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Carter McCormick Date

Relationship of Demographic Variables and Classification of Leprosy Cases in Georgia since the early 1900s.

By

Carter McCormick
Master of Public Health

Hubert Department of Global Health

_____

Jessica K. Fairley, MD, MPH
Committee Chair

Relationship of Demographic Variables and Classification of Leprosy Cases in Georgia since the early 1900s.

By

Carter McCormick
Bachelor of Arts
University of North Carolina at Chapel Hill, 2015

Thesis Committee Chair: Jessica K. Fairley, MD, MPH

An abstract of
a thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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2018

Abstract

Relationship of Demographic Variables and Classification of Leprosy Cases in Georgia since the early 1900s.

By: Carter McCormick

Introduction: Leprosy (also known as Hansen's Disease) is a disease that is diagnosed in approximately 160 people in the USA each year. Recent studies have shown different forms of transmission in the southern US (zoonotic versus person-to-person), but epidemiologic data are lacking about factors associated with multibacillary infection, the most infectious form.

Purpose: To examine if location of birth, dichotomized between domestic (United States) born and born abroad, is related to disease presentation (multibacillary versus paucibacillary) in cases of leprosy in Georgia when controlling for other demographic characteristics.

Methods: Data was collected from surveillance reports on 123 leprosy patients from the National Hansen's Disease Program who had been reported by or lived in the state of Georgia since the early 1900's. Two logistic regression models were built, one using all years and one using post-1995 cases. Location of birth was the variable of interest and the outcome was type of leprosy (multibacillary vs. paucibacillary). Sex, age, and ethnicity was controlled for.

Results: While the model showed no significant relationship between country of origin and type of leprosy, being Asian or Pacific Islander (97.36% of which were foreign born) was associated with a higher risk of multibacillary infection when controlled with the other variables (aOR = 5.714; 95% CI: 1.254 – 26.287). This trend was repeated in the model using post-1995 data.

Conclusion: Leprosy is known to be highly endemic in Micronesia and other areas in Asia. There have been several articles describing the epidemiological data of Asians and Pacific Islanders in the USA, such as the Marshallese in Arkansas and Micronesians in Hawaii. However, more research should be done to see if these population is at greater risk for multibacillary leprosy. With the global community dedicated to the elimination of leprosy, understanding which populations are at greater risk for this more infectious type of leprosy is important to create targeted interventions and prevention strategies.

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Chapter 1: Introduction

Background

Leprosy (also known as Hansen's Disease) is a disease that has been affecting people since biblical times. It is a chronic condition caused by the bacillus *Mycobacterium leprae (M. lepare)*, which can affect the skin, the peripheral nerves, mucosa of the upper respiratory tract, and also the eyes[20]. The common clinical presentation is skin lesions, with pigmentation different from that of the surrounding skin, combined with sensory loss at the site[30]. Patients may also present with thickened nerves, commonly of the peripheral nerves, and complications associated with this symptom such as muscle weakness[30]. The disease can lead to permanent disability due to damage of the nerves, as well as negative health outcomes associated with stigma and discrimination that individuals with leprosy face by their community[20]. Transmission of *M. leprae* is by droplets from the nose and mouth during close and frequent contact with untreated patients[20]. Other methods of transmission have been studied in recent years and are discussed in further sections.

Leprosy is classified by clinical presentation, based on the number of skin lesions, and by histopathology from a skin biopsy[30]. Skin smears are utilized to measure the amount of *M. leprae* bacilli on the skin[4]. Within United States the Ridley-Jopling classification is used, which diagnoses patients as having indeterminate, tuberculoid, borderline tuberculoid, mid-borderline, borderline lepromatous, and lepromatous leprosy[4]. The global classification that is commonly used is that of the World Health Organization, which classifies patients with less than 5 lesions as paucibacillary (PB) and those with 5 or more lesions as multibacillary (MB)[4].

If detected early enough and treated appropriately, patients can prevent the long term disability associated with the disease[20]. Current recommended treatment strategies for leprosy by the World Health Organization is multidrug therapy (MDT)[20]. The specifics of the MDT used to treat a patient depends on the type of leprosy, differing between multibacillary and paucibacillary, with a combination of monthly and daily medications lasting from six to 24 months[32].

Global prevalence of leprosy has dropped 90% since the early 1990's due in part to the use of MDT and better surveillance[1]. Now global leprosy burden affects low- and middle-income countries predominately, with about 200,000 – 300,000 cases reported annually[1]. India, Brazil, and Indonesia have the most cases reported annually[10]. India has consistently had the most reported cases on Leprosy with 135,485 cases reported in 2016[10]. Brazil and Indonesia had 25,218 and 16,826 cases reported in 2016 respectively[10]. This is compared to the cases reported from a higher income country, such as 5 cases for the Netherlands in 2016[10]. The United States sits at a slightly higher case number per year, with 168 cases reported in 2016[10].

Problem Statement

As the United States continues to have cases of leprosy annually, there is a clear need to assess the trends and patterns of cases, to better understand the disease manifestations and communities at risk. Additionally, there is a need to determine if the relationship between demographic variables are related to the diagnosed classification of leprosy so interventions can be tailored to specific populations to decrease the number of cases. Performing this study in a southern state, where armadillo transmission is present, allows us to evaluate two groups

of patients with different potential transmission risks, thus contributing to the gap of knowledge of the relationship of transmission method and type of leprosy diagnosed [28].

Purpose Statement

The purpose of this study is to examine if location of birth, dichotomized between domestic (United States) born and born abroad, is related to disease presentation (multibacillary versus paucibacillary) in cases of leprosy in Georgia when controlling for other demographic characteristics.

Research Question

Is country of origin, stratified as domestic (USA) born and born abroad (non-USA born), related to the classification of Hansen's Disease, either as paucibacillary leprosy or multibacillary leprosy?

Significance Statement

As there continues to be leprosy in the United States, there needs to be more attention placed on the disease and how it is impacting people, especially if patients from some populations are more at risk for the more infectious multibacillary disease. Understanding how domestic born citizens versus immigrants are being impacted by leprosy is important to ensure that tailored interventions can be targeted to these specific populations. It may also help understand the overall epidemiology and transmission patterns in other contexts.

Chapter 2: Literature Review

Leprosy in the United States Among Immigrants

Leprosy has been present in the United States prior to the country's founding, with the Acadian people from Canada bringing cases of leprosy to French Louisiana in the mid 1700's[14]. Cities with main ports of entry into the country had higher burdens of leprosy due to the immigrant populations there, such as Miami in Florida with the population from the Caribbean and West Indies[14]. A "Leper Home" was set up to care for individuals with leprosy in the late 1800's in Lousiana[13]. In 1917, the United States Senate passed Senate Bill 4086, which created a National Leprosarium in Carville, Louisiana[13]. This Leprosarium became the base of the National Hansen's Disease Program (NHDP), who's center was later moved in 1998 to Baton Rouge, Louisiana[13]. In recent decades, leprosy cases in the United States have been low but steady, hovering around 160 cases reported per year[10].

Most of the cases of leprosy seen in the United States are among immigrant patients from countries where leprosy is endemic. The rate of diagnosis of leprosy among immigrants was 14 times higher than among domestic born citizens in 2011[22]. This can be seen in numerous case reports and case series of individuals who have immigrated to the United States and did not start presenting clinical symptoms of leprosy until they resided in the United States[3; 11; 12; 16; 19; 23; 25; 29]. The symptoms of leprosy presented differ from case to case, as well as the type of leprosy. One case study by Choe (1994) documented a 16-year-old Vietnamese immigrant that presented with a unilateral foot drop due to damage from leprosy of the peroneal nerve[3]. This differs widely from the 20-year-old Vietnamese immigrant that presented with skin abnormalities in the case report from Goldenring and Castle (1984)[11]. In the case

series by Hartzell et al. (2004), a 26-year-old Micronesian man presented with a rash on his abdomen and decreased sensation to touch on his legs, left arm, and right cheek[12]. The other two patients in the case series, a 21-year-old Marshallese man and a 26-year-old Micronesian man, both presented with anesthetic skin lesions on their upper extremities[12]. Diversity in presentation can be seen again in the 22-year-old Cambodian patient who suffered from persistent carpel tunnel syndrome due to neuropathy of the median nerve in the wrist as a result of leprosy in the Koss et al. (1993) case study[16].

One study by Mastro et al. (1992) looked at cases of leprosy in the United States between 1978-1988 and found that 90% of cases during that time were imported cases[21]. They noted that a spike in cases in the mid-1980's came from refugees coming in the early 1980's from Vietnam, Cambodia, and Laos[21]. This trend of imported cases greatly outnumbering United States born cases can be seen still in more recent data. Leon et al. (2016) looked at patients diagnosed with leprosy at the Emory TravelWell Center, a satellite clinic of the U.S. Department of Health and Human Services National Hansen's Disease Program, between 2002 to 2014 and found that 86% of cases were among immigrants[18]. The top two countries of origin among these patients were Brazil and Mexico[18].

In the United States, Micronesian and Marshallese immigrants in the United States make up a significant portion of cases each year[33]. The Marshall Islands and the Federated States of Micronesia are both endemic for leprosy[10]. Woodall et al. (2011) examined leprosy data of these immigrant populations from 1990 - 2009[33]. The study found that of the 686 cases of leprosy in the United States between 2004 - 2008, 90 were among Marshallese and Micronesian patients[33]. Over half of the reported cases among these populations occur in

Hawaii, where there is a larger number of these immigrants living[33]. Between 2000-2009, there were 29 Hawaii-residing Micronesian cases and 43 Hawaii-residing Marshallese cases, which represents 55% of Micronesian and Marshallese cases in the United States during that time[33]. While few Micronesians live in a concentrated area on continental United States, there is a sizeable population of Marshallese people living in Arkansas that is roughly equivalent in size to the Hawaii-residing Marshallese population (approximately 8,000)[33]. Between 1990 – 2009, there were 17 cases reported in the Arkansas-residing Marshallese population[33]. This represents one third of all leprosy cases among Marshallese people living on continental United States during that time[33]. While these cases numbers may seem low, the Micronesian and Marshallese source population only totaled approximately 170,00 during this time[33]. From 2009-2012, the Arkansas-residing Marshallese population new case rate of leprosy was 77 per 100,000 people, compared to 0.05 per 100,000 people for the entire United States, which is well above the threshold for hyperendemic leprosy, at greater than 40 new cases per 100,000 people annually[2; 24].

Leprosy in the United States Among Domestic Born Citizens

While a majority of cases of leprosy in the U.S. are among immigrants, domestic born patients have also been diagnosed with leprosy. The most comprehensive study that looked at a large number of U.S. born citizens with leprosy was done by Joseph et al. (1985)[15]. This study examined data on 1,309 leprosy patients born in the continental United States between 1932 – 1981[15]. The study found that of the 740 cases from 1952 – 1980 that included data on place of birth, patients born in Texas accounted for over half of the cases, contributing to the 73% of

cases that occurred in southern states[15]. Of the 466 cases that data on history of contact was available for, only 138 cases had contact with a person with leprosy[15]. The remaining 328 cases had no known contact with an individual with leprosy[15].

In some cases of no known prior contact with individuals with leprosy, transmission likely occurred while traveling to areas where leprosy is endemic. One such case study by Sen et al. (2001) documented a 70-year-old female who had traveled previously to China and Hawaii and is believed to have acquired *M. leprae* at some point during one of her trips, although she reported no contact with a person with leprosy[26]. Another method of transmission that has been shown to be probable is transmission from the nine-banded armadillo (*Dasypus novemcinctus*), which is the only other mammalian reservoir of *M. leprae*[28]. Truman et al. (2011) investigated this theorized link and proved a genetic similarity between *M. leprae* sequenced in captures armadillos and United States patients who resided in the area where armadillo exposure was possible[28]. This study was done in the southern United States[28]. Another study by Sharma et al. (2015) further investigated zoonotic leprosy in the southeastern United States[27]. In the study, 645 armadillos from 8 locations in the southeastern United States were captured and tested for *M. leprae*[27]. The 8 locations were chosen because they had not previously been known to have enzootic leprosy[27]. The study found *M. leprae* infected armadillos at all locations, suggesting a potential of infected armadillos being located in more areas of the United States[27].

Several case studies also help to confirm this probable transmission route. One case study by Lane et al. (2006) documented at 57-year-old woman from Georgia who presented with several skin lesions[17]. She reported her husband killing armadillos and burying them near

her garden, as well as armadillos burrowing in the same area[17]. This indirect armadillo contact was deemed to be the probable cause of her leprosy, as she had not been in contact with other people known to be infected and had not traveled to an endemic area[17]. A case study by Elsayed et al. (2015) documented a 41-year-old Florida man who presented with a severe skin rash on his upper trunk[7]. He had not traveled outside the state of Florida but did have contact with armadillos after trying to snare them after causing property damage, and was later confirmed to have leprosy after lab testing[7]. In a case series by Domozych et al. (2016) four patients in Central Florida presented with probable transmission due to contact with armadillos[6]. Two of the four patients reported direct contact with armadillos or armadillo carcasses, with no travel to areas endemic for leprosy, and the other two patients reported indirect contact with armadillos, with only one reporting travel to areas with low endemicity[6]. In Brazil, a case-control study was carried out by Deps et al. (2008) to look at armadillo contact as a risk factor[5]. The study had 506 cases and 594 controsl[5]. The study found that armadillo contact doubled the odds of leprosy when controlled for by age, sex, health unit recruited from, place of birth and residence[5].

Paucibacillary vs. Multibacillary Cases in the United States

There are very few studies that examine the differences in type of leprosy, between paucibacillary and multibacillary, among immigrants and U.S. born citizens. The Mastro et al. (1992) study of cases from 1971 - 1988 found that 67.8% of immigrant cases of leprosy were multibacillary, with individuals from the Philippines and Indochina more likely to have paucibacillary[21]. The Joseph et al. (1985) study shows a similar trend is present among patients

born on the continental United States between 1952 – 1980, with 66% of these cases being multibacillary[15].

Other studies that identify the type of leprosy among patients did not specify the stratification by immigrant versus United States born. In Leon et al. (2016), it is reported that 70% of patients at the Emory TravelWell Center between 2002 to 2014 had multibacillary leprosy[18]. Four of the 30 cases of leprosy in that study were among U.S. born citizens, but there is no data given to determine how many of the multibacillary cases were among immigrants versus United States born patients[18].

One systematic literature review on *M. leprae* transmission by Bratschi et al. (2015) found two interesting points in the 79 studies included in their review[1]. The first is that individuals with household contacts of multibacillary cases were at higher risk of transmission than of those individuals with household contacts of paucibacillary cases[1]. The second was that most secondary cases of leprosy in the review were paucibacillary cases[1]. Bratschi et al. does highlight the importance of considering the temporal constraints of studies that could have prevented the ability to detect multibacillary cases, but the dichotomy of most primary cases being multibacillary and most secondary cases being paucibacillary is an interesting and warrants further study[1].

Chapter 3: Manuscript (For Submission to Emerging Infectious Diseases)

Relationship of Demographic Variables and Classification of Leprosy Cases in Georgia since the early 1900s.

Contribution of Student

For this manuscript, the student collected the data (with the help of the National Hansen's Disease Program), conducted all statistical analysis presented, created the figures and tables, and wrote the manuscript, with editorial assistance from Dr. Jessica Fairley.

Abstract

Introduction: Leprosy (also known as Hansen's Disease) is a disease that is diagnosed in approximately 160 people in the USA each year. Recent studies have shown different forms of transmission in the southern US (zoonotic versus person-to-person), but epidemiologic data are lacking about factors associated with multibacillary infection, the most infectious form.

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Results: While the model showed no significant relationship between country of origin and type of leprosy, being Asian or Pacific Islander (97.36% of which were foreign born) was associated with a higher risk of multibacillary infection when controlled with the other variables (aOR = 5.714; 95% CI: 1.254 – 26.287). This trend was repeated in the model using post-1995 data.

Conclusion: Leprosy is known to be highly endemic in Micronesia and other areas in Asia. There have been several articles describing the epidemiological data of Asians and Pacific Islanders in the USA, such as the Marshallese in Arkansas and Micronesians in Hawaii. However, more research should be done to see if these population is at greater risk for multibacillary leprosy. With the global community dedicated to the elimination of leprosy, understanding which populations are at greater risk for this more infectious type of leprosy is important to create targeted interventions and prevention strategies.

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Global leprosy burden affects low- and middle-income countries predominately, with about 200,000 – 300,000 cases reported annually[1]. India, Brazil, and Indonesia have the most cases reported annually, making up about half of the cases reported in 2016[10]. Cases reported from higher income countries tend to be much smaller, such as 5 cases for the Netherlands in 2016[10]. However, the United States sits at a slightly higher case number per year, with 168 cases reported in 2016, which is consistent with the number of cases reported in prior years[10].

The United States has had a long history of Leprosy, even before its founding, with the Acadian people from Canada bringing cases of leprosy to French Louisiana in the mid 1700's[14]. In 1917, the United States Senate passed Senate Bill 4086, which created a National Leprosarium in Carville, Louisiana[13]. This leprosarium became the base of the National Hansen's Disease Program (NHDP), whose center was later moved in 1998 to Baton Rouge, Louisiana, and continues to be the main clinical, epidemiologic, and diagnostic reference in the United States for leprosy today[13].

Most of the cases of leprosy seen in the United States are among immigrant patients from countries where leprosy is endemic. The rate of diagnosis of leprosy among immigrants was 14 times higher than among domestic born citizens in 2011[22]. Between 1978-1988, 90% of reported cases were among immigrants[21]. Recent data still confirms this trend continues, with 86% of cases at the Atlanta NHDP affiliated clinic between 2002 to 2014 being among immigrants[18]. Leprosy in domestic born citizens tend to be traced back to either transmission while traveling in a leprosy endemic country or probable armadillo transmission[17;7;6].

There are very few studies that examine the differences in type of leprosy, between PB and MB, among immigrants and U.S. born citizens. Studies have shown that both domestic born

and immigrant cases of leprosy tend to be MB in both populations (between 60-68% for either group in both studies), but there is no evaluation of which population is more likely to be MB or PB versus the other population[15; 21]. Since MB disease is associated with a higher risk of complications and secondary transmission, it is important to understand the patterns of disease manifestations and any epidemiologic associations with this type of leprosy[1]. Whether one has MB disease is thought to be based on host predisposition, but there is little known about the patterns of disease presentation based on the potential type of transmission (zoonotic versus person-to-person). There is also a clear literature gap that exists to evaluate the relationship between location of birth, between being born in the United States and being born abroad, and the type of leprosy diagnosed with, especially in southern states where zoonotic transmission is more common[28]. Therefore, this paper seeks to answer the question if location of birth is associated with either MB or PB leprosy with the goal to better understand the epidemiology of leprosy in a Southern US state and to better target interventions.

Methods

Data on age, ethnicity, location of birth, leprosy diagnosis, and sex were extracted from surveillance reports from the National Hansen's Disease Program of cases in Georgia. Leprosy is a reportable disease in Georgia and is monitored primarily through passive surveillance. Inclusion criteria for the study was any patient who had ever lived in Georgia or was reported by a clinic in Georgia during any year.

From the data, chi-squared tests and t-tests were done to assess differences between the domestic and foreign-born populations. An epidemiological model, using logistic regression,

was built with controlling variables of interest (age, sex, and ethnicity) based on peer-reviewed literature. This logistic model was built with type of leprosy, dichotomized as paucibacillary and multibacillary, as the outcome variable. Country of origin was the primary variable of interest. Age was an included controlling variable due to the long duration of contact need for transmission of leprosy. It was theorized that older people would have a greater chance of contracting a less infectious form leprosy because they have had more years to potentially be in contact with the bacteria. Sex was included as a control due to the higher cases of MB leprosy in men[8; 15; 21]. Similarly, ethnicity was included to control for individuals in subpopulations that may have a higher burden of multibacillary versus paucibacillary disease, and vice versa[21]. A second model was built only using data from after 1995, when the WHO started providing MDT for all leprosy patients, to see if temporal changes impacted the relationship[31]. Interaction was assessed in both models.

For this study, birth location refers to the birth place of the patient, with domestic cases referring to patients who were born in one of the 50 US states, and abroad locations referring to patients who were not born in the United States and displayed symptoms either before or after moving to the United States.

This study deemed exempt from review by the Emory University Institutional Review Board. SAS version 9.4 was utilized for analysis.

Results

Of the 138 cases that met inclusion criteria at the National Hansen's Disease Program, 123 cases were included in the final model. The 15 cases not included had missing data for one

or more of the variables and were thus excluded in this complete case analysis. The demographics of study population are displayed in Table 1. Of the 123 cases, 39 (31.71%) were born domestically and 84 (68.29%) were born abroad. For both groups, most have multibacillary leprosy (n=27, 69.23% of those born domestically and n=53, 63.10% of those born abroad). Both groups were also mostly male (n=30, 76.92% of those born domestically and n=54, 64.29% of those born abroad). Most cases born domestically were white (n=27, 69.23%) while most cases born abroad were Asian or Pacific Islander (n=37, 44.05%). The domestic born cases were on average older (mean: 45.95, SD: 14.24) than those cases born abroad (mean: 35.56, SD: 13.74). A trend of increasing MB cases, and overall number of reported cases, can be seen starting in the 1970's (Figure 1). This is also the time period that a switch in which birth location makes up a larger proportion of the leprosy cases reported (Figure 2).

The full logistic model run for all years is shown in Table 2. The model shows that location of birth is not significantly associated with the type of leprosy diagnosed (aOR: -0.7861; 95% CI: 0.116 – 1.796) when controlling for age, sex, and ethnicity. While almost all other variables do not show an association, being ethnically Asian or Pacific Islander versus white does have a significant relationship with more MB leprosy diagnosed (aOR: 5.741, 95% CI: 1.254 – 26.287) when also controlling for age, sex, and location of birth. Interaction did not have an effect on the relationship for this model.

In the model built using data after 1995, shown in Table 3, we see a similar relationship. The relationship between birth location and type of leprosy was not statistically significant (aOR: 0.528; 95% CI: 0.193 – 1.446) when controlling for age, sex, and being Asian or Pacific Islander. Due to low number of cases for all ethnicities in the 55 cases reported after 1995, we

could not utilize the full ethnicity variable for analysis. We re-structured the variable to consider Asian or Pacific Islanders versus all other ethnicities as that is the ethnicity that appeared as a risk factor. Given then potential interaction with location of birth and ethnicity, interaction was assessed and there were no interactive effects found in this model.

Discussion

This analysis of cases of leprosy in the state of Georgia is the first of its kind and we found several interesting things. The younger average age of the population born abroad compared to the domestically born cases is of note, as it suggests more active transmission in the host country. This would make sense, as these immigrants are likely coming from countries that have higher prevalence of leprosy compared to the United States[10]. This is confirmed when looking at those cases that do have data on their country of origin. The increasing trend in both number of MB cases and foreign-born cases after the 1970's suggests changes in surveillance or a change associated with disease distribution. It is interesting to see these increases occur at the same time, but yet our results suggest that the location of birth does not have an association with the type of leprosy diagnosed between multibacillary and paucibacillary among patients reported by, or who have lived in, Georgia. However, the number of MB and PB cases among domestic born cases compared to cases born abroad is almost equal (PB: 30.77% vs. 36.90%; MB: 69.23% vs. 63.10%). This is approximately the same split seen in prior studies[15; 21].

The finding that only cases with ethnicity of Asian or Pacific Islander are at greater odds of MB disease is interesting. Pacific Islanders are the only ethnicity group of people living in the United States that have been studied for leprosy as an individual ethnic group. In the study on

Micronesian and Marshallese people living in the United States, MB was more prevalent than PB, hovering around 75% with MB[33]. The odds ratio for this variable in the full model also had large confidence intervals (aOR: 5.714; 95% CI: 1.254 – 26.287), meaning this estimate is not very precise. We performed a post-hoc analysis with just this ethnicity variable and we see a more precise estimate (aOR: 3.759; 95% CI: 1.520 – 9.298), suggesting that this relationship exists but is understated without controlling for the other variables. One explanation could be that there is a higher likelihood of MB disease in Asian or Pacific Island countries, possibly suggesting factors such as micronutrient deficiencies, or other co-morbidities that alters the immune response to M. leprae[9]. These immigrant groups may be, thus, at higher risk of secondary transmission of leprosy in their communities, given that MB is more infectious, so attention should be paid to thorough contact examinations. However, there is not identifiable literature that explains why this ethnic class would have greater odds of having multibacillary.

In the model built using data after 1995, we were unable to utilize the full ethnicity variable due to insufficient numbers of cases in each ethnicity category for both birth location groups. As such, since being Asian or Pacific Islander was identified as a risk factor in the first model, we recoded the data to have an Asian or Pacific Islander variable where the reference group was being any other ethnicity. While birth location was still not associated with type of leprosy, being Asian or Pacific Islander still showed a statistically significant association with MB leprosy. This analysis was chosen because in 1995, the World Health Organization started providing MDT to all leprosy patients, and felt that this could signify the possibility of less person-to-person transmission post-1995 and potentially more armadillo transmission[31]. Interestingly, we also see a continuation of an upward trend of MB cases in the 1990's (Figure

1), which could indicate improved surveillance, or worse surveillance for PB cases that may be going undetected, but could also indicate changes in distribution and transmission for the disease.

There are several limitations to this study. While leprosy is a reportable disease in Georgia, there is always the potential for underreporting of cases. We would assume that the surveillance data is a complete population of those that have leprosy living in Georgia, but there is always the possibility of missed data entry on surveillance reports, individuals who are misdiagnosed and therefore not reported, or those who do not seek care. All of these situations would exclude those cases from our study. With such a small number of cases, the loss of 15 cases due to incomplete data could have significantly impacted the results.

There were several variables that we would have liked to include but were not possible to attain the data for. First, we would have liked to control for potential transmission method by having data on both prior armadillo contacts and contact with known leprosy patients. We also would have liked to control for socioeconomic status (SES), as it can be theorized that individuals with lower SES may live in more crowded conditions, which is known to be associated with increased cases of leprosy, or potentially could be related to factors that predispose an individual to having MB leprosy. For a more thorough analysis, we would have liked to be able to control for location of birth by country as opposed to a simple dichotomy, but many reports and records did not indicate the exact country, rather only the ethnicity and if they were born internationally. In order to ensure enough data, we dichotomized to address this problem.

Since the sample used is only of cases from Georgia, we cannot generalize these findings to leprosy cases from other states. A more complete study should be done utilizing all cases from the 50 states to better assess the relationship between birth location and type of leprosy diagnosed. This would also give a more holistic view of the epidemiology of leprosy in the United States. The ability to add more controlling variables would help evaluate the true relationship of place of birth and type of leprosy diagnosed.

As it stands, leprosy research, specifically research that focuses on United States leprosy patients, is fairly limited. As an increasingly globalized world where movement of people is easier now than ever before, leprosy cases will continue to appear all around the world. The upward trend of cases seen since the 1990's in the Georgia is an impetus to further study of this disease within the state to ensure containment. Unique analyses, such as this study, would illuminate better understanding of the disease. These further studies would allow for more targeted treatment and prevention strategies to help achieve the disease elimination goals.

Chapter 4: Conclusion & Recommendations

This analysis of cases of leprosy in the state of Georgia is the first of its kind and we found several interesting things. The younger average age of the population born abroad compared to the domestically born cases is of note, as it suggests more active transmission in the host country. This would make sense, as these immigrants are likely coming from countries that have higher prevalence of leprosy compared to the United States[10]. This is confirmed when looking at those cases that do have data on their country of origin. The increasing trend in both number of MB cases and foreign-born cases after the 1970's suggests changes in surveillance or a change associated with disease distribution. It is interesting that this increasing can be seen to occur at the same time, but yet our results suggest that the location of birth does not have an association with the type of leprosy diagnosed between multibacillary and paucibacillary among patients reported by, or who have lived in, Georgia.

The finding that only cases with ethnicity of Asian or Pacific Islander are at greater odds of MB disease is interesting. Pacific Islanders are the only ethnicity group of people living in the United States that has been studied for leprosy as an individual ethnic group. In the study on Micronesian and Marshallese people living in the United States, MB was more prevalent than PB, hovering around 75% with MB[33]. The odds ratio for this variable in the full model also had large confidence intervals (aOR: 5.714; 95% CI: 1.254 – 26.287), meaning this estimate is not very precise. We performed a post-hoc analysis with just this ethnicity variable and we see a more precise estimate (aOR: 3.759; 95% CI: 1.520 – 9.298), suggesting that this relationship exists but is understated without controlling for the other variables. One explanation could be that there is a higher likelihood of MB disease in Asian or Pacific Island countries, possibly

suggesting factors such as micronutrient deficiencies, or other co-morbidities that alters the immune response to M. leprae[9]. These immigrant groups may be, thus, at higher risk of secondary transmission of leprosy in their communities, given that MB is more infectious, so attention should be paid to thorough contact examinations. However, there is not identifiable literature that explains why this ethnic class would have greater odds of having multibacillary.

In the model built using data after 1995, we were unable to utilize the full ethnicity variable due to insufficient numbers of cases in each ethnicity category for each birth location group. As such, since being Asian or Pacific Islander was identified as a risk factor in the first model, we recoded the data to have an Asian or Pacific Islander variable where the reference group was being any other ethnicity. While birth location was still not associated with type of leprosy, being Asian or Pacific Islander still showed a statistically significant association with MB leprosy. This analysis was chosen because in 1995, the World Health Organization started providing MDT to all leprosy patients, and felt that this could signify the possibility of less person-to-person transmission post-1995 and potentially more armadillo transmission[31]. Interestingly, we also see a continuation of an upward trend of MB cases starting in the 1997's (Figure 1), which could indicate improved surveillance, or worse surveillance for PB cases that may be going undetected, but could also indicate changes in distribution and transmission for the disease. We also see an increasing trend of cases born abroad making up a large proportion of cases starting at the same time (Figure 2).

Most cases of leprosy in the United States, both among those born abroad and those born domestically, are multibacillary[21; 22]. However, there is currently no way to make an educated guess as to what kind of leprosy an individual has based on any demographic

characteristics or a confirmatory test. Prior contact with leprosy infected patients or armadillos is the best-known indicator, but due to the long latency period of leprosy before someone is symptomatic, it can be hard to determine where exactly someone acquired the disease from. For a disease that often stigmatizes individuals and may be misdiagnosed, being able to identify the type of leprosy an individual from an area is most likely to have would be beneficial to increase targeted interventions.

We live in an increasingly globalized world where movement of people is easier than ever. As conflicts continue to displace individuals and environmental changes potentially bring more individuals into contact with armadillos, there will continue to be leprosy cases in the United States. However, the body of literature on leprosy in the United States, especially in recent years, is limited. There must be more research done on leprosy so that we are able to create targeted, efficient, and cost-effective interventions. A unique analysis, such as this, should be applied to more states to understand the epidemiologic trends of the disease in their states. Due to the crippling disability this disease can cause, there must be more focus on the disease which is likely to impact those that already face other barriers, such as low socioeconomic status. The world is working towards control of leprosy, but this will not happen without the research to address the gaps in literature.

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Appendix

Table 1 – Demographic Characteristics of Cases in the Study

	Born Domestic n=39 (31.71%)	Born Abroad n=84 (68.29%)	p-value
Leprosy Type, n (%)			
PB	12 (30.77)	31 (36.90)	0.5067
MB	27 (69.23)	53 (63.10)	
Sex, n (%)			
Female	9 (23.08)	30 (35.71)	0.161
Male	30 (76.92)	54 (64.29)	
Ethnicity, n (%)			
White	27 (69.23)	6 (7.14)	<0.0001
Black	10 (25.64)	10 (11.90)	
Hispanic	1 (2.56)	23 (27.38)	
Asian or Pacific Islander	1 (2.56)	37 (44.05)	
Indian or Middle Eastern	0 (0.00)	8 (9.52)	
Age, Mean (SD)	45.95 (14.24)	35.56 (13.74)	0.0002

Table 2 – Logistic Regression Model for all Years

Parameter	Estimate	P-Value	Adjusted Odds Ratio	95% Wald CI
Birth location				
Domestic	Ref			
Abroad	-0.7861	0.2614	0.456	0.116-1.796
Sex				
Female	Ref			
Male	-0.3542	0.4174	0.702	0.298-1.652
Ethnicity				
White	Ref			
Black	0.00298	0.9950	1.855	0.498-6.910
Hispanic	-0.3481	0.4774	1.306	0.245-6.960
Asian or Pacific Islander	1.1326	0.0043	5.741	1.254-26.287
Indian or Middle Eastern	-0.1725	0.8078	1.557	0.184-13.178
Age	-0.0211	0.1562	0.979	0.951-1.008

Table 3 – Logistic Regression Model for cases after 1995

Parameter	Estimate	P-Value	Adjusted Odds Ratio	95% Wald CI
Birth location				
Domestic	Ref			
Abroad	-0.6387	0.2140	0.528	0.193 - 1.446
Sex				
Female	Ref			
Male	-0.3387	0.4354	0.713	0.304 - 1.669
Ethnicity				
All other ethnicities	Ref			
Asian or Pacific Islander	1.4045	0.0031	4.074	1.604 - 10.344
Age	-0.0224	0.1249	0.978	0.950 - 1.006

Figure 1

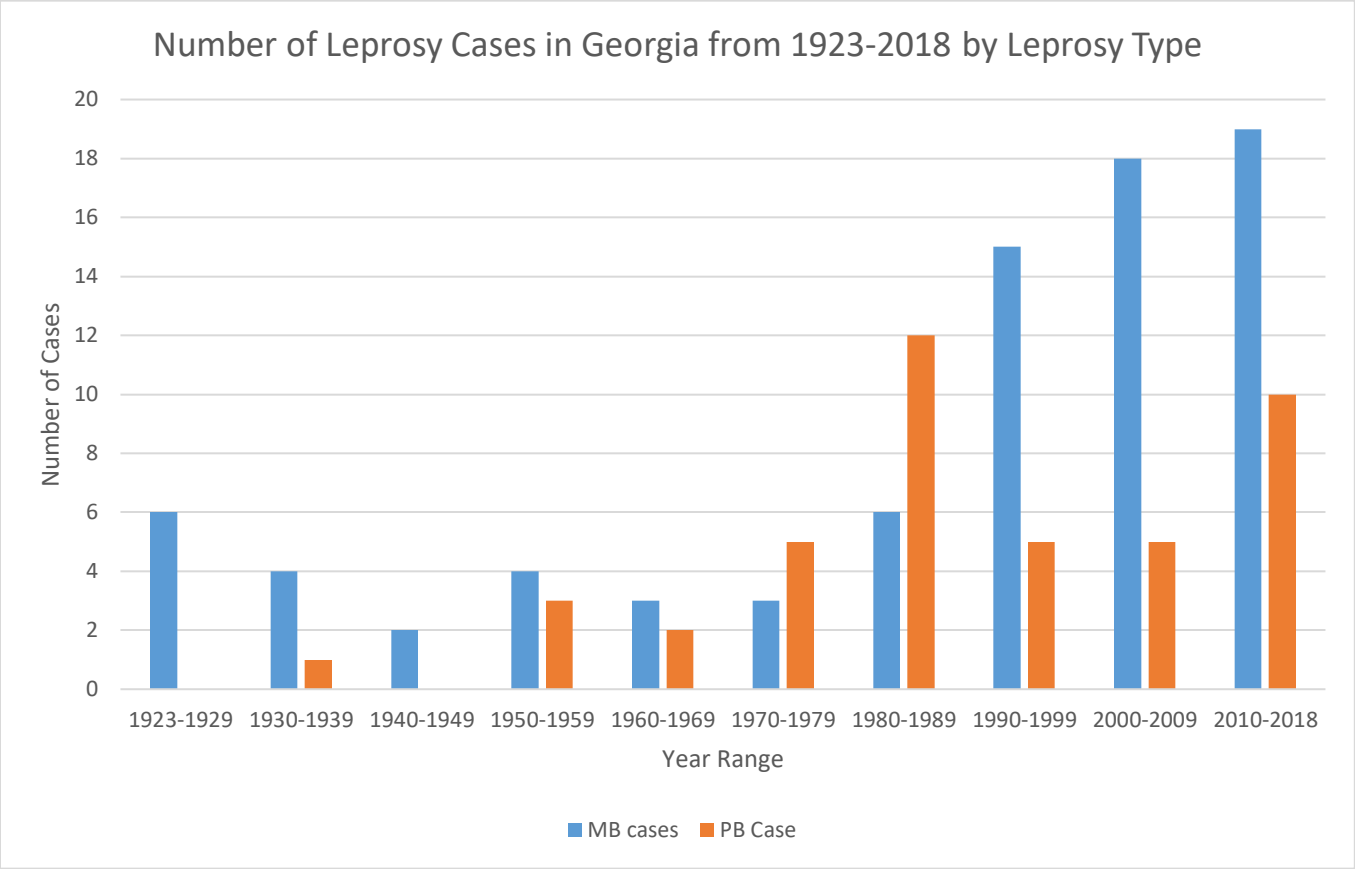
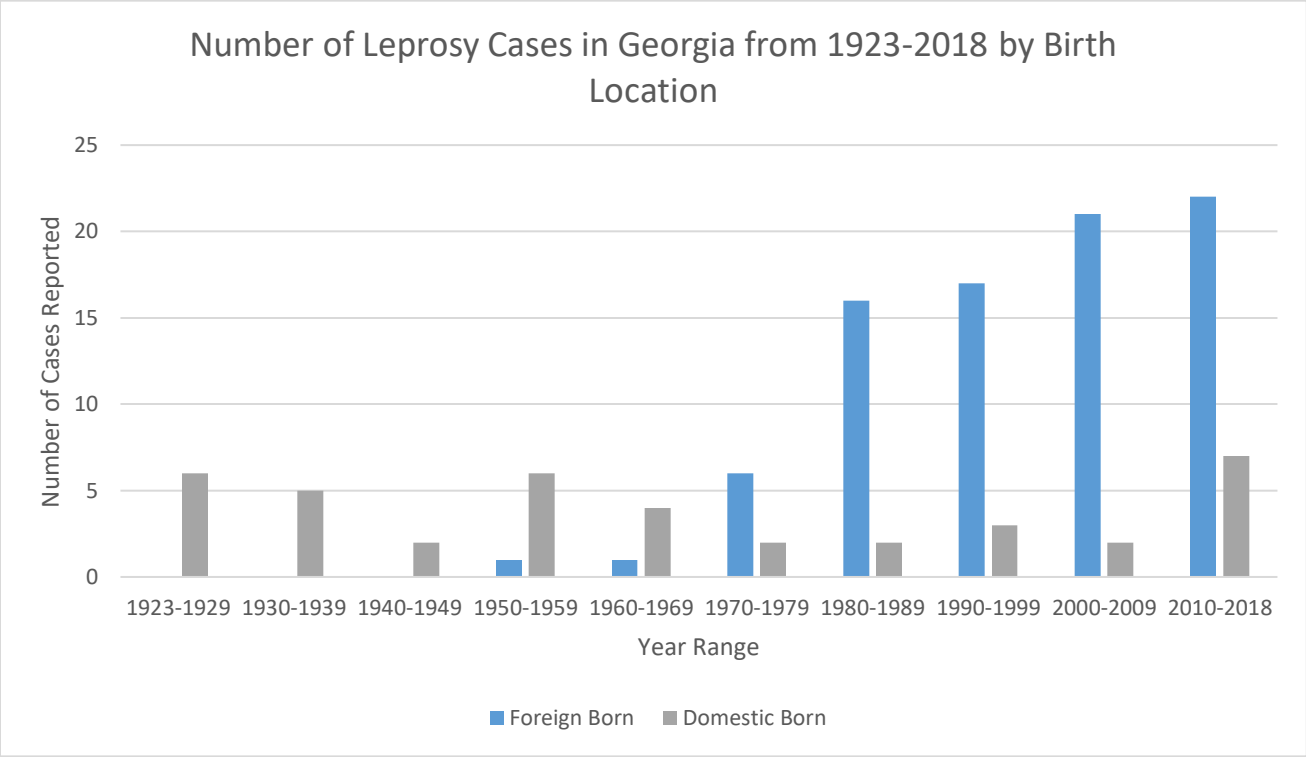

Number of Leprosy Cases in Georgia from 1923-2018 by Leprosy Type
Number of Cases
20
18
16
14
12
10
8
6
4
2
0
1923-1929
1930-1939
1940-1949
1950-1959
1960-1969
1970-1979
1980-1989
1990-1999
2000-2009
2010-2018
Year Range
MB cases
PB Case

Figure 2


Number of Leprosy Cases in Georgia from 1923-2018 by Birth Location
Number of Cases Reported
25
20
15
10
5
0
1923-1929
1930-1939
1940-1949
1950-1959
1960-1969
1970-1979
1980-1989
1990-1999
2000-2009
2010-2018
Year Range
Foreign Born
Domestic Born