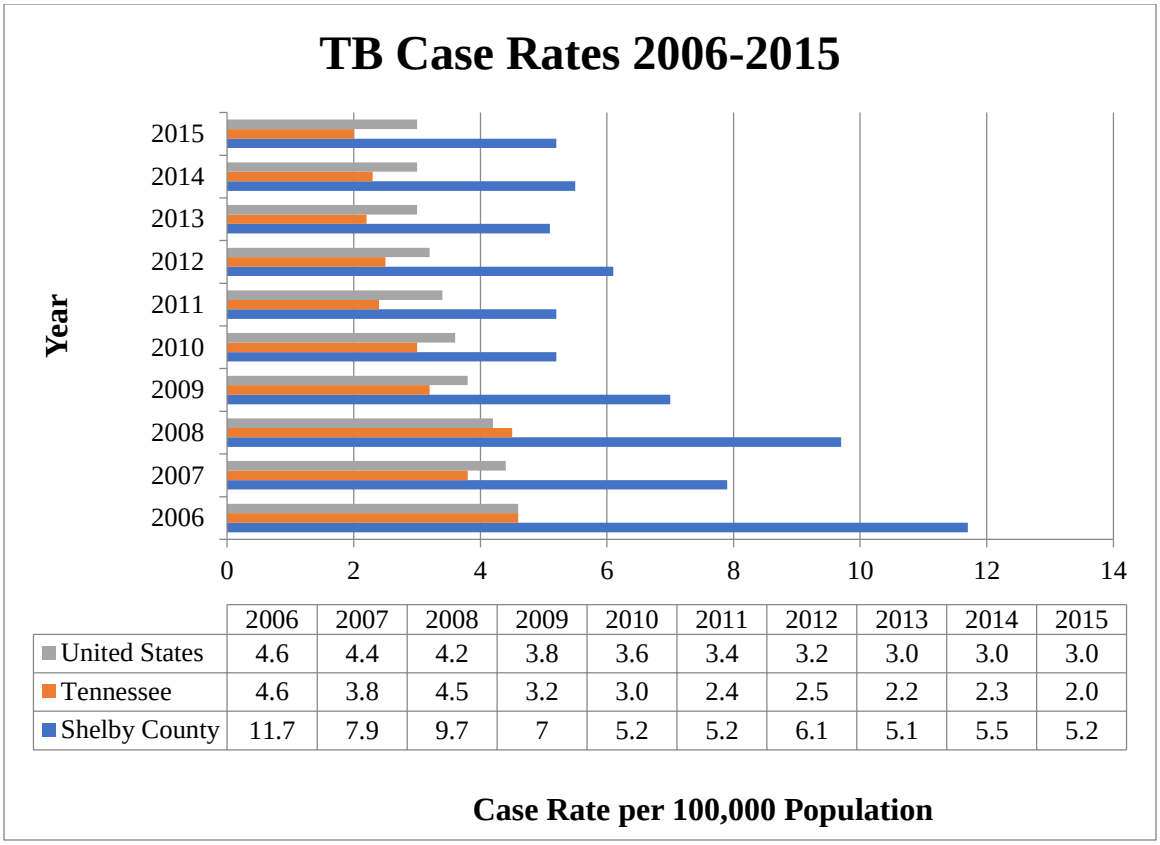


Figure 2. Shelby County and Tennessee TB Incidence 2006-2015. A comparison of two populations, Shelby County, Tennessee and the whole state of Tennessee, were used in this 10-year trend. Data labels in the blue column are for Shelby County TB incidence, while the data in the orange column is the remainder of the Tennessee incidence excluding Shelby County. The count on the top of each column is the total TB incidence for the state of Tennessee corresponding to that year.[8,11-21]



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
United States	4.6	4.4	4.2	3.8	3.6	3.4	3.2	3.0	3.0	3.0
Tennessee	4.6	3.8	4.5	3.2	3.0	2.4	2.5	2.2	2.3	2.0
Shelby County	11.7	7.9	9.7	7	5.2	5.2	6.1	5.1	5.5	5.2

Figure 3. **Tuberculosis case rates per year for the United States, Tennessee, and Shelby County during 2006 to 2015.** The case rates listed represent the United States, the state of Tennessee, and Shelby County, Tennessee.[8,11-21] During this 10-year period, the drastic difference of Shelby County can be seen compared to the other two populations.

From 2010 to 2015 TB rates in Shelby County stayed almost unchanged, while it was trending lower both in Tennessee and the United States (Figure 3). During these six years, the TB incidence experienced little fluctuation and ranged between 48 to 57 cases per year. The plateau may be due to prevention and/or treatment measures used in Shelby County that are less effective than those of Tennessee or the United States in general to combat TB. For these reasons, it is pertinent to examine factors that are potentially associated with TB prevention among TB cases' contacts in Shelby County to understand what measures need to be done to decrease the incidence of TB in Shelby County. Data from Shelby County TB cases in the years 2013 to 2015, and their contacts, were

analyzed to understand how many contacts are needed to go through preventive treatment to avert one new case of TB. This will allow for assessing missed opportunities for preventive therapy.

The Study Objective

The principal goal is to understand what actions need to be done to decrease TB incidence in Shelby County, Tennessee. The focus is on finding out how many past contacts have become sick with Tuberculosis disease (TBD) and how many received TB treatment of any kind. If they did not receive the appropriate treatment, we want to know if there was a missed opportunity to intervene. The following specific aims will be performed to address the study objective.

1. Identify Shelby County TB cases between 2010 to 2015 from existing databases at the Shelby County Health Department (SCHD).
2. Match the identified TB cases to a data set of over 943,000 TB, HIV, STD, and other test results to find the earliest test date for each case and calculate the fraction of cases that have previous test results in the SCHD system.
3. Identify contacts of each TB case by abstracting the patient chart for each case in the TB Clinic indexed on each case's unique ID.
4. Identify the number of contacts who were diagnosed with TBD, TB Suspect, and Latent tuberculosis infection (LTBI).
5. Calculate the proportion of contacts that were diagnosed with TBD, TB Suspect, or LTBI, who were offered the preventive treatment, and the proportions of contacts who accepted or rejected treatment. Additionally, calculate the proportion completed and did not complete the treatment among those who

accepted. The number of individuals who have previously been diagnosed as LTBI or TBD and gone through treatment will also be calculated.

6. Perform data analysis using logistic regression to understand missed opportunities of prevention, the risk of transmission between cases and their contacts compared to their diagnosis, and what population is at most risk for transmission of TB considering age group, race, sex, and prior positive test.

Research Question: How many TB contacts need to receive preventive therapy in order to prevent one case of TB?

Hypothesis 1: Contacts specified as 'high' risk on their investigation sheet have a greater chance of developing TBD or becoming a TB suspect compared to individuals with a 'low' or 'moderate' risk specified.

Hypothesis 2: Individuals who have evidence of a prior positive TB test before they were named as a contact have a greater chance of developing TBD or becoming a TB Suspect compared to individuals without a prior positive test.

Rationale

This study aims to examine factors that may explain the current plateauing of TB cases in Shelby County despite the overall decrease in TB incidence in Tennessee and the United States. This research potentially will contribute greatly to improve the health of Memphis and Shelby County communities by providing important information to improve preventive treatment for TB. Information of TB case contacts can give us insight into how to prevent the spread of the disease. This research will benefit the populations in Shelby County that are affected by this deadly disease by providing valuable information on how to decrease the incidence of TB in Shelby County, Tennessee.

CHAPTER 2

LITERATURE REVIEW

Infectious diseases are found throughout history causing epidemics around the globe.[22] It was believed that remarkable progress was made in the effort of eliminating these diseases and in the near future many developed countries would show positive results from using vaccinations and newer medications. However, this belief was short lived. In the 1980s, the world witnessed a pandemic of a new deadly disease AIDS.[22] This syndrome is caused by an emerging new viral pathogen, HIV infection that became more prominent during this time.[23] Not only was there the issue of the new pandemic, but an additional infectious disease re-emerged during this period. That infectious disease was TB; a potentially deadly airborne transmissible disease. There was a resurgence of TB incidence between 1985 and 1992 due to increased numbers of HIV/TB co-infected individuals who activated TBD after they became immunosuppressed.[24]

Emerging and re-emerging infectious diseases are a burden for many developing and industrialized countries worldwide. These infectious diseases challenge public health systems and there is need to develop effective policies and programs to control them.[25] With TB it is essential to understand the organism behind the infection, the different types of TB that can be contracted, and risk factors associated with the disease in hopes to decrease the incidence worldwide and one day eradicate this public health issue all together.

Tuberculosis Organism

TB has been around for centuries and is one of the oldest diseases recorded by mankind.[26] Traces of TBD have been found in the spine of ancient skeletal remains.

However, it is unclear how the organism that causes TB came about. Speculation shows that the causal organism of TB may have appeared throughout water and soil then adapted to other hosts, such as animals and humans, throughout time.[27]

A group of five mycobacteria is responsible for causing TB infection. This group of tubercle bacilli is known as the *Mycobacterium tuberculosis* complex (MTC).[22] Even though all the MTC pathogens have been shown to cause infection throughout the human population, *Mycobacterium tuberculosis* (*M. tuberculosis*) primarily causes most cases of TB in the United States.[28] This pathogen is transmitted through the air from person-to-person. Transmission can occur through coughing, sneezing, singing, or speaking.[8] Another person can become infected after breathing in air that has been contaminated by small particles of this bacterium. Yet, this type of bacteria is considered moderately infectious. Out of the individuals who breathe in air contaminated by a case with *M. tuberculosis*, only 20% to 30% of them will become infected.[29] After the bacteria is breathed in, the body activates defense mechanisms to regulate the infection. There are two types of TB an individual may develop requiring separate treatment regimens; TBD and LTBI.[30]

Tuberculosis Disease and Latent Tuberculosis Infection

TB is found in two clinical forms; TBD and LTBI. TBD is the symptomatic, infectious form that affects an individual while LTBI is the presence of the dormant state of a bacterium in the body without causing symptoms due to the immune system being able to control it.[24] When an individual becomes infected, TB starts out as LTBI.[22] The issue here is that some individuals may never know they have this infection unless they get tested since it is asymptomatic. If LTBI goes untreated, there is a possibility of the

infection turning into the full-blown TBD.[22] About 90% to 95% of people who become infected with LTBI, will never develop the infectious disease.[30] However, the remaining 5% to 10% will at some point in their life develop TBD. Depending on whether an individual has LTBI or TBD, there are separate treatment approaches to rid the body of the bacteria.

Diagnosis and Treatment of Tuberculosis

Symptoms associated with TBD are triggered due to the bacteria multiplication in the body. This results in an immune response throughout the host that may present symptomatically in the form of cough, fever, sweats, chills, chest pain, bloody sputum production, or weight loss.[22] Presence of symptoms is just one of the ways TBD can be diagnosed clinically. Various laboratory tests such as Mantoux tuberculin skin test (TST), Interferon-Gamma Release Assays (IGRA), sputum culture, sputum smears, nucleic acid amplification (NAA), biopsies, and chest radiographs are also used to determine the difference between someone diagnosed as TBD or LTBI.[10,22] During a typical TB screening, TST and IGRA blood tests are used to assess if an individual is infected with TB bacteria.[31] However, other tests listed above, like chest radiographs or sputum samples, are needed to differentiate if an individual is infected with a dormant bacterium or has TBD.[8,22]

Following the determination of an individual's diagnosis, various treatment options are then put into play depending on what type of TB that person has. The Food and Drug Administration (FDA) oversees approval of drugs used for TB treatment. Currently, the FDA has permitted ten drugs that can be used to treat TBD. Out of these ten drugs, four of them are considered "first-line anti-TB agents" per the CDC.[8] These

four agents include isoniazid (INH), ethambutol (EMB), rifampin (RIF), and pyrazinamide (PZA). A combination of these drugs will be given to an individual over a six to nine-month period. The type of treatment will be determined based on drug susceptibility, age, HIV status, and other criteria.[8] TBD treatment differs from the treatment of LTBI.

LTBI is the asymptomatic form of *M. tuberculosis* infection. A person can go an extended amount of time without knowing they are infected with *M. tuberculosis* because laboratory tests are required to determine if an individual is infected. These tests will determine if the body has a response to a TB antigen.[22] Like the diagnosis of TBD, LTBI is first identified by a TST or IGRA test. A positive TST or reactive IGRA test will show the infection of *Mycobacterium tuberculosis* in the body. Though, there is different criteria for what is considered a positive test depending on other risk factors that individual has (Table 1).[8,22]

Table 1. Tuberculin Skin Testing.[8]

Classification of the Tuberculin Skin Test Reaction		
*An induration of **5 or more** millimeters is considered positive in*	*An induration of **10 or more** millimeters is considered positive in*	*>An induration of **15 or more** millimeters is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.*
HIV-infected persons	Recent immigrants (< 5 years) from high-prevalence countries	
A recent contact of a person with TB disease	Injection drug users	
Persons with fibrotic changes on chest radiograph consistent with prior TB	Residents and employees of high-risk congregate settings	
Patients with organ transplants	Mycobacteriology laboratory personnel	
Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-a antagonists)	Persons with clinical conditions that place them at high risk	
	Children < 4 years of age	
	Infants, children, and adolescents exposed to adults in high-risk categories	

Tuberculosis (TB). Centers for Disease Control and Prevention Web site. https://www.cdc.gov/tb/default.htm Updated April 14, 2016. Accessed February 19, 2017.

Once determined that the patient has a positive test result and is diagnosed as LTBI, treatment options will be determined. LTBI treatment is designed to eliminate *M. tuberculosis* in the infected individual. Elimination of the bacterium will cure the disease

and the possibility of transmission and/or recurrence.[32] There are four main preventive regimens that are approved by the CDC for LTBI: 6-month INH, 9-month INH, Isoniazid with Rifapentine (3HP), and RIF (Table 2).[8] In the past, the favored treatment for LTBI was the INH for 9 months. However, comorbidities and health status take a role in choosing which type of preventive therapy is best suited for an individual (Table 2). The new preventive therapy regimen 3HP has become more popular within treatment options because it is shorter, easier to administer, and is less toxic to the liver than INH regimen.[33-35] There is no evidence, however, as to which treatment is more effective. Sterling, et al. studied the effects of 3HP compared to INH and found 3HP was as effective as INH for 9 months in the preventive treatment of LTBI.[36]

Table 2. Treatment Regimens for LTBI.[8]

Drug	Duration	Interval	Comments
Isoniazid (INH)	9 months	Daily	*Preferred treatment for:*
			Persons living with HIV, Children aged 2-11, Pregnant Women (with pyridoxine/vitamin B6 supplements)
		Twice weekly*	*Preferred treatment for:*
			Pregnant Women (with pyridoxine/vitamin B6 supplements)
Isoniazid (INH)	6 months	Daily	
		Twice weekly*	
Isoniazid with Rifapentine (3HP)	3 months	Once weekly*	*Treatment for:*
			Persons 12 years or older
			Not recommended for persons who are:
			Younger than 2 years old, Living with HIV/AIDS taking antiretroviral treatment, Presumed infected with INH or RIF-resistant *M. tuberculosis*, Women who are pregnant or expect to become pregnant within the 12-week regimen.
Rifampin (RIF)	4 months	Daily	
*Use Directly Observed Therapy (DOT)			

Tuberculosis (TB). Centers for Disease Control and Prevention Web site. https://www.cdc.gov/tb/default.htm Updated April 14, 2016. Accessed February 19, 2017.

Recently in late 2015, the treatment regimen 3HP was introduced in Shelby County, Tennessee as an alternative to 9-month INH because 3HP is a combination of INH and Rifapentine (RPT). The half-life of RPT is 5 times longer than RIF which enables the treatment 3HP to be administered once per month compared to the once daily

treatment of RIF.[35] Depending on how and when the medication will be administered will rely on which treatment is best suited for an individual.

When regimens are taking weekly, DOT can be used. This strategy was invented as an adherence to monitor the patient taking their medication.[37] DOT entails the individual being monitored while taking the medicine either in their home or at the clinic where they are being treated. This can be done by family members, public health professionals, or volunteers.[37] If an individual is not using DOT, then the medication will be self-administered. Self-administration may become a problem with individuals who skip or decide to stop taking their medications. During instances of stopping therapy early, now more than ever the problem of antibiotic-resistance has come into play.[8,22] Antibiotic-resistance occurs when the is ineffective against the bacteria. This can make it difficult to properly treat the patient. Not only does this issue cost more money, depending on the type of antibiotic-resistance is encountered will determine what procedures need to be done accordingly.[38]

At risk children, who are under the age of 5, may be put on what is called "Window Therapy" or "Window Prophylaxis." This treatment option will be offered to young children who are close contacts to an active TB case.[28] Even if the child does not test positive with a TST test, this preventive therapy may be utilized to prevent further spread of TBD. Once a child has been considered TB-free with a chest radiograph, they will go through window therapy until all three conditions are met for discontinuation: infant is 6 months or older, the second TST is negative, and the second TST has been performed at least 8 weeks of the child being exposed to the active TB case.[28]

Foreign Born

In the United States, two-thirds of the TB cases per year are individuals who are born in a country other than the United States; known as foreign-born. These individuals have a TB incidence that is around 13 times greater than the TB incidence among United States born (US-born) persons: 15.1 cases per 100,000 vs. 1.2 cases per 100,000, respectively.[24] Foreign-born individuals typically develop TBD years after they arrived in the United States, which indicates a progression of LTBI to TBD in most cases.[24] When LTBI goes untreated, it can progress to TBD. Reasons for this could be due to these individuals not being properly treated in their country of origin, which may also have high rates of TB transmission.

China, Vietnam, India, the Philippines, and Mexico are the top countries where foreign-born individuals in the United States originate. These five countries account for 45.2% of the population considered foreign-born in the United States. Similarly, these countries account for 56.6% of the TB cases in all foreign-born individuals throughout the world.[24]

Risk Factors Associated with Developing Tuberculosis

There are multiple risk factors involved with an individual becoming infected with *M. tuberculosis* whether latently or actively. Environmental factors can lead to an increase risk of infection. Crowding in places such as barracks, shelters, and prisons can leave people vulnerable for contracting TB.[39] In these tight quarters, it is easier for the bacteria to be spread through the air from person-to-person due to the proximity. Similarly, the duration of time spent with an active case of TB can increase the risk of

transmission to the contact. The severity of disease and cough frequency of the active TB case can contribute to risk of infection to a contact.[39]

Much of the LTBI individuals that progress to TBD do so within the first 2 years after infection. Though, the risk of infection becomes higher after the 5th year of having an exposure to an active case.[29] Additionally, HIV infection is identified as the highest effective biologic risk factor to develop TB. Individuals with HIV have an increased risk of TB reactivation.[22] About 40% of individuals with HIV will progress to TBD several months after the initially TB infection.[40]

CHAPTER 3

METHODOLOGY

Approval #4268 from the Institutional Review Board (IRB), at the University of Memphis, was obtained on June 15, 2016.

Study Area and Sampling Plan

The study was performed at the Office of Epidemiology and the TB Clinic of the Shelby County Health Department (SCHD) in Memphis, Tennessee between May 2016 to February 2017. Initial data was extracted from the National Electronic Disease Surveillance System (NEDSS) by the Office of Epidemiology to include TB cases from the years 2013, 2014, and 2015; including 149 cases total. These years were chosen due to the data being available compared to preceding years and they also have better contact investigation data included in each patient chart. Starting in 2013, documenting contact investigations became more advanced in Shelby County which allowed for improved data that are easily available. The 2013 to 2015 TB cases were matched to a dataset of over 943,000 test results to find the earliest TB test on record at the SCHD for each case. For each case, the duration between the date the case was counted as diseased minus the first recorded TB test was calculated. This duration was categorized into three intervals: >30 days, >60 days, and >90 days. The cases with >30 days were utilized to obtain their patient records in the TB Clinic. From the 149 TB cases of the years 2013 to 2015, 95 (64%) made up the >30 days group. The patient records on each of the 95 cases were used to extract contact investigation information that included self-identified contacts or possible contacts for each case. Once contacts were obtained for each specified case, existing TBD/LTBI datasets in Microsoft Excel created by the SCHD were used to match

with the list of contacts acquired from the case patient files. In the end, 1,327 contacts were gathered from the patient files and used for analysis.

Data Collection and Organization

Preliminary data for the 149 TB cases from the years 2013 to 2015 were stored into one dataset by the Office of Epidemiology at the SCHD and included 281 variables. This "Case" dataset was used to match with another database of over 943,000 TB, HIV, and sexually transmitted disease (STD) test results from the years 2001-2015 and the fraction of cases with evidence of a prior TB test was calculated. The first name, last name, social security number, date of birth, and sex were used to match cases to names from the "Test" dataset. In some instances, race, ethnicity, and zip code were also used in the matching process to guarantee the accuracy. There were four main objectives in this matching process. First, identify the earliest TB test date on record for each TB case. Second, determine if the case was tested prior to the year of diagnoses. Third, identify the type of test that is the first on record for each case. Lastly, find the difference in days from the first TB test date on record to the date counted as diseased for each TB case. TB tests included TST, IGRA, and chest radiography which were the main ones observed. Evidence of a prior positive TB test was pertinent to this investigation because it may have meant there was a former opportunity to intervene with that individual before they became a case. It also gave us insight to whether they were previously diagnosed with TBD, TB suspect, or LTBI.

In the original Case dataset that was extracted from the NEDSS, TB test dates were recorded. The TB test dates specified in the Case dataset were matched with the ones in the Test dataset. The reason for matching was to make sure the dates were the

same and to see if the case had been in the SCHD system previously for another type of test. Also, it was relevant to understand if the earliest test date for that individual was due to something other than TB: HIV or STD. After matching the individuals from the Case dataset to tests in the Test dataset, 144 of the 149 were found with a TB test. The 5 remaining TB case's name, date of birth, and social security numbers could not be matched in the Test dataset. However, these 5 had test dates specified in the Case dataset and those were used. TB tests including TST, IGRA, NAA, culture, smear, and chest radiography were specified in the case dataset.

After the two datasets were matched, a new Microsoft Excel spreadsheet was created using a copy of the original to include material from each dataset regarding TB cases from the years 2013-2015. The new dataset included variables that allowed examination if any case was tested before they were diagnosed with TB, diagnosis date, first test on record at SCHD, and first TB test date. The interval between the date the case was counted as diseased and the first recorded test date was calculated. In this research, date counted was used because that is the day the CDC and the SCHD reports yearly for TB cases and it is used as the diagnosed date.

The cases with the calculated intervals of >30 days were included in this study due to time constraints. The one-month gap between the two dates is noteworthy to consider the potential for opportunity to intervene. The individuals who had a difference between the count date and test date of greater than 30 days were included in the final analysis, which included around 64% of the 2013-2015 TB case list; 95 cases. Dates calculated ranged from -55 to 7,750 days. Negative numbers were not included with the variables because the presence of a negative variable meant that the case was counted as

diseased prior to the first test date on record at the SCHD. Twelve of the 54 cases (22%) not included in the study had a negative difference or no difference. Due to the study focusing on missed opportunities to prevent, these cases would not have given any indication towards the hypothesis because they did not have a preventive opportunity. The remaining 42 of the 54 cases not included in the study, had a difference of 1-30 days from the date of testing to the date of diagnosis and were not included due to time constraints.

Patient charts for the 95 TB cases that were included in the study were acquired through the TB Clinic at the SCHD. Using the case's state ID number, local patient ID number, first name, last name, date of birth, and genotype if given, members of the TB Clinic pulled charts to allow for data abstraction. Contacts in the patient charts were acquired using a chart abstraction tool that was developed for this study (Figure 4). The charts were reviewed to gather information on all contacts named through the contact investigation upon diagnosis of the case. Contacts in patient charts included the ones that were self-identified by the case and ones that were possible contacts named by the school, prison, shelter, or institution to which some patients belonged. For each contact, the following information was abstracted: first name, last name, demographics, date of birth, social security number, relation to case, address, phone number, date listed as contact, first exposure date, last exposure date, test type, test date, test result, evidence of prior positive, risk of transmission, diagnosis, diagnosis date, previous diagnosis date, whether LTBI treatment was offered, type of LTBI treatment, LTBI treatment initiation date, and LTBI treatment end date. If the contact was later diagnosed with TBD, additional information about type of TB treatment, TB type, TB treatment initiation date,

TB treatment end date, culture test result, smear test result, genotype, and whether the contact was fully evaluated was collected. Out of the 95 cases, 16 did not have contacts listed within their patient charts. Many of the 16 cases were diagnosed with extrapulmonary TB and therefore were not contagious and contact investigation was not needed. The information about the contacts was used to create a new "Contacts" dataset and included 1,325 contacts.

Next, the Contacts dataset was compared to a "LTBI" dataset from the TB Clinic in the SCHD made up of patients who come on Wednesdays to their clinic hours that are homeless or have been named as contacts in previous investigations. The Wednesday clinic hours were designated as a TB and HIV testing facility to the homeless population in Shelby County. These tests are free. Among the patients that came to Wednesday clinic, those who were diagnosed as LTBI were identified and matched with the TB case's state ID number and county ID number from the Contacts dataset. If state- or patient ID numbers matched between the two datasets, then the contacts listed in the Wednesday TB Clinic dataset were added to my Contact dataset. To prevent duplication, the first name, last name, demographics, social security number, address, and phone number of each contact were matched within the two datasets. Much of the contacts listed were already on the contacts dataset and were not needed to be added again. During the matching process, if updated information regarding tests or diagnosis of the contact were found, the Contact dataset was updated. This action ensured all recorded contacts of each case are identified, linked to that case, and included all information available about the contact for analysis.

Statistical Analysis

The 95 cases that were used in the study were compared to the total 149 cases in the original SCHD dataset to see if there were any differences in distribution of age group, sex, race, and ethnicity between the two groups. The contacts were also compared with their cases in terms of age, sex, race, and ethnicity. Frequencies were calculated using SAS (SAS Institute, Cary, NC) to determine the demographic makeup of the 2013-2015 TB cases and contacts.

Next, the number of contacts to each case, the number of cases linked to each contact, the number of cases who shared contacts, and the number of cases named as a contact to another case were calculated. The percent of contacts that newly developed or were previously diagnosed as TBD, TB Suspect, or LTBI were also determined. Of each of these three contact categories, the proportion offered preventive therapy and the proportion accepted the offer of preventive therapy were calculated. Of those who accepted the preventive therapy, the proportions who completed, did not complete, or stopped preventive therapy were determined. The number of contacts who had a previous positive TST or IGRA test prior to being named a contact was also identified.

The "relationship" variable, listed on the contact investigation sheets, showed the relationship between the case and their contact. Relationships were classified into 8 broad groups; casual, congregate setting, extended family, friend, healthcare setting, immediate family, other household contacts, and school/work setting. The "risk" variable specified the risk of transmission to the contact. The different risk categories, low, moderate, and high, were assessed in the relationship groups that had the highest frequency. In the risk variable, frequencies were assessed between the three categories. Logistic regression was

used to determine the association between risk and the diagnosis of TBD or TB Suspect. Logistic regression was used to examine the adjusted associations of age group, race, and sex with susceptibility to TB. Additionally, logistic regression was utilized to assess the relationship between prior positive TB test and the diagnosis of TBD or TB Suspect.

All statistical analyses were performed using SAS statistical software (SAS Institute, Cary, NC) and Epi Info. The significance level used was alpha of 0.05.

CHAPTER 4

RESULTS

The total number of TB cases in Shelby County, Tennessee between the years 2013 to 2015 was 149. Roughly 64% of the cases, 95, were utilized to gather contact information from their patient charts in the TB Clinic. Distributions of sex, age group, race, and ethnicity were compared between the two case cohorts (Table 3).

Table 3. Case Distribution Comparison. The overall cohort of 149 cases was compared to the study cohort of 95 cases to understand the distribution between four variables; sex, age group, race, and ethnicity.

	Overall Cohort (n=149)	**Study Cohort (n=95)**
Sex	**Frequency (Percent)**	
Male	96 (64%)	56 (59%)
Female	53 (36%)	39 (41%)
Age Group		
0-14	21 (14%)	19 (20%)
15-24	20 (13%)	11 (12%)
25-44	50 (34%)	28 (29%)
45-64	43 (29%)	27 (28%)
65+	15 (10%)	10 (11%)
Race		
Asian	10 (7%)	6 (6%)
Black or African American	107 (72%)	68 (72%)
White	32 (21%)	21 (22%)
Ethnicity		
Hispanic or Latino	23 (15%)	14 (15%)
Not Hispanic or Latino	126 (85%)	81 (85%)

The two cohorts had similar demographic characteristics. However, there were small variations in some categories. The majority were males in both cohorts compared (64% of the overall cohort and 59% of the study cohort). The median ages were 39 and 38 in the overall and the study cohorts, respectively. Racial distributions were similar

with the majority being Black or African American (72% in both cohorts). Lastly, ethnicity was similar with 85% of the cases not Hispanic or Latino.

Eleven percent of the 95 cases tested positive for HIV and 12% stated homelessness status within the year before being diagnosed. About 69 cases (73%) were born in the United States. The proportion of US-born TB cases in Shelby County is different from that in the whole United States. A majority of TB cases in the United States are foreign-born.

Around 48% of the individuals were diagnosed with pulmonary TB, while 35% were diagnosed with extra pulmonary TB and 17% diagnosed with both. The 48% diagnosed with pulmonary TB are those who are able to transmit the disease to others. Most cases were verified by clinical case definition (54%) or positive culture (38%). The other 8% were verified by a positive NAA or verified by a provider's diagnosis. The reasons for TB evaluation were TB symptoms (39%), abnormal chest radiograph (26%), case-contact investigations (20%), and incidental lab results (11%). The remaining 4% were diagnosed through employment or during an immigration medical exam.

Contact Cohort

After chart abstraction of the 95 TB cases and matching to the Wednesday TB Clinic dataset, there were a total of 1,327 contacts to be evaluated. Sixteen of the 95 cases did not have contact investigation charts in their files. This could be because the case was diagnosed with extrapulmonary TB, the case passed away prior to investigation, or the case did not have any contacts. To assess the similarities of the cases to their contacts, distributions of age, sex, race, and ethnicity were obtained and compared (Table 4).

However, not every contact gave their demographic information to the contact investigation (Table 4).

The number of contacts to each case, the number of cases linked to each contact, the number of cases who shared contacts, and the number of cases named as a contact to another case were identified. On average there were around 14 contacts to 1 of the 95 cases. Excluding the 16 cases without contacts, changed the average to 17 contacts per 1 of the 79 cases. There were 88 individuals who were named as a contact to multiple cases and 10 of the 88 (11%) were named in three or more contact investigations. Of the 79 cases, 19 had similar contacts between at least one of the other cases and 7 of the 19 (34%) cases shared contacts with at least two other cases. Lastly, 14 of the 95 cases were named as a contact within another case's contact investigation. In all 14 of the cases, there is no known prior offer of treatment before becoming a case.

Table 4. Study Cohort and Contact Cohort Comparison. The study cohort of 95 cases was compared to the contacts collected. The total contacts collected do not equal the amount of contacts (1,327) due to a number of individuals not specifying demographics during the contact investigation.

	Study Cohort (n=95)	**Contact Cohort (Collected)**
Sex	**Frequency (Percent)**	
Male	56 (59%)	508 (49%)
Female	39 (41%)	538 (51%)
Age Group		
0-14	19 (20%)	206 (19%)
15-24	11 (12%)	248 (23%)
25-44	28 (29%)	317 (29%)
45-64	27 (28%)	267 (24%)
65+	10 (11%)	53 (5%)
Race		
Asian	6 (6%)	34 (4%)
Black or African American	68 (72%)	722 (76%)
Race		
Native Hawaiian or Other Pacific Islander	.	7 (0.7%)
White	21 (22%)	186 (20%)
Ethnicity		
Hispanic or Latino	14 (15%)	135 (15%)
Not Hispanic or Latino	81 (85%)	788 (85%)

Three comparisons were made to better understand the differences between the cases and their contacts. Frequencies of sex, age group, race, and ethnicity were calculated. Comparisons were made in the study cohort to the contact cohort collected in the study. The distribution of sex was different (59% were male in case cohort vs. 49% were male in the case contacts collected). The age distribution differed slightly between the two cohorts. The median age in the contact cohort was 30. The majority in both cohorts were Black or African American at 76% vs. 72% in contacts and case cohorts.

Previous Positive and Risk of Transmission

Throughout the contact investigation sheets, an area was specified for comments by the provider, nurse, or investigator. Included within these comments were the reasons

why individuals did not get fully evaluated and if they have been tested positive for TB prior to the meeting. Sixty individuals, accounting for 5% of the contacts with the previous positive variable, stated they have tested positive for TB prior to the investigation. Out of the 60 individuals, 4 were diagnosed as TBD or TB suspect and 15 were diagnosed LTBI.

Another important variable is the risk of transmission specified on the contact investigation sheets as high, moderate, or low. A majority of the contacts were recorded either at a moderate or high risk of transmission from the active TB case; 531 (49%) and 473 (43%) contacts, respectively. Only 87 individuals were considered at low risk of transmission that accounted for 8% of the collected contacts.

Relationship of Contact to Case

The relationship of each contact to their associated case was specified in the contact investigation sheets and included for analysis (Figure 5). Establishing the relationship between cases and their contact will allow for understanding the mode of transmission within these individuals.

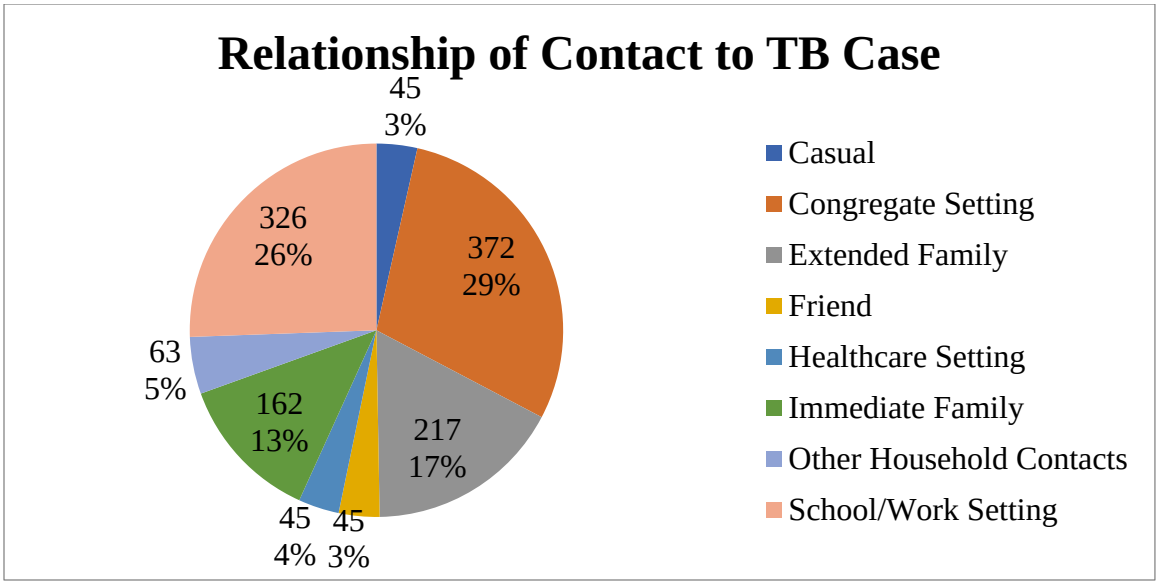


Figure 5. Relationship of Contact to TB Case. Relationships listed for individuals were put into 8 categories. Fifty-two contacts did not have specified relationships on their contact investigation sheet and therefore are missing from the percentages.

The largest group of contacts was in the "congregate setting" category (372, 29%). These individuals included people that the case came in contact with at a shelter or prison. Whether it was the case's arresting officer, dorm mate, staff at the prison/shelter, resident at the shelter, or inmate, these were all included within the congregate or large group setting category. The next largest group was the "school/work setting" (326, 26%). Owners, managers, supervisors, coworkers, bus drivers, classmates, teachers, and school employees were included in this category.

Family was classified into two categories; extended and immediate family. "Extended family" included aunts, uncles, cousins, in-laws, godparents, unspecified family members, grandparents, grandchildren, nephews, nieces, and stepparents. While the "immediate family" category included parents, siblings, and children. Extended family accounted for 17% of the contacts while immediate family accounted for 13%. Individuals who may be at the case's home for an extended period of time or visit on a

regular basis were included within the "other household contacts" group. These individuals were significant others, spouses, significant others to family members, caregivers, and roommates. Other household contacts accounted for 5% of the contacts. Close friends were put in their own category, because they may be seen in multiple setting throughout each case; school, work, home, etc. Individuals included in the "friend" category were only ones who were close to the actual case, and not friends of family members. This group accounted for another 3% of the contacts' relationships collected.

There were 45 individuals accounting for 3% of the contacts who were in the casual category. Lastly, the "health-care setting" was used as a category. These individuals included employees of the hospital/clinic, funeral home workers, doctors, specialists, and roommates while in the hospital. There were 45 health-care setting contacts (3%).

After establishing the relationships between the case and their contacts, risk of transmission was included within the investigation alongside the relationship variable. Since congregate setting (Figure 6) and school/work setting (Figure 7) were the largest categories for the relationships, analysis was performed to see the distribution of the risk variable within these two groups.

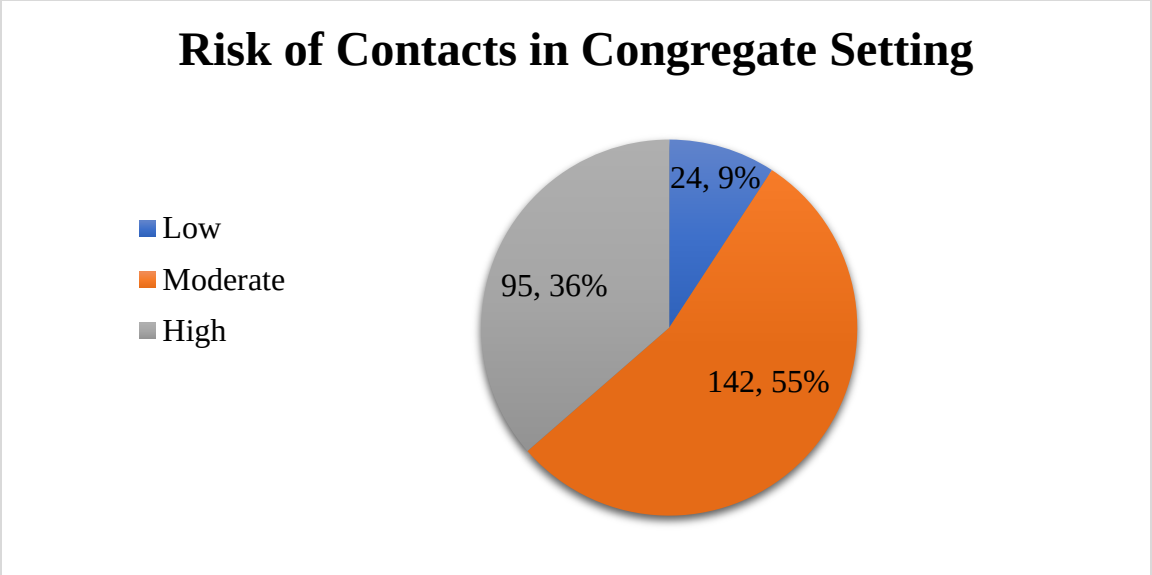


Figure 6. Risk of Contacts in Congregate Setting. Individuals listed as contacts within the shelter or prison setting and the distribution of transmission risk.

Within the congregate setting, a majority of individuals (91%) were considered moderate or high risk of TB transmission on their contact investigation sheet (Figure 6). This gave only 9% of individuals a low chance of transmission between the active case and the specified contact. After breaking up the moderate and high categories, moderate has a higher frequency at 54% than high (36%). However, individuals within the high or moderate category should be carefully evaluated to understand the transmission risk.

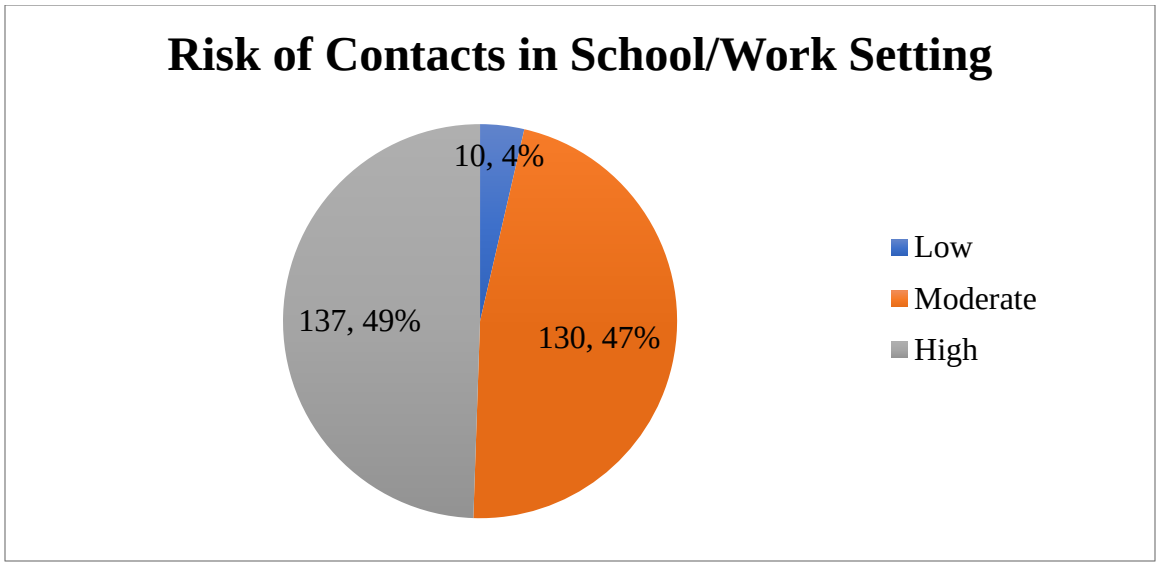


Figure 7. Risk of Contacts in School/Work Setting. Individuals listed as contacts within the school or work setting and the distribution of transmission risk.

Individuals in the school/work setting had different risk of transmission distribution than that of the congregate setting (Figure 7). Only 4% had a low risk of transmission, while 96% had a moderate or high risk of transmission. Unlike the congregate setting, the moderate and high risk had a closer to even distribution, but the high risk category was more (49%). The moderate risk accounted for 47% of the moderate and high risk.

Diagnosis of Contacts

Once the risk of transmission was understood, it was pertinent to find individuals who developed TBD, LTBI, or became a TB Suspect. Diagnosis was put into four categories, TBD or TB suspect, LTBI, previous diagnosis, and no diagnosis (Figure 8).

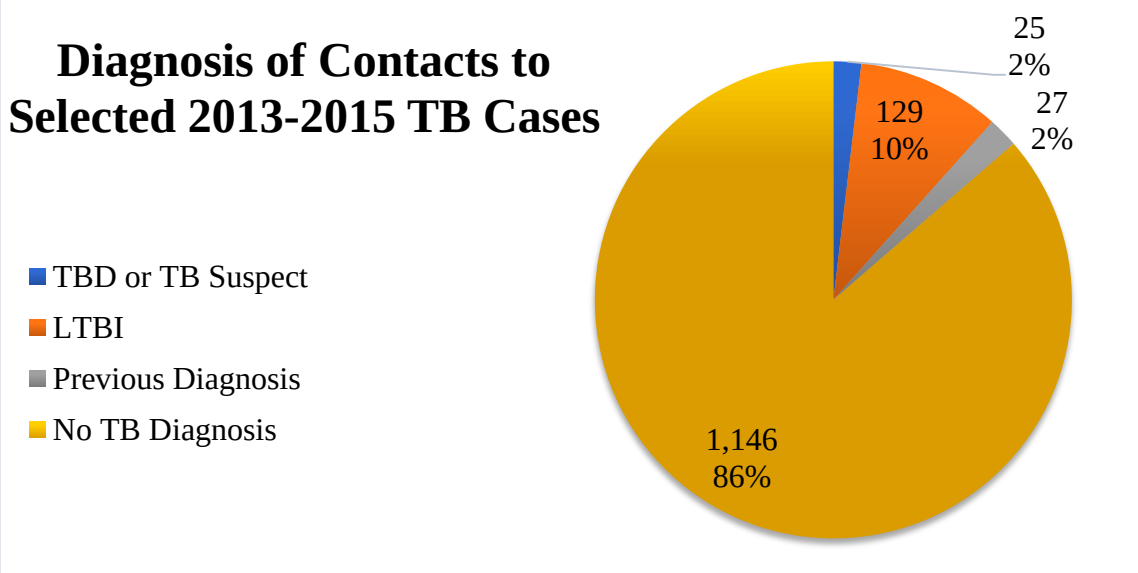


Figure 8. Diagnosis of Contacts to Selected 2013-2015 TB Cases. Diagnosis of the 1,327 contacts after the contact investigation. Four categories of diagnosis were discovered; TBD or TB Suspect, LTBI, Previous Diagnosis, and No TB Diagnosis.

Individuals with previous diagnosis (2%) included previous TBD, previous TB suspect, and previous LTBI. Individuals with no TB diagnosis accounted for 86% of the contacts. Individuals who had a missing diagnosis variable on their contact sheet were considered "not specified" and accounted for 37% of the ones considered "no TB diagnosis." Among all 1,327 contacts assessed during this study, 21 were diagnosed with TBD and another 4 diagnosed as TB Suspect; accounting for 2% of the contacts. Sixteen of the 25 (64%) TBD or TB Suspect diagnosed individuals were at high risk of transmission, 5 of the 25 (20%) were at moderate risk of transmission, 1 of the 25 (4%) was at low risk of transmission, and 3 of the 25 (12%) did not have the risk of transmission specified. Of the 25 diagnosed with TBD or TB suspect, 13 had their type of TB ascertained during their contact investigation. Sixty-two percent were diagnosed as pulmonary TB from the individuals with the type of TB specified in the contact investigation; leaving the remaining 38% diagnosed with extra pulmonary or both types

of TB in their body. Age of 0-14 years, male sex, and black or African American race were risk factors for TBD in the contacts.

There were 129 contacts diagnosed as LTBI during the study. Within the 1,327 contacts, 39 individuals have been previously treated for LTBI prior to the contact investigation. Excluding the individuals who have previously been treated, there were 180 offered LTBI preventive therapy treatment (Figure 9). The 10% of the contacts diagnosed as LTBI, as well as other contacts at risk (young children, immigrants, ones with medical conditions associated with weakening the immune system, individuals recently infected with TB, etc.), were offered LTBI treatment.[8] Of the 180 individuals offered therapy, 63% completed it. Even though this number is over half, it needs to be higher. Individuals who did not complete their treatment or refused to receive treatment constituted 21% and 6%, respectively, of the 180 who were offered preventive therapy. Ten percent of the individuals had missing data on completion of preventive therapy.

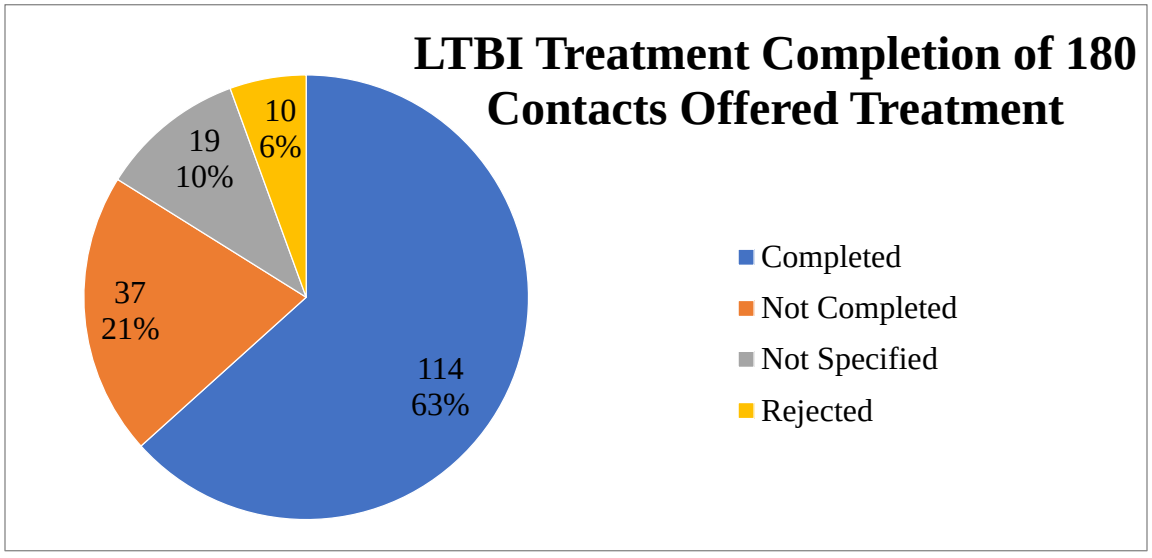


Figure 9. LTBI Treatment Completion of 180 Contacts Offered Treatment. Individuals were assessed as Completed, Not Completed, Not Specified, or Rejected LTBI therapy.

The next step to understand treatment delivery was to determine which group was more likely to be offered treatment. As one might expect, those with high or moderate risk were offered LTBI treatment more often. Eighty-one of the 473 individuals with a high risk of transmission (17%), 69 of the 531 individuals with moderate risk of transmission (13%), and 11 of the 87 individuals with low risk of transmission (13%) were offered preventive therapy. There were 19 of the 180 individuals who were offered treatment that did not have a risk of transmission stated in their contact investigation sheet.

Only 103 (57%) of the 180 contacts offered preventive therapy had the type of LTBI treatment identified on their contact sheet. Among the ones identified, 58% went through INH, 37% went through window therapy, 3% was given 3HP, and the remaining 2% either took RIF or switched from INH to RIF. An analysis of interest was looking into each treatment regimen and seeing which one had the highest completion rate (Table 5).

Table 5. LTBI Treatment Regimen and Treatment Completion Status. 3HP, INH, RIF or INH/RIF, and Window Therapy were the four types of treatment that were specified during the contact investigation. No individuals that rejected treatment had the type of LTBI treatment specified and were not included within the table.

LTBI Treatment Regimen and Treatment Completion Status					
Completion Status	**LTBI Treatment Regimen**				
	3HP	INH	RIF or INH/RIF	Window Therapy	Total
Completed	2	28	0	35	65
Not Completed	0	20	1	1	22
Not Specified	1	12	1	2	16
Total	3 (3%)	60 (58%)	2 (2%)	38 (37%)	103

3HP had a completion of 67%, INH had a completion of 47%, RIF or INH/RIF had a completion rate of 0%, and window therapy had a completion of 92%. The window therapy category included INH, window therapy and other window therapy that did not have a specified regimen; however, it was most likely INH due to the recommended treatment regimens specified by the CDC.[8] This category was separated to show individuals that may have not been diagnosed LTBI, but went through therapy due to their age or other risk factors.

Bivariate and Multivariable Analyses

A crude analysis of risk variable and diagnosis was evaluated using logistic regression. Risk was considered the explanatory variable while diagnosis as the outcome. The outcome variable was the log odds of an individual being diagnosed with TBD or TB Suspect. Moderate was used as the reference level because it was the most commonly reported risk category.[41] Moreover, comparison between the moderate risk factors and high risk factors was desired because these are the individuals who may have comorbidities. Individuals with high risk have factors that are significant to transmission; contact with TB infected individual, elder population, HIV, or transmission through an institute. Ones considered at a moderate risk of transmission were malnourished individuals, smokers, diabetics, and the poor.[42] The test found a significant association with high risk developing TBD or TB Suspect. The odds of developing TBD or being a TB Suspect and being at high risk was 3.7 (95% CI: 1.3, 10.1) times the odds of an individual at a moderate risk (Table 6).

An adjusted analysis was performed with the outcome of TBD or TB Suspect diagnosis and race, age group, and sex as explanatory variables. During the procedure,

possible quasi-complete separation was noted in the log showing that some variables did not converge. Multiple attempts were made to fix this separation by changing the iterations; however, the estimates did not converge. Reference levels were specified in the categories of each variable that had the greatest frequency.[41] Additionally, the age group of 25-44 was used as the reference level because this group has shown an increase in TB compared to other groups. The higher TB prevalence may be due to being the primary group affected by HIV/AIDS.[7,28,43] The 25-44 age group, Black or African American, and Female were the reference in each variable. The model found, individuals 0-14 years of age have an 8.2 times the odds of developing TBD or being a TB Suspect (95% CI: 1.8, 37.5) compared to those 25-44 years old, after holding all other variables constant (Table 6).

The final logistic model tested whether prior TB test status was associated with the diagnosis of TBD and TB Suspect. No presence of prior positive TB test was used as the reference.[41] Those with a positive prior TB test have 3.8 (95% CI: 1.271, 11.622) times the odds of developing TBD or being TB Suspect compared to an individual who does not have a prior positive TB test (Table 6).

Table 6. Significant Findings through Bivariate and Multivariable Analyses. Through analysis, odds ratio (OR), confidence interval (CI), and the p-value were obtained within each regression.

Significant Findings through Bivariate and Multivariable Analyses			
	OR	**95% CI**	**P-value**
Risk			
High vs. Moderate	3.682	(1.339, 10.129)	0.0116
Age Group			
0-14 vs. 25-44	8.248	(1.812, 37.535)	0.0063
Prior Positive and Diagnosis			
Prior Positive vs. TB Diagnosis	3.843	(1.271, 11.622)	0.0171

Stratified Analysis of Tuberculosis Diagnosis

According to the study, 2% of individuals were diagnosed as TBD or TB suspect; with 48% of them being diagnosed as pulmonary TBD. Some of these individuals were named as contacts within multiple investigations. Due to this, the TBD and TB suspect diagnosed individuals were de-duplicated to answer the research question in this study. The de-duplication left 20 of the 25 individuals; accounting for 1.5% of the contact cohort. This suggests that for every 100 people who go through preventive therapy, 1.5 individuals may be prevented from developing TB. Likewise, for every 1,000 people who go through LTBI preventive therapy, 15 cases of TB may be prevented.

Stratified sampling was done for the individuals diagnosed as TBD or TB suspect to see what the preventive opportunity is based on the groups with the highest odds ratio in logistic regression. Three different strata were considered for individuals diagnosed TBD or TB suspect; adult versus child, foreign versus US-born, and low versus high risk of transmission. Pediatric cases are considered 14 years of age and below while adults are 15 years of age and higher. Forty-five percent of the de-duplicated TB cases were pediatric, 45% were adults, and 10% did not specify age. The stratified preventive opportunity for age did not differ between the two groups (0.68 per 100 people or 6.8 per 1,000 people). With risk, 5% of the de-duplicated TB cases were at low risk, 20% were at moderate risk, 60% were at high risk, and 15% did not have risk of transmission defined. The preventive opportunity for individuals at a low risk of transmission is 0.08 per 100 people (0.8 per 1,000 people) who go through preventive therapy, while individuals at a high risk of transmission are 0.9 per 100 people (9 per 1,000 people) who go through preventive therapy. Lastly, there are a higher percentage of US-born individuals with TB

in Shelby County, Tennessee compared to the United States. Of the de-duplicated TB cases, 70% were US-born, 5% were foreign-born, and 25% did not have country of birth specified in their contact investigation sheet. The preventive opportunity for US-born is 1.1 per 100 persons, or 11 per 1,000 people, who go through preventive therapy. Individuals who are foreign-born in Shelby County have a 0.08 per 100 people (0.8 per 1,000 people) preventive opportunity of not developing TB if treated properly. The two countries of origin figures may not be generalized to the United States population due to a majority of TB cases in the nation being foreign-born.

CHAPTER 5

DISCUSSION

This study focuses on the importance of infectious disease surveillance and control in regards to TB. This potentially deadly, airborne disease is endemic to a multitude of countries and is also found within the United States.[8] With rates that are slowly declining, TB may be a candidate for eradication in the future.[22] In Shelby County, Tennessee between 2010 and 2015 the incidence of TB has been at a plateau with little variance from year to year.[11-21]

Individuals who had evidence of a prior positive TB test had an approximately four-fold chance of developing TBD or becoming a TB suspect compared to the individuals who did not have a prior positive TB test. These individuals needed to be analyzed to understand why the diagnosis was missed that they developed TBD after the positive test. These individuals could be amongst the 5% to 10% that will develop TBD from LTBI at some point in life.[30] However, they may have been unaware that they were infected with TB in the first place.[22] Missed diagnosis of LTBI or TBD can be detrimental to not only that individual, but to ones they come in contact with on a regular basis.

Individuals within the relationship groups of congregate setting and school/work setting had the highest proportion. Individuals that the active case came in contact with would be anyone at prison, shelter, school, or work. Another 32% of the individuals in the study cohort were between 0-24 years of age. Indicating, a good portion of these individuals may be in some type of schooling system, which may expose students to TB,

especially given that the young age group was shown to be at a much increased risk of the disease middle-aged groups.

Not only is it important for surveillance to be a part of elimination of TB, control methods are needed to sustain past endeavors. TB control efforts include vaccination and treatment options. In countries where TB is at high prevalence, the Bacillus Calmette–Guérin (BCG) vaccination has been used to control the spread of TB.[22] In these same countries, or ones that do not use the BCG vaccine (United States), preventive therapy is offered to individuals who may have a higher risk of transmission.[8] An important factor is making sure the patient is truly taking their medication and not stopping it too early.[37] If the treatment is completely finished then prevention of TB should occur.

Limitations

Time constraints were a major limitation to this study. We were able to abstract data of only 64% of TB cases from 2013 to 2015 to find their contacts, which may have introduced selection bias to the study. The second limitation is the small size of cases. This can be avoided in the future by collecting data from more years.

The third limitation to this study is extracting data from multiple sources to form one contact dataset from the 2013 to 2015 TB cases. If matched properly, this restraint should not be an issue. However, errors from multiple merging and matching different datasets can occur and affect the data quality.

Recommendations

In future research, these limitations should be addressed. By accounting for the limitations, additional cases can be used to acquire contacts for the analysis and a superior method of data collection from one source can be utilized. Having an increased

number of contacts will increase the accuracy that the data is representing the whole TB community of Shelby County, Tennessee.

Surveillance and data collection procedures need to be improved as well in order to decrease TB and understand the distribution of cases in Shelby County. Increasing surveillance efforts will enhance the ability to find active TB cases. Performing contact investigations for each contact within each case of reported TB will allow locating individuals who may soon develop TBD from LTBI. Contact investigations also assist with diagnosis of LTBI since it is asymptomatic and an individual could go years without knowing they are infected. Data collection from these contact investigations need to be thorough. In-depth investigations may decrease the amount of missing variables and ultimately help in analysis.

The major recommendation from this study is to increase the amount of individuals who go through preventive therapy. It is recommended that more individuals be offered preventive therapy to decrease the incidence of LTBI that may eventually advance to TBD. It is suggested that every 100 people put through preventive therapy for LTBI may prevent up to 1.5 cases of TB. If the proposed finding is addressed and more individuals go through preventive therapy, TB numbers will be down in Shelby County. Ultimately, it will be decreasing the mode of transmission between active cases to contacts. It would also benefit public health programs by treating individuals who are specified as high risk of transmission.

Additionally, increasing the amount of DOT may assist with individuals completing therapy. When a patient is being observed, they are more likely to complete

the therapy out of courtesy. If allowed to take the medication on their own, there's potential for missed administration or skipping the treatment entirely.

CHAPTER 6

CONCLUSION

Understanding what makes Shelby County, different than the rest of the United States is important. A majority of the TB population of Shelby County is US-born, which naturally is not the case throughout the nation that shows a vast number of foreign-born diagnosed individuals.[22] This may lead to the necessity of improvement of contact investigations and standardizing TB surveillance data collection.

One way to address this public health issue and improve TB prevention and treatment in Shelby County is to identify contacts of new confirmed cases and provide timely preventive treatment to prevent them from contracting the disease. Through contact investigations, missed opportunities for prevention can be found leading to the result of a multitude of cases. Additionally, preventive therapy is needed to be offered to more people in order to prevent persons with LTBI developing to TBD cases. The recommendations found from this study should be taken to make administration of preventive therapy regimens easier, more precise, and ultimately effective. Constant surveillance and control efforts need to be sustained to decrease the incidence or eradicate TB in the future.

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APPENDIX

Chart Abstraction Tool

CASE

First Name _____ Last Name _____

State Number _____ County Case Number _____ DOB _____

Age ____ Sex _____ Race _____ Ethnicity _____ Genotype _____TB Type _____ Culture ____

Smear ____ Infection Period _____ Date Counted _____ Zip _____

CONTACT

First Name _____ Sex _____ Race _____ Ethnicity _____ DOB _____ Age ____

Last Name _____ Phone Number_____ SSN_____

Address _____

Date Listed as Contact _____First-Last Exposure Date _____

Relationship to Case _____ Risk Level _____ Prior positive? ☐ Yes ☐ No Date_____

Test Date 1) 2) 3)

Test Type 1) ☐ CXR ☐ TST/PPD ☐ IGRA 2) ☐ CXR ☐ TST/PPD ☐ IGRA 3) ☐ CXR ☐ TST/PPD ☐ IGRA

Test Result 1) ☐ + ☐ - ☐ Indeterminate 2) ☐ + ☐ - ☐ Indeterminate 3) ☐ + ☐ - ☐ Indeterminate

Diagnosis? ☐ TBD ☐ LTBI ☐ Previous ☐ No ☐ Not Specified

Date Diagnosed _____ Previously Diagnosed Date _____

Type of TBD ☐ Pulmonary ☐ Extrapulmonary ☐ Both

Culture _____ Smear _____ Genotype _____

Offered treatment? ☐ Yes ☐ No ☐ TBD ☐ LTBI ☐ Accepted ☐ Rejected ☐ Not offered ☐ Previously Treated

Initiation Date _____ Treatment Regimen _____

☐ Completed ☐ Not completed ☐ Lost ☐ Provider's Decision to Stop ☐ Other

Completion Date _____ Stop date_____

Fully Evaluated? ☐ Yes ☐ No If not, why _____

Figure 4. Chart Abstraction Tool. This tool was created in particular for this study through Microsoft Word. Each sheet allowed for 1 case and 4 contacts to be extracted. This tool was essential in data abstraction and cut down on time from acquring data in the patient files of the TB Clinic.

IRB Approval

Hello,

The University of Memphis Institutional Review Board, FWA00006815, has reviewed and approved your submission in accordance with all applicable statuses and regulations as well as ethical principles.

PI NAME: Leah Reish
CO-PI:
PROJECT TITLE: Prevention of Tuberculosis Disease in Previously Infected Individuals of Shelby County, Tennessee
FACULTY ADVISOR NAME (if applicable): Fawaz Mzayek
IRB ID: #4268
APPROVAL DATE: 6/15/2016
EXPIRATION DATE:
LEVEL OF REVIEW: Exempt

Please Note: Modifications do not extend the expiration of the original approval

Approval of this project is given with the following obligations:

1. If this IRB approval has an expiration date, an approved renewal must be in effect to continue the project prior to that date. If approval is not obtained, the human consent form(s) and recruiting material(s) are no longer valid and any research activities involving human subjects must stop.

2. When the project is finished or terminated, a completion form must be completed and sent to the board.

3. No change may be made in the approved protocol without prior board approval, whether the approved protocol was reviewed at the Exempt, Exedited or Full Board level.

4. Exempt approval are considered to have no expiration date and no further review is necessary unless the protocol needs modification.

Note: Review outcomes will be communicated to the email address on file. This email should be considered an official communication from the UM IRB.