ASSOCIATIONS BETWEEN EVER-SMOKING AND TUBERCULOSIS
AMONG HISPANICS RESIDING IN THE UNITED STATES

A Thesis
Presented to the
Faculty of
San Diego State University

In Partial Fulfillment
of the Requirements for the Degrees
Master of Arts in Latin American Studies and Master of Public Health
with a Concentration in
Epidemiology

by
Erik Michael Hendrickson
Spring 2014
SAN DIEGO STATE UNIVERSITY

The Undersigned Faculty Committee Approves the

Thesis of Erik Michael Hendrickson:

Associations Between Ever-Smoking and Tuberculosis Among Hispanics

Residing in the United States

Thomas Novotny, Chair
Graduate School of Public Health

Ramona Pérez
Center for Latin American Studies

Suzanne Lindsay
Graduate School of Public Health

11/25/13
Approval Date
Copyright © 2014
by
Erik Michael Hendrickson
All Rights Reserved
ABSTRACT OF THE THESIS

Associations Between Ever-Smoking and Tuberculosis Among Hispanics Residing in the United States
by
Erik Michael Hendrickson
Master of Arts in Latin American Studies and Master of Public Health with a Concentration in Epidemiology
San Diego State University, 2014

Nearly one-third (2.3 billion cases) of the world is infected with latent tuberculosis infection (LTBI), making the prevention and control of this disease one of the top public health priorities. Smoking tobacco is a major risk factor for tuberculosis morbidity and mortality and is a critical point to intervene. The act of smoking creates a local inflammatory response in the lungs, while the nicotine in tobacco suppresses the immune response to that inflammation. Tuberculosis is unequally distributed according to demographic and geographic factors and has been found to be more prevalent among ethnic-minorities that are foreign-born. In the United States, Hispanics are the largest foreign-born populations originating from countries that have higher endemic incidence rate of tuberculosis. However, there is little known about the relationship between ever-smoking and tuberculosis among Hispanics and specifically when differentiating between multiple types of Hispanics. This study investigates the association between ever-smoking and tuberculosis among Hispanic subgroups residing in the United States and surveyed using data from the Hispanic Health and Nutrition Examination Survey (HHANES) conducted by the National Institutes of Health (NIH). This study has a main dependent and outcome variable of whether a participant had ever been told by a doctor that they had tuberculosis. The main independent variable was ever-smoking at least 100 cigarettes in their life while testing other variables, diabetes, per capita income, age, gender, foreign birth, and educational level, for confounding relationships. Wald Chi-Square and logistic regression were used to analyze the data. After adjusting for all other variables, Mexican Americans with a history of smoking were 1.21 (95% CI 0.98-1.48) times more likely to have been diagnosed with TB by their doctor than those without a history of smoking. Cuban Americans with a history of smoking were 1.06 (95% CI 0.20-5.51) times more likely to have been diagnosed with TB by their doctor than those without a history of smoking. Puerto Ricans with a history of smoking were 1.18 (95% CI 0.51-2.78) times more likely to have been diagnosed with TB by their doctor compared to those without a history of smoking. Although results did not reach statistical significance, smoking cessation may be an effective measure to both prevent and control tuberculosis.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>SECTION</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vii</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>viii</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>ix</td>
</tr>
<tr>
<td>CHAPTER</td>
<td></td>
</tr>
<tr>
<td>1 INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>Statement of the Problem</td>
<td>2</td>
</tr>
<tr>
<td>Hypotheses</td>
<td>3</td>
</tr>
<tr>
<td>Basic Assumptions</td>
<td>3</td>
</tr>
<tr>
<td>2 LITERATURE REVIEW</td>
<td>4</td>
</tr>
<tr>
<td>Overview of Tuberculosis</td>
<td>4</td>
</tr>
<tr>
<td>Microbiology and Pathology of Tuberculosis</td>
<td>5</td>
</tr>
<tr>
<td>Global Burden of Tuberculosis</td>
<td>6</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td>9</td>
</tr>
<tr>
<td>Sex, Gender, and Age Groups</td>
<td>9</td>
</tr>
<tr>
<td>HIV</td>
<td>10</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>10</td>
</tr>
<tr>
<td>Tobacco Smoking</td>
<td>12</td>
</tr>
<tr>
<td>3 METHODS</td>
<td>14</td>
</tr>
<tr>
<td>Study Design</td>
<td>14</td>
</tr>
<tr>
<td>Data Collection</td>
<td>15</td>
</tr>
<tr>
<td>Variables</td>
<td>15</td>
</tr>
<tr>
<td>Confounding Variables</td>
<td>17</td>
</tr>
<tr>
<td>Statistical Analysis</td>
<td>18</td>
</tr>
<tr>
<td>4 RESULTS</td>
<td>20</td>
</tr>
<tr>
<td>Descriptive Statistics</td>
<td>20</td>
</tr>
<tr>
<td>Bivariate Analysis</td>
<td>22</td>
</tr>
<tr>
<td>Table</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>1</td>
<td>Descriptive Data of Risk Factors for Reported Tuberculosis Among Hispanic Respondents to HHANES, United States 1982-1984, Stratified by Ethnic Subgroup</td>
</tr>
<tr>
<td>2</td>
<td>Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Mexican American Respondents to HHANES, United States 1982-1984</td>
</tr>
<tr>
<td>3</td>
<td>Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Cuban American Respondents to HHANES, United States 1982-1984</td>
</tr>
<tr>
<td>4</td>
<td>Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Puerto Rican Respondents to HHANES, United States 1982-1984</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

Figure 1. Ethnic stratification of hispanic persons residing in the United States and were interviewed with the adolescent and adult questionnaire: Ages 12-74 years of the HHANES during 1982-1984.................................................................16
I would like to acknowledge those who were integral in the preparation and process of this project, both the thesis and myself. Specifically I would like to note all the love and support that my parents and family have provided, I would be lost without their continual efforts to ground orient me. Valerie for her compassion, sacrifices, and perpetual company, in both the light and dark times. My friends and colleagues from SDSU for the constant debates, critical insights, and general camaraderie, that is the true meaning of graduate school. Dra. Ramona L. Pérez for her empathy, encouragement, and investments, I am a better and more mature person because them. Dr. Thomas Novotny for his guidance into a new way of being and his support in my success, they are priceless. Dr. Suzanne Lindsay for her inspirational vision for public health practice, that break the clichés of old, and work to effectively serve communities.
Cigarette smoking is a major risk factor for tuberculosis (TB) morbidity and mortality, and thus smoking cessation may be a critical intervention for TB prevention and control (Ariyothai et al., 2004; Bates et al., 2007; Lin, Ezzati, Chang, & Murray, 2009; Schneider & Novotny, 2007; Shulte, Valway, McCray, & Onorato, 2001). In 2011, there were 8.7 million new TB infections globally, 1.4 million deaths from TB (World Health Organization [WHO], 2012a), and of the total global TB cases, 20% were attributed to cigarette smoking (WHO, 2013). Most research has found that those who smoke are 2 to 4 times more likely to acquire TB infection than those who do not smoke (Davies et al., 2006; WHO, 2009). This is biologically plausible because cigarette smoking produces a local inflammatory response in the lungs, and the nicotine found in cigarette smoke suppresses the specific immune response to that inflammation (Bothamley, 2005; Kirkham, Spooner, Ffoulkes-Jones, & Calvez, 2003; Nouri-Shirazi & Guinet, 2003; Sköld, Lundahl, Hallden, Hallgren, & Eklund, 1996). The inflammation and suppression of the immune system, exacerbates the transmission of TB particulates from exposed persons to non-exposed persons (Center for Disease Control and Prevention [CDC], 2011b).

In the United States, the majority of TB cases are among foreign-born populations and ethnic minorities (CDC, 2011a). While Hispanics were second to Asians in the incidence rate and the total number of cases of TB in 2011 (Asians: n=3,148, Hispanics n=3,008), this is a relatively recent phenomenon (CDC, 2013). Prior to 2011, and particularly so during the resurgence of TB in the 1980’s when the Hispanic Health and Nutrition Examination Survey (HHANES) was conducted, Hispanics had an overall incidence rate of 23.2 cases per 100,000, compared to the national average of 12 cases per 100,000 persons (CDC, 1982). Current estimated rates among foreign-born persons with TB indicate Mexico as the largest single country of origin, accounting for 23% of all foreign born cases reported in 2009 (CDC, 2011c). As one of the largest ethnic/racial populations with the highest incidence and prevalence of TB residing in the United States, Hispanics could benefit greatly from a
focused cigarette smoking prevention and cessation intervention coupled with TB treatment and prevention programs.

**STATEMENT OF THE PROBLEM**

There is little research exploring the relationship between cigarette smoking and TB among Hispanic populations residing in the United States. Without a deeper understanding of this specific relationship, there is limited capacity to develop health policies and intervention programs targeting Hispanic populations with the highest need. The purpose of this study is to provide further insight into the relationship between cigarette smoking and TB among Hispanic subgroups residing in the United States. The secondary purpose of this study is to explore other predictive risk factors for TB among the Hispanic subgroups. To achieve these purposes, a secondary analysis of the Hispanic Health and Nutrition Examination Survey (HHANES) was conducted.

The HHANES is a large health survey of a national representative sample of Mexican-American, Cuban-Americans, and Puerto Ricans residing in the United States, collected during 1982-1984. While the HHANES collected a comprehensive set of socio-demographic, health behavioral, and health status data, for the purposes of this study only the interview data from the Adolescent and Adult History Questionnaire for respondents aged 12-74 years was used. Furthermore, HHANES variables found to be significantly associated with TB were included in the analyses (ever-smoked, age, sex, per capita income, foreign-birth, diabetes).

The relationship between ever-smoking cigarettes and other risk factors and history of TB infection will be reported. All data and analyses were stratified by Hispanic subgroups in accordance with the original intent in the sampling design and the recommendations for analysis by the National Center for Health Statistics (NCHS). Results from this study will contribute to the growing literature concerning cigarette smoking prevention and cessation as a critical intervention to prevent and control for TB. Results may also provide insight as to how TB prevention and control efforts can be focused towards Hispanic populations in the United States that are at highest risk for TB.
HYPOTHESES

- H0: There is no association between TB and ever smoked cigarettes among respondents aged 12-74 years to the HHANES, Adolescent and Adult History Questionnaire, 1982-1984.
- H1: There is an association between TB and ever smoked cigarettes among respondents aged 12-74 years to the HHANES, Adolescent and Adult History Questionnaire, 1982-1984.

BASIC ASSUMPTIONS

1. The study population sampled in the HHANES allows analysis with external validity and results may be generalized to the Mexican-American, Cuban-American, or Puerto Rican populations residing in the United States.
2. The HHANES Adolescent and Adult History Questionnaire has adequate internal validity, supported by sufficient construct validity, content validity, and limited selection or response biases.
CHAPTER 2

LITERATURE REVIEW

OVERVIEW OF TUBERCULOSIS

TB is a disease with a long history and substantial impact among human populations. Theoretically, TB and *homo sapiens* have evolved side-by-side for nearly 40,000 years, both originating from the Horn of Africa (Blouin et al., 2012; Wirth et al., 2008) and known to exist together during Neolithic Times, more than 9,000 years ago (Hershkovitz et al., 2008; Wirth et al., 2008). In antiquity, philosopher-physicians such as Hippocrates, Aristotle, and Galen identified an illness they called *phthisis* that is very similar to the disease we currently know as TB. TB affected a large proportion of the ancient population, especially persons in their working years, and was characterized by cough, fever, and subsequent ‘consumption’ of the body. However, it wasn’t until the 18th and 19th centuries that TB gained the attention of medical and public health scientists. In response to a dramatic increase of annual mortality rates of TB in major cities of Western Europe reaching 800-1000 per 100,000 persons (Daniel, 2006), medical and public health scientists such as René-Théophile Laennec, Jean-Antonette Villemin, and Robert Koch identified the pathogenesis, transmission modality, and etiologic agent, responsible for the TB infection and disease (Daniel, 2006). These fundamental discoveries created the foundation for further innovations such as the tuberculin skin test (TST) by Clemens von Pirquet and Charles Mantoux in 1907 (Daniel, 2006), the *Bacille Calmette-Guérin* (BCG) vaccine by Albert Calmette and Camile Guérin in 1921, as well as a series of antibiotic treatments developed in the 1940’s and 1950’s such as Streptomycin, Isoniazid and Rifampin (Barnes, 2000; Daniel, 2006; McCarthy, 2001).

Recently, TB mortality and morbidity has increased due to multiple drug resistant varieties, bringing global public health agencies such as the World Health Organization’s (WHO) to declare in 1993 that TB is a public health emergency of global proportion (“WHO calls tuberculosis a global emergency”, 1993). While attention and efforts to prevent and control TB have increased since the WHO declaration, TB’s burden of disease is still a great concern.
to the global public health community with 1.2 million global deaths and 49,000 DALY’s in 2010 (Institute for Health Metrics and Evaluation [IHME], 2010).

**Microbiology and Pathology of Tuberculosis**

*Mycobacterium tuberculosis* is the etiologic agent that causes TB infection and disease in human populations. It is a non-motile, non-sporulating, weakly gram-positive, acid-fast bacillus with extremely thick waxy hydrophobic cell walls which lend to its ability to resist drying, acidity/alkalinity, and multiple types of antibiotics, and to its ability to stay dormant for long periods of time (Lawn & Zumla, 2011; Sakamoto, 2012). *M. tuberculosis* ranges in size from 1-4 μm in length and 0.3 to 0.6 μm in width and divides at a very slow rate of 15-20 hours. It favors large amounts of oxygen and as a result finds the human respiratory system an ideal host environment (WHO, 2012a). However, once *M. tuberculosis* is expelled from the respiratory system via a cough or sneeze, it is able to survive in the air for several hours depending on certain environmental factors such as temperature and humidity (CDC, 2011b; Rieder, 1999). An infectious dose of *M. tuberculosis* ranges from 1 to 200 bacilli per person, and a single aerosol droplet can contain anywhere from 1 to 400 bacilli (Sakamoto, 2012). *M. tuberculosis*’ characteristics of resiliency, airborne transmission routes, and virulence lends to its high prevalence and attack rate (Reingold & Phares, 2006).

When *M. tuberculosis* enters the human respiratory system, it initially adheres to the alveolar cell wall with two potential outcomes: ingestion by alveolar macrophages and establishing latent tuberculosis infection (LTBI), or are removed by the macrophages prior to this establishment (Reider, 1999; CDC, 2011b). To establish LTBI, alveolar macrophages incorporate the bacillus into “phagosomes [where it is] subject to killing via a variety of mechanisms” such as phagocytosis, the process where phagosomes fuse with lysosomes and digest foreign agents (Reider, 1999). During this process, *M. tuberculosis* prevents the fusion of the phagosome with the lysosome as well as the acidification of the phagosome, evading digestion and surviving in the alveolar macrophage or externally in the granulomatous scars (Sakamoto, 2012). LTBI can often be observed in chest x-rays because of calcified alveolar macrophages and granuloma scars that are known as Ghon’s complex. Once LTBI is established, it remains a “chronic asymptomatic infection, followed by reactivation and transmission years later” (Sakamoto, 2012).
Persons infected with LTBI remain asymptomatic and have a 10% lifetime chance of becoming active TB cases, but persons who are immune-compromised, such as persons living with HIV or diabetes, or who smoke tobacco, are at a higher risk of acquiring LTBI, progressing from LTBI to active TB disease, and dying from active TB (Sakamoto, 2012; Mainous III & Pomeroy, 2010; WHO, 2013). For persons with LTBI and a normal immune system, tissue destruction and necrosis from the infection is usually countered by the healing process and subsequent fibrosis of the local nidus of infection. During periods of active TB disease, the cavities that previously hosted dormant LTBI break down to spread infection throughout the lungs and into the bloodstream, creating new foci of extra-pulmonary infection (CDC, 2011b; Grosset, 2003). Persons with active TB are able to infect up to 10-15 persons per year (WHO, 2013) via the sputum they expel when coughing, sneezing, singing, or spitting (CDC, 2011b).

**GLOBAL BURDEN OF TUBERCULOSIS**

The burden of disease is measured in terms of its prevalence, incidence, and mortality caused by a disease in a given period of time. TB in this regard has an enormous burden, standing as one of the world’s greatest killers from a single infectious agent (WHO, 2012a), secondary only to HIV/AIDS. In 2011, there were 12 million prevalent cases (170 cases per 100,000 person) of TB in the world, with 8.7 million incident cases (125 cases per 100,000 persons), 1.4 million deaths including HIV-associated deaths (equivalent to 20 cases per 100,000), and 49,000 DALY’s (IHME, 2010; WHO, 2012a). One-third of the world’s populations (2.3 billion cases) are infected with LTBI (WHO, 2013). TB infection and disease is disproportionately distributed according to socioeconomic status (SES) evident by 95% of all TB deaths occurring in low and middle-income countries (WHO, 2013). This is also illustrated by the uneven distribution of overall disease burden: Asia (59%), Africa (26%), Eastern Mediterranean (7.7%), Europe (4.3%), and the Americas (3%) (WHO, 2012a).

In 2012, the United States had 9,951 new TB cases, an incidence of 3.2 cases per 100,000 persons (CDC, 2013). The rate in foreign born persons was 11.5 times higher than in U.S. born persons (CDC, 2013). TB rates are also unequally distributed geographically and center in regions that have large urban centers, among foreign-born populations, and ethnic
minorities. Four states: California, New York, Texas, and Florida, each reported more than 500 cases in 2012 and when aggregated represented nearly half of all the nationwide cases for that year (49%) (CDC, 2011c, 2011e, 2013). These states have some of the largest urban centers in the nation and also possess large foreign-born populations: California (25.4%), New York (10.8%), Texas (10.4%), and Florida (9.2%) (Grieco et al., 2012). They are also four states with the largest Hispanic populations: California (38.1%), Texas (38.1%), Florida (22.8%), and New York (18%) (Pew Research Center & Per Hispanic Center, 2011).

Furthermore, the majority of foreign-born persons residing in these states identified themselves as Hispanic (Bennet et al., 2008).

TB among foreign-born persons residing in the United States is increasing. According to the CDC, in 2002 TB cases among foreign-born persons in the United States accounted for the majority (51.2%) of reported TB cases (CDC, 2011c). In 2010, the CDC found 33 states with at least 50% of its TB cases being foreign-born (CDC, 2011c). In 2011, 62% (6,527) of 10,528 reported TB cases in the United States were among foreign-born persons, a rate of 17.2 cases per 100,000 persons, again 11.5 times higher than among US-born persons with 1.5 cases per 100,000 (CDC, 2011a). This is compared to 21.6% (4,925) of 22,800 reported cases of TB in 1986; 29.6% (7,346) of 24,817 cases in 1993; and 41.6% (7,591) of 10,675 cases in 1998 (McKenna, McCray, & Onorato, 1995; Talbot, Moore, McCray, & Binkin, 2000). Among the 6,243 TB cases among foreign-born persons in the United States during 2012, 1,303 (20.9%) were from Mexico, 768 (12.3%) were from the Philippines, 529 (8.5%) were from India, 450 (7.2%) were from Vietnam, and 351 (5.6%) were from China (CDC, 2013). Furthermore, 55% of foreign-born persons with TB in the United States reported being in the country for at least 5 years or more prior to diagnosis, with Mexico as the highest percentage of country origin (60%) (CDC, 2011c). This becomes even more significant considering that Hispanics consisted of 16.7% (51,927,158 persons) of the United States population in 2011 (310,000,000 persons), of which 6% (18,788,300) were Hispanics that were also foreign-born. The CDC found that 84% of all TB cases in the United States in 2011 were among ethnic and racial minorities; the largest being Hispanics and Latinos (29%), with 2,999 cases (5.8 cases per 100,000 persons) (CDC, 2011c, 2012a, 2013).

While Hispanic and Latino as racial/ethnic categories includes a diverse array of subgroups, for the purpose of this study and remaining in accordance with the sample
population used in the Hispanic Health and Nutrition Examination Survey (HHANES) collected in the 1980’s, we will only include Mexican-Americans, Cuban-Americans, and persons from Puerto Rico. Hispanics have remained an ethnic minority with higher rates of TB than both non-Hispanic white populations as well as other ethnic minority groups since the 1980’s. In 1980, the CDC reported that tuberculosis among Hispanics in the United States had an overall case rate of 23.2 per 100,000 persons, twice that for other persons (CDC, 1982). In 1985, the CDC again reported TB among Hispanics in the United States had an overall case rate of 18.1 per 100,000 persons, 4 times the rate of 4.5 per 100,000 persons for non-Hispanic white populations (CDC, 1987). The majority of TB cases in Hispanics residing in the United States were in three states alone: California with 40%, Texas with 23%, and New York with 13% (CDC, 1987).

Mexican-Americans were 65% of the total Hispanic and Latino American populations in 2011, of which 34.7% were foreign born (U.S. Census Bureau, 2011). This large population of Mexican-Americans can be attributed to Mexico’s 115 million population (measured in 2011) and its geographic proximity to the United States. Mexico as a country of origin was found in 2011 to have a TB prevalence rate of 28 per 100,000 persons and an incidence rate of 23 per 100,000 persons (WHO, 2011a). In 1999, Mexico was the country of origin for 23% (1,753) of all foreign-born persons with TB. Of TB cases among Mexican-born persons, 75% reported from the four United States bordering Mexico: California (82%), Texas (36%), Arizona (67%), and New Mexico (17%)” (CDC, 2001). Over 60% of Mexican-Americans reside in California and Texas (Ennis, Rios-Vargas, & Albert, 2011) and these estimates do not include the estimated seven million undocumented Mexicans that are living and working in the United States (Passel & Cohn, 2009). Mexican-Americans “according to a 2000 survey of the US-born population…were almost 5 times as likely as Caucasians to be infected [with TB]” (American Lung Association [ALA], 2010). Mexicans/Mexican-Americans are also estimated to have a higher LTBI infection rate compared to Caucasians (9.4% vs. 1.9%) (Bennet et al., 2008).

There are only a few ways that TB is brought into the United States from Mexico. Persons in Mexico with active TB disease can cross the border, persons from Mexico with LTBI become active after arrival to the United States, or a United States resident visits Mexico and acquires TB prior to returning to the United States (CDC, 2001).
Cuban-Americans consist of 3.6% of the total Hispanic and Latino American population in 2011, of which 57.6% were foreign-born (U.S. Census Bureau, 2011). Cuba as a country of origin in 2011 had a population of 11 million with a TB prevalence rate of 12 per 100,000 persons and an incidence rate of 9.3 per 100,000 persons (WHO, 2011a). In a study of TB among Cubans ages 6 months to 74 years old in Dade County drawn from the 1982-1984 HHANES, 5-14% of persons were positive for LTBI among the 901 persons of Cuban descent tested (CDC, 1992). Furthermore this study reported that Cubans born outside the United States had much higher prevalence of LTBI than those born in the United States and that those who ever smoked (12%) were almost twice as likely as those who were nonsmokers to have LTBI (7.1%) (CDC, 1992).

Puerto Ricans consist of 9.5% of the total Hispanic and Latino American populations in 2011 (U.S. Census Bureau, 2011). Puerto Rico’s population in 2011 was 3.7 million, with a TB prevalence rate of 2 per 100,000 persons and an incidence of 1.8 per 100,000 persons (WHO, 2011a).

**Socioeconomic Status**

TB is a disease that has long been associated with poverty and low socioeconomic status (SES), both in US-born and foreign-born populations in the United States (Olson et al., 2012). In the United States, rates have been highest in the lowest SES quartiles of both US-born and foreign-born populations, but while TB rates were greater in low SES than high SES in both these populations, foreign-birth was only weakly associated with poverty as a determinant for TB (Olson et al., 2012). SES accounts for much of the increased risk that is also associated with race/ethnicity (Cantwell, McKenna, McCray, & Onorato, 1998).

**Sex, Gender, and Age Groups**

TB is a disease that disproportionately affects persons by sex and age. Men are more affected by TB than women, with a global ratio of 1.9 male TB cases for every female case (WHO, 2012a). This is attributed to socio-cultural factors that shape gender, suggesting males have more social contacts and therefore are at greater risk of exposure to contagious diseases as well as possessing immune systems that are more susceptible to TB (Onifade et al., 2010). Women, however, are less affected by the psychosocial and economic risks for TB
that could be due to higher amounts of access and use of health services by women in many regions of the world (Onifade et al., 2010). One study suggests that when controlling for smoking and alcohol use, females have a higher case-rate of LTBI than do males. Both TB infection and disease is more strongly associated with age group, mainly affecting persons in their primary working years (WHO, 2013). For persons in the United States during 2010, 64% of all cases were 25-64 years old, and 20% were older than 65 years (CDC, 2011c). Stratified by gender, males over the age of 65 years had the highest incidence (8 per 100,000 persons) and lowest in the 5-14 year age group (1 per 100,000 persons) (CDC, 2011c). Females ≥ 65 years of age also had the highest incidence (4 per 100,000 persons) and those aged 5-14 years had the lowest (1 per 100,000 persons) (CDC, 2011c). Thus, it appears as though age may influence rates of TB more than does gender (WHO, 2002).

**HIV**

There were 2.5 million people living in the world with both HIV and TB in 2011, this represents 40% of global TB cases (WHO, 2012a). Tuberculosis is also the leading cause of HIV-related deaths worldwide (25%), with 430,000 persons dying of the co-infection in 2011 (WHO, 2012c, 2013). Furthermore, co-infected persons are 21 to 34 times more likely to develop active TB disease than those without HIV (WHO, 2013). This is due to the suppression of the immune system by HIV, affecting CD4+ T cells, macrophages, and microglial cells such that cell-mediated immunity is not able to contain LTBI or new exposures. Those with HIV and LTBI are therefore more likely to develop active TB disease than those without HIV and they are also more likely to die as a result of these co-morbidities (WHO, 2012a).

**Diabetes Mellitus**

Multiple studies have found diabetes mellitus to be a risk factor for TB (Barmejo et al., 1995; Boucot, 1957; Coker et al., 2006; Dyck et al., 2007; Jabbar, Husain, & Khan, 2006; Jick, Lieberman, Rahman, & Choi, 2006; Kim, Hong, Lew, Yang, & Lee, 1995; Leung et al., 2008; Mboussa et al., 2003; Olmos et al., 1989; Pablos-Mendez, Blustein, & Knirsch, 1997; Perez, Brown, & Restrepo, 2006; Ponce-De-Leén et al., 2004; Shah & Hux, 2003; Shetty, Shemko, Vaz, & D’souza, 2006; Swai, McLarty, & Mugusi, 1990). A study of the NHANES
II found that persons with diabetes mellitus have higher odds of developing active TB, 2.31 (95% CI 1.36-3.93), after controlling for race, ethnicity, and age (Corris, Unwin, & Critchley, 2012; Jeon & Murray, 2008; Marks, 2011; WHO, 2011b). Diabetes mellitus and TB are synergistic in causing active TB disease by depressing the immune system, especially among those that have chronic high blood sugar levels (Boucot, 1957; Dooley & Chaisson, 2009; Leung et al., 2008; Olmos et al., 1989; Root, 1934; Swai, Maclarty, & Mugusi, 1990) via hyperglycemia, cellular insulinopenia, and the indirect effects of those on macrophage and lymphocyte function (Dooley & Chaisson, 2009). Diabetes mellitus in particular affects chemotaxis, phagocytosis, and macrophage activation, as well as antigen presentation by phagocytes (Dooley & Chaisson, 2009). One study found that TB patients with diabetes mellitus had less activated alveolar macrophages and decreased hydrogen peroxide production than those without diabetes (Wang, Yu, Lin, Liu, & Kuo, 1999). The decreased phagocyte and T-cell functions contribute to insulin deficiency, a major cause for the impairment of internalization by the Fe-rector-bound material, a vital part of phagocytosis (Dooley & Chaisson, 2009).

TB co-existing with diabetes mellitus is a major public health concern, and 10% of global TB cases (1.2 million) are linked to diabetes mellitus (WHO, 2011b). Diabetes mellitus affects 350 million and kills 3.4 million, with a prediction to increase 50% in disease burden by 2030 (WHO, 2011b). In the United States alone, diabetes mellitus affects 25.8 million people and killed 231,404 in 2007, costing $174 billion from direct and indirect medical costs (CDC, 2011d). National survey data from 2007-2009 for adults aged ≥20 years of age found diabetes mellitus prevalence to be 66% higher among Hispanics compared to non-Hispanic whites (CDC, 2011d). Furthermore among Hispanics, Mexican-Americans were found to have 87% higher prevalence, Puerto Ricans 94% higher prevalence, and Cubans/Central and South Americans equivalent to non-Hispanic white populations (CDC, 2011d). The convergence of these two epidemics is of great concern for both low-income and high-income countries (Dooley, Tang, Golub, Dorman, & Cronin, 2009; Lindoso et al., 2008; Restrepo et al., 2007; Stevenson et al., 2007).
Tobacco Smoking

Previous studies indicate that smokers have a higher prevalence of TB and are at increased risk for infection, for developing active TB disease, and for dying from TB than those who are not smokers (Bates et al., 2007; Hassmiller, 2006; Leung et al., 2010; S den Boon et al., 2005). Persons who smoke tobacco are 2-4 times more likely of acquiring TB than those who do not smoke (Davies et al., 2006; WHO, 2009). In addition, a dose-response relationship between smoking and TB infection has also been found (Davies et al., 2006). This may be due to the pathophysiology related to both tobacco smoke and TB infection as they both induce apoptosis of alveolar macrophages (Aoshiba, Tamaoki, & Nagai, 2001; Bothamley, 2005). Cigarette smoke specifically produces a local inflammatory response, and the nicotine in tobacco smoke suppresses the presentation function of antigens necessary to develop a specific immune response to this inflammation (Bothamley, 2005; Kirkham et al., 2003; Nouri-Shirazi & Guinet, 2003; Sköld et al., 1996). According to Davies et al. (2006), “nicotine in tobacco smoke is exploiting the final effector pathway of this major physiological anti-inflammatory mechanism”. The nicotine in tobacco smoke also turns off the production of TNF cytokines in the lungs, and those are responsible for destroying alveolar macrophages containing tubercle bacilli (Dheda, Johnson, Zumla, & Rook, 2004; Tomita et al., 2002). Type II pneumocytes are thought to be the initial site that TB infects and where it multiplies (Bermudez & Goodman, 1996). “Smoking during exposure to tubercle bacilli is likely to induce delayed hypersensitivity [and] more likely to produce disease” (Bothamley, 2005, p. 528).

More than 20% of global TB cases are attributable to tobacco smoke (WHO, 2013). With over 7,000 chemicals, tobacco smoke can cause multiple health effects and six million deaths per year are attributed to smoking globally (WHO, 2007, 2012b). This amount is projected to reach 8.4 million by 2020 (Murray & Lopez, 1997). There are more than one billion smokers (29% of the global population) in the world and 80% of them reside in Lower and Middle Income Countries (LMIC) (WHO, 2007, 2012b). The health effects of tobacco smoke additionally may also result in 600,000 deaths from exposure to second-hand smoke (SHS) (WHO, 2012b), and issues regarding third-hand smoke are also emerging as public health concerns (Newland, 2009). In the United States there are 45 million adults (19%) who currently smoke cigarettes, with 13 million (29% of current cigarette smokers) living under
the poverty line (CDC, 2011c). Tobacco smoke in the United States “resulted in at least 443,000 premature deaths, 5.1 million Years of Potential Life Lost (YPLL), and $96.8 billion [annually] in productivity loss” (CDC, 2008). Cigarette smoke has numerous effects on human physiology contributing to non-communicable diseases such as cardiovascular diseases, chronic respiratory diseases, and certain types of cancers.

Hypotheses regarding duration of smoking, current vs. previous smoking, and the relationship to development of active pulmonary TB are currently being explored, with increasing evidence supporting smoking as a major risk-factor for TB infection and disease (Bothamley, 2005). Policy makers and public health personnel should consider tobacco cessation as part of TB control (Lin et al., 2009) because it is a risk-factor that is modifiable through behavior change and policy (Bates et al., 2007). There are multiple publications that have emphasized smoking cessation as a critically important intervention for preventing and controlling TB (Ariyothai et al., 2004; Bates et al., 2007; Lin et al., 2009; Schneider & Novotny, 2007; Shulte et al., 2001).
CHAPTER 3

METHODS

STUDY DESIGN

A secondary analysis of cross-sectional data from the National Hispanic Health and Nutrition Examination Survey (HHANES) was conducted to investigate the association between ever-smoking cigarettes and TB infection reported by three Hispanic subgroups: Mexican-Americans, Cuban-Americans, and Puerto Ricans, 12-74 years of age. The HHANES is among the most comprehensive Hispanic health surveys and physical examinations carried out in the United States to date (Delgado, Johnson, Roy, & Treviño, 1990). It was the first special population survey undertaken by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of Hispanics residing in the United States, specifically focusing on certain selected chronic conditions, and it serves as a baseline for other surveys of Hispanics (Delgado et al., 1990).

NCHS conducted the HHANES to acquire nationally representative samples of Hispanic subgroups that would establish baseline comparisons for future studies about Hispanic health in the United States. The HHANES consists of a set of special population surveys and examinations that were administered to 15,924 Hispanic persons ages six months-74 years of age (CDC, 2012b) during 1982-1984. Of this sample population there were 9,894 Mexican-Americans (8,554 interviewed/ 7,462 examined) from Texas, Colorado, New Mexico, Arizona, and California during July 1982 through November 1983; 2,244 Cuban Americans (1,766 interviewed/ 1,357 examined) residing in Dade County, Florida during January 1984 through April 1984; and 3,786 Puerto Ricans (3,369 interviewed/ 2,834 examined) residing in the New York City area during May 1984 through December 1984 (Delgado et al., 1990; CDC, 2012b). This sample population drew from a survey universe that represents 76% of the total 1980 census estimate for US Hispanic non-institutionalized civilian population ages six months through 74 years (Delgado et al., 1990).

This particular study draws from the interview data gathered through the Adolescent and Adult History Questionnaire for Ages 12-74 Years of the HHANES during July 1982.
and December 1984. This questionnaire was administered to 9,643 Hispanics: 5,773 Mexican-Americans, 1,454 Cuban-Americans, and 2,416 Puerto Ricans in their respective regions. The dataset was edited by dropping those who did not answer questions about educational level, TB infection, per capita income, foreign-birth, and diabetes; the final study population consisted of 8,578 respondents: 5,122 Mexican-Americans, 1,308 Cuban-Americans, and 2,148 Puerto Ricans (Figure 1).

**Data Collection**

The HHANES methodology was reported and summarized by Delgado et al. (1990). Data were collected using direct physical examinations, diagnostic testing, anthropometry, laboratory analysis, and personal interviews. Data were collected on chronic conditions such as diabetes, hypertension, and depression along with other issues such as TB infection, immunization, alcohol and tobacco consumption, dental health, digestive diseases, diet and nutritional status, as well as some environmental exposures. Bilingual staff members conducted interviews in either the subject’s house or in a mobile trailer, while all physical examinations were performed in the mobile center.

A household interview consisted of a Household Screener Questionnaire (HSQ) administered at each selected address, followed by a Family Questionnaire administered for each family unit, an Adult Sample Person Questionnaire for persons 12-74 years of age, and a Child Sample Person Questionnaire for persons 6 months to 11 years of age. The National Institute of Health Statistics (NHIS) provided the database from their online public domain servers along with SAS formatting for further research.

**Variables**

TB was the dependent variable and the main outcome of interest in this study. This variable was measured using a single item from the questionnaire: “Were you ever told by a doctor that you had tuberculosis?” The responses to this question was trichotomous, 1=Yes, 2=No, and 8=Blank but applicable. For the purposes of this study, the variable was dichotomized by excluding those who answered 8=Blank but applicable.
Figure 1. Ethnic stratification of hispanic persons residing in the United States and were interviewed with the adolescent and adult questionnaire: Ages 12-74 years of the HHANES during 1982-1984.

Ever-smoked cigarettes was the main independent variable and exposure of interest in this study. The variable was measured using a single item from the questionnaire: “Have you smoked at least 100 cigarettes in your entire life?” This question was provided separately to person’s ages 12-19 years old in a supplemental questionnaire from those 20-74 years old delivered in the standard questionnaire, but both are included within the Adolescent and
Adult data tape. These two variables were created by a single question but were delivered to two age groups. The two variables were combined into a single variable for ease of data analysis among the entire age range. The responses to this question were trichotomous, 1=Yes, =No, and 8=Blank but applicable. For the purposes of this study, the variable was dichotomized by excluding those who answered 8=Blank but applicable.

CONFOUNDING VARIABLES

The HHANES Adolescent and Adult Questionnaire: Ages 12-74 Years included an extensive array of demographic and socioeconomic variables that could confound the potential relationship between TB history and ever smoking status. Therefore, this analysis controlled for the following cofactors identified in the literature to be potential confounders for TB: age, per capita income, sex, diabetes, education, and foreign birth. Other cofactors for TB identified in the literature such as HIV were not included in the analysis because the HHANES survey did not collect these data.

Age was a continuous variable computed by NHIS according to “Age at interview (computed)”, however, for bivariate analysis the following age groups were created for illustrative purposes: under 18 years of age; 18-24 years of age; 25-34 years of age; 35-44 years of age; 45-54 years of age; 55-64 years of age; and persons 65 and older. Per Capita Income was also a continuous variable computed by NHIS according to “Per capita income (computed)”, however, for bivariate analysis it was also categorized according to the 1980 US Census quintiles for Household Income levels among those with Hispanic origin. This consisted of the lowest-fifth earning less than $6,088; the second-fifth of earners ranging from $6,088-$10,850; the third-fifth of earners ranging from $10,851-$16,700; the forth-fifth of earners ranging from $16,701-$25,324; and the highest fifth earning $25,325 and above1 (U.S. Census Bureau, 2013).

All other independent variables were categorical variables: sex, diabetes, education level, foreign birth. Sex was scored as a dichotomous variable with 1=Male and 2=Female. Diabetes was measured by the question “Do you have diabetes or sugar diabetes?” and was

---

1 Income categories adjusted for 2010 dollar values were: less than $16,013; $16,014-$30,000; $30,00-$47,602; $47,603-$76,020; more than $76,021.
scored as a trichotomous variable with 1=Yes, 2=No, and 8=Blank but applicable. For the purposes of this study, the variable was dichotomized by excluding those who answered 8=Blank but applicable.

Education was measured by the question “What is the highest grade or year of regular school, sample person has ever attended?” and was scored as 00=Never attended or kindergarten only, 01-08=Elementary Grades, 09-12=High School grade, 13-16=College, 17=Graduate School, and 88=Blank but applicable. For the purposes of this study, the variable was dichotomized according to <12=Less than 12 full years of school and 12-17=At Least 12 full years of school, and by excluding those who answered 88=Blank but applicable. For the purposes of this study the variable was dichotomized as those who were foreign-born and those who were not foreign-born. This was achieved by combining scores 2= Second Generation (One of both parents born in Mexico/Cuba/Puerto Rico) with 3=Third or higher generation (Neither parent born in Mexico/Cuba/Puerto Rico); those who answered 8=Blank but applicable were excluded.

**Statistical Analysis**

All analyses were conducted using SAS, version 9.3. The analyses were performed using NHIS-HHANES provided weights to account for the complex sampling design and to obtain proper variance estimations. Missing values were excluded from all analyses. Descriptive statistics included frequencies and associated percentages calculated for all study variables to describe overall demographic and health factors related to TB and ever-smoking cigarettes. Bivariate analysis provided crude odds ratios (OR) and 95% confidence intervals (CI), and Wald Chi-square was used to evaluate the strength, direction, and significance of the relationship between TB and the independent variables of interest: ever-smoked cigarettes, sex, foreign-birth, diabetes, educational level, per capita income, and age.

Multivariate logistic regression was used for the final analysis, specifically implementing the forward stepwise logistic regression model-building process to select
variables for the final model. The main independent variable and exposure of interest (ever-smoked cigarettes) always remained in the model while other potential confounders were tested one-by-one for statistical significance to indicate whether they should be included or excluded from the final model using a p-value of 0.05. These included sex, foreign-birth, diabetes, educational level, per capita income, and age as well as several interaction terms (ever-smoked*sex, ever-smoked*foreign-birth, ever-smoked*diabetes, ever-smoked*educational level, ever-smoked*per capita income, and ever-smoked*age). The interaction between age*foreign-birth was also included due to differential relationships between those who are older and foreign-born and having TB. An alpha level of 0.05 determined whether a variable succeeded through the forward stepwise process from the full model to the final multivariate logistic regression model. To address the overall fit of the model, a generalized goodness-of-fit test was performed including the overall R values.
CHAPTER 4

RESULTS

DESCRIPTIVE STATISTICS

The majority of the 5,122 Mexican-Americans were male (50.3%), were not foreign-born (67.2%), had <12 full years of education (60.5%), were not diabetic (95.9%), had never-smoked cigarettes (54.6%), and were not told by a doctor that they had TB (97.9%). Among the Mexican-Americans, mean age was 32.3 (± 0.29) years old and mean per capital income was $5,224 (± 180.71)$^2$ (see Table 1).

The majority of the 1,308 Cuban-Americans were female (53.2%), were foreign born (90.2%), had 12 full years of education or more (51.1%), were not diabetic (97.9%), had never-smoked cigarettes (54.6%), and were not told by as doctor that they had TB (99.6%). Among the Cuban-Americans, mean age was 39.5 (± 0.60) years old and mean per capital income was $6,861 (± 172.36)$^3$ (see Table 1).

The majority of the 2,148 Puerto Ricans were female (58.3%), were foreign born (60.7%), had <12 full years of education (57.8%), were not diabetic (95.8%), had never-smoked cigarettes (55.1%), and had not been told by a doctor that they had TB (98.3%). Among the Puerto Ricans, mean age was 32.4 (± 0.61) years old and mean per capital income was $5,034 (± 446.31)$^4$ (see Table 1).

All three Hispanic subgroups had comparable rates of reported TB, ever-smoking cigarettes, and diabetes, but unequal demographically with respect to sex, foreign birth, age, per capita income, and educational level. Puerto Mexican-Americans had the highest rate of US-born persons compared to Cuban-Americans with the lowest. Cuban-Americans were on average the oldest population, had the highest per capita income, and highest rate of persons with at least 12 years of education.

---

$^2$ $11,437$ adjusting for the 2010 dollar value
$^3$ $15,021$ adjusting for the 2010 dollar value
$^4$ $11,021$ adjusting for the 2010 dollar value
Table 1. Descriptive Data of Risk Factors for Reported Tuberculosis Among Hispanic Respondents to HHANES, United States 1982-1984, Stratified by Ethnic Subgroup

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mexican-Americans (n=5,122)</th>
<th>Cuban Americans (n=1,308)</th>
<th>Puerto Ricans (n=2,148)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency (%)</td>
<td>Weighted Frequency (%)</td>
<td>Frequency (%)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>114 (2.22)</td>
<td>129,851 (2.06)</td>
<td>6 (0.46)</td>
</tr>
<tr>
<td>No</td>
<td>5,008 (97.78)</td>
<td>6,159,519 (97.94)</td>
<td>1,302 (99.54)</td>
</tr>
<tr>
<td>Missing Freq.</td>
<td>1 (0.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2,382 (46.51)</td>
<td>3,162,264 (50.28)</td>
<td>613 (46.87)</td>
</tr>
<tr>
<td>Female</td>
<td>2,740 (53.49)</td>
<td>3,127,106 (49.72)</td>
<td>695 (53.13)</td>
</tr>
<tr>
<td>Ever-Smoked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2,145 (41.88)</td>
<td>2,777,263 (45.44)</td>
<td>547 (41.82)</td>
</tr>
<tr>
<td>No</td>
<td>2,802 (54.71)</td>
<td>3,335,110 (54.56)</td>
<td>713 (54.51)</td>
</tr>
<tr>
<td>Missing Freq.</td>
<td>175 (3.42)</td>
<td>48 (3.70)</td>
<td></td>
</tr>
<tr>
<td>Foreign Birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1,639 (31.99)</td>
<td>1,936,484 (32.78)</td>
<td>1,109 (84.79)</td>
</tr>
<tr>
<td>No</td>
<td>3,193 (62.34)</td>
<td>3,971,514 (67.22)</td>
<td>136 (10.40)</td>
</tr>
<tr>
<td>Missing Freq.</td>
<td>290 (5.66)</td>
<td>63 (4.82)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>238 (4.65)</td>
<td>259,184 (4.12)</td>
<td>41 (3.13)</td>
</tr>
<tr>
<td>No</td>
<td>4,884 (95.35)</td>
<td>6,030,186 (95.88)</td>
<td>1,267 (96.87)</td>
</tr>
<tr>
<td>Missing Freq.</td>
<td>1 (0.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 12 Years</td>
<td>3,330 (65.01)</td>
<td>3,806,775 (60.53)</td>
<td>683 (52.21)</td>
</tr>
<tr>
<td>12 Years or more</td>
<td>1,792 (34.99)</td>
<td>2,482,595 (39.47)</td>
<td>625 (47.78)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (Std. Err.)</th>
<th>Mean (Std. Err.)</th>
<th>Mean (Std. Err.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per Capita Income</td>
<td>5224.14 (± 180.71)</td>
<td>6821.12 (± 172.36)</td>
<td>5034.66 (± 446.31)</td>
</tr>
<tr>
<td>Age</td>
<td>32.30 (± 0.29)</td>
<td>39.45 (± 0.60)</td>
<td>32.37 (± 0.61)</td>
</tr>
</tbody>
</table>
Bivariate Analysis

Among Mexican-Americans, chi-square analyses revealed statistically significant relationships (p<0.05) between TB and the following exposure variables: ever-smoked cigarettes, foreign-birth, and most age-groups; there was no association between TB and gender, between TB and diabetes, between TB and educational level, or between TB and per capita income. Mexican-American participants who had ever-smoked cigarettes were 1.26 times (95% CI: 1.04-1.52) more likely to have been told by a doctor that they had TB compared to those who have never-smoked. Furthermore, foreign-born Mexican-Americans were 1.78 times more likely (95% CI: 1.14-2.80) more likely to have been told by a doctor that they had TB compared to those who were not foreign-born. Mexican-Americans were 2.24 times more likely (95% CI: 1.11-4.50) to have been told by a doctor that they had TB among 25-34 year olds; 2.60 times more likely (95% CI: 1.32-5.15) among 35-44 year olds; 2.47 times more likely (95% CI: 0.96-6.34) among 45-54 year olds; 4.14 times more likely (95% CI: 1.50-11.43) among 55-64 year olds; and 4.48 times more likely (95% CI: 1.63-12.31) among those 65 years of age and older when compared to those under 18 years of ages.

Among Cuban-Americans, a relationship was found between TB and the following variables: diabetes and age; no associations were found between TB and ever-smoked cigarettes, between TB and sex, TB and per capita income, or between TB and educational level. Cuban-American participants who had diabetes were 7.86 times (95% CI: 1.24-49.49) more likely to have been told by a doctor that they had TB, compared to those who did not have diabetes.

Among Puerto Ricans, a relationship was found between TB and sex, foreign-birth, and age; there was no association found between TB and ever-smoked cigarettes, between TB and diabetes, TB and educational level, or TB and per capita income. Puerto Rican participants who were female were 3.79 times (95% CI: 1.51-9.52) more likely to have been told by a doctor that they had TB than those who were male. Furthermore, foreign-born Puerto Rican participants were 3.42 times (95% CI: 1.12-10.47) more likely to have been told by a doctor that they had TB than those who were not foreign-born. Puerto Ricans were 3.84 times (95% CI 1.27-11.67) more likely to have been told by a doctor that they have TB
among 35-44 year olds and 10.14 times more likely (95% CI 2.12-48.5) among 45-54 year olds when compared to those under 18 years of age.

**Multivariate Logistic Regression**

For Mexican-Americans, the odds of having been told by a doctor that they have TB are 1.21 times (95% CI: 0.98-1.48) higher among those who have ever-smoked (>100 cigarettes smoked in their entire life) compared to those who have never-smoked (<100 cigarettes smoked in their entire life), adjusting for sex, foreign-birth, age, and the interaction between age and foreign-birth (see Table 2). The adjusted OR for Mexican American females having been told by a doctor that they have TB was 2.23 (95% CI: 1.11-4.47). The adjusted OR for foreign-born Mexican-Americans having been told by a doctor that they have TB was 9.42 (95% CI: 8.34-10.51). Older age was found to be a risk for Mexican-Americans who were told by a doctor that they had TB. For Mexican-Americans, the risk of having TB is related to the effect of foreign-birth on age, such that Mexican Americans with TB are more likely to be foreign-born and older compared to younger and US-born Mexican Americans with TB. A goodness-of-fit test was accepted and concluded that the model is a good fit for our sample ($R^2 = 1.00$, $X^2 = 25.57$, $df = 5$, $p < 0.0001$) (see Table 2).

For Cuban-Americans, the odds of having been told by a doctor that they have TB are 1.06 times (95% CI: 0.20-5.51) higher among those who have ever-smoked (>100 cigarettes smoked in their entire life) compared to those who have never-smoked (<100 cigarettes smoked in their entire life), adjusting for age. For Cuban Americans, one-unit of age was found to be associated to having TB at a rate of 1.17 (95% CI: 1.11-1.23), adjusting for those who have ever-smoked cigarettes. A goodness-of-fit test was accepted and concluded that the model is a good fit for our sample ($R^2 = 0.96$, $X^2 = 35.35$, $df = 2$, $p < 0.0001$) (see Table 3).

For Puerto Ricans, the OR of having been told by a doctor that they have TB is 1.18 (95% CI: 0.51-2.78) higher among those who have ever-smoked (>100 cigarettes smoked in their entire life) compared to those who have never-smoked (<100 cigarettes smoked in their entire life), adjusting for sex and age (see Table 4). For Puerto Ricans, one-unit of age was found to be associated with TB at with OR of 1.03 (95% CI: 1.01-1.05), adjusting for sex and those who have ever-smoked cigarettes. The adjusted OR for Puerto Ricans females was 3.73.
Table 2. Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Mexican American Respondents to HHANES, United States 1982-1984

** Mexican-Americans (n=4663**)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever Smoked</td>
<td></td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Yes</td>
<td>1.21</td>
<td>0.98-1.48</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2.23</td>
<td>1.11-4.47</td>
<td></td>
</tr>
<tr>
<td>Foreign Birth:</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>9.42</td>
<td>8.34-10.51</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.04</td>
<td>1.02-1.06</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age * Foreign-Birth</td>
<td>0.96</td>
<td>0.93-0.98</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*OR of having been told by a doctor that you have tuberculosis

** Missing Frequencies from response or explanatory variables=459

(\(R^2=1.00\), \(X^2=25.57\), \(df=5\), \(p<0.0001\))

Table 3. Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Cuban American Respondents to HHANES, United States 1982-1984

** Cuban American (n=1260**)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever Smoked</td>
<td></td>
<td></td>
<td>0.95</td>
</tr>
<tr>
<td>Yes</td>
<td>1.06</td>
<td>0.20-5.51</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.17</td>
<td>1.11-1.23</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*OR of having been told by a doctor that you have tuberculosis

** Missing Frequencies from response or explanatory variables=74

(\(R^2=0.96\), \(X^2=35.35\), \(df=2\), \(p\)-value <0.0001)
Table 4. Multivariate Analyses of Risk Factors for Reported Tuberculosis Among Puerto Rican Respondents to HHANES, United States 1982-1984

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever smoked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.18</td>
<td>0.51-2.78</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td></td>
<td>0.009</td>
</tr>
<tr>
<td>Female</td>
<td>3.74</td>
<td>1.38-10.13</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.03</td>
<td>1.01-1.05</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*OR of having been told by a doctor that you have tuberculosis

** Missing Frequencies from response or explanatory variables=74

(R^2 =0.97 , X^2 =25.32 , df= 3 , p<0.0001)

(95% CI: 1.38-10.13) for having TB. A goodness-of-fit test was accepted and concluded that the model is a good fit for our sample (R^2 =0.97, X^2 =25.32, df= 3, p<0.0001) (see Table 4).
CHAPTER 5

DISCUSSION

This study shows no significant association between those who were told by their doctor that they have TB and those who had ever smoked at least 100 cigarettes in their life, among Hispanic respondents to the HHANES, 1982-1984. This is inconsistent with other research that has found significant associations between cigarette smoking and TB (Hassmiller, 2006; S den Boon et al., 2005), specifically among Hispanics (Dietz, Novotny, Rigau-Perez, & Schultz, 1991; McCurdy, Arretz, & Bates, 1997). While this study did not find a significant relationship (p<0.05) between those who were told by a doctor that they had TB and ever smoked cigarettes, the direction of the relationships was positive with Mexican-Americans having the highest adjusted OR. Descriptive analysis found the following diseases and risk factors to be similar among the three Hispanic subgroups included in this study: TB, diabetes, and ever smoked cigarettes. However, demographic factors such as sex, foreign-birth, educational level, per capita income, and age differed among the three groups of respondents included in this study. This finding illustrates the need to differentiate and stratify analyses by Hispanic subgroups when determining the relationship between disease outcomes and risk factors.

Mexican-Americans had a higher proportion of males with Puerto Ricans having the lowest. This is notable when considering the sampling method that used the head of the household as a main determinant for eligibility. Puerto-Rican households in New York City, and surrounding regions could be more matriarchal than Mexican-American households sampled in southwestern states. Mexican-Americans had the highest proportion of persons that were US-born, with Cuban-Americans having the lowest. The high proportion of Mexican-Americans being US-born illustrates the unique relationship that Mexico has with the United States due to its proximate land border, the desire for Mexican immigrants to initially raise families in the United States, and the continued attraction for younger Mexican-Americans to remain in the United States for work. Cuban-Americans were the oldest, had the highest average per capita income, the highest proportion of persons with 12 or more
years of completed education, and were a majority foreign-born. This speaks to the longstanding political-economic tensions that Cuba and the United States have had for the last half-century. Cuban-Americans residing in the United States were for the majority foreign-born, older, wealthier, and more educated: potentially being the social elites who were able to leave Cuba prior to the formal establishment of the communist party in the 1950’s, and the subsequent US embargos held against them in the 1960’s.

Bivariate analyses revealed that the relationship between ever-smoking cigarettes and TB was only significant for Mexican-Americans. However, the strength of the relationship between ever-smoking cigarettes and TB was comparable among all of the Hispanic subgroups. This similarity can be understood as an effect of differential sample sizes, Mexican-Americans having the largest. The positive association between ever-smoking cigarettes and TB among the three Hispanic subgroups on using only bivariate analyses agrees with prior research and suggests that further investigation into this relationship is needed. Bivariate analyses also revealed age to be significantly related to TB among all Hispanic subgroups. For Puerto Ricans, gender and foreign-birth were significantly associated with TB and had a relatively strong relationship. The odds that a female Puerto Rican had TB were twice that of Mexican-American females. The odds that a foreign-born Puerto Rican had TB were twice that of foreign-born Mexican-Americans. This speaks further to the demographic results that indicate a higher proportion of Mexican-Americans being male and US-born as well as to the high proportion of Puerto Ricans being female and foreign-born.

Multivariate analysis found that after adjusting for covariates associated with TB (sex, age, foreign-birth, and the interaction between age and foreign-birth), the association between ever smoked cigarettes and TB among Mexican Americans became insignificant. Results indicated that sex, foreign-birth, age, and the interaction between age and foreign-birth were significantly associated with TB. Mexican-American females are more likely to have TB than Mexican-American males. Foreign-born Mexican-Americans are more likely to have TB than US-born Mexican-Americans. Older Mexican-Americans are more likely to have TB than younger Mexican-Americans. The interaction between age and foreign-birth indicates that TB differentially affects persons who are foreign-born at an older age than those at a younger age. For Cuban-Americans, results indicated that age was significantly
associated with TB. Thus, older Cuban-Americans were more likely to have TB than younger Cuban-Americans. Furthermore among all the Hispanic subgroups samples in this study, older Cuban-Americans have the highest ORs of having TB. For Puerto Ricans, females were more likely to have TB than Puerto Rican males. Older Puerto Ricans were more likely to have TB than younger Puerto Ricans.

Multivariate results found that Mexican-American and Puerto Rican females were disproportionately affected by tuberculosis and also were inconsistent with findings at a global level by the World Health Organization (WHO, 2012a). These findings should be further investigated to determine what factors are creating the disparity for these Mexican-American and Puerto Rican females residing the United States.

LIMITATIONS

This study was limited in its sampling design by addressing only three Hispanic subgroups residing in particular regions of the United States from 1982-1984. The final sample was only able to investigate the diversity within three major Hispanic subgroups, but was not able to produce a national probability sample of Hispanics in general. Furthermore, it is questionable that this sample is actually 76% of the 1980 Census populations and a nationally representative sample. Since the HHANES was conducted in the 1980’s there is also a lack of information regarding other known TB cofactors such as HIV. Finally, self-report data is a reliable form of data collection, yet highly variable, when compared to data from physical examination or serologic testing (Evridiki et al., 1989). As such, it also lacks an ability to measure exposures to second-hand smoke and third-hand smoke.

This study was limited by not evaluating the missing frequencies for potential sampling bias. It was also limited in its use of head of household income as the measure for socioeconomic status, since it doesn’t capture the individual or household income levels. And its use of ever smoked as greater or less than 100 cigarettes smoked in a lifetime, as it does not capture nuances such as the sharing of cigarettes, a known characteristic of Hispanic and Latino social gatherings.

FUTURE DIRECTIONS

In future studies, using biologic ascertainment of smoking status and latent tuberculosis infection (LTBI) as well as physical examination would be best to reduce
respondent bias and increase test sensitivity. One recommendation is to use QuantiFERON-TB Gold to test blood samples from patients for LTBI and active TB disease, as it is currently the “gold standard” instrument used in TB research as well as prevention and control programs. A second recommendation is to focus on the relationship between current smoking cigarettes and TB instead of ever-smoking cigarettes; this would relate more towards the known physiological effect that smoking cigarettes has on the immune and pulmonary systems. Furthermore, a third recommendation is to test for cotinine as the main measure for current smoking because it is a metabolite of nicotine, a dependable referent for active exposure, and is also sensitive enough to incorporate measurement of passive exposure.

While the HHANES was a major achievement to create a baseline sample of racial/ethnic minorities residing in the United States, it is outdated, was not able to be analyzed at the level of Hispanic and Latino, and did not incorporate a diverse array of Hispanic subgroups in its sampling frame. Furthermore, the HHANES needs to be evaluated whether it is a nationally representative sample consisting of 76% of the 1980 US Census population and the population that was not included within the sample. Future research should be specifically conducted on a nationally representative random sample of Hispanic and Latinos in general as well as the subgroup level that would gather socio-demographic, health, and environmental exposure information using physical examinations and serologic testing. In these future studies, it would also be beneficial to include a stronger socioeconomic status measure that uses a broader array of proxy measures than Individual Income Levels or Total Household Income. This research is needed in part due to the changes in the Hispanic population since the 1980’s with a dramatic increase from 14.6 million in 1980 to 52 million in 2011 (U.S. Census Bureau, 2012). This recommendation could be achieved using a nationwide representative dataset, such as the NHANES, that used QuantiFERON-TB Gold and cotinine as their main measures for TB and tobacco smoke exposure, and ensuring it has the ability to stratify for Hispanic and Latino racial/ethnic groups and subgroups.
REFERENCES


Tomita, K., Caramori, G., Lim, S., Ito, K., Hanazawa, T., Oates, T., … Adcock, I. M. (2002). Increased p21(cip1/waf1) and b cell lymphoma leukemia-x(l) expression and reduced
apoptosis in alveolar macrophages from smokers. *American Journal of Respiratory and Critical Care Medicine, 166*(5), 724-731.


